eISSN 2465-891X
www.thenerve.net

The Nerve

Vol.9, No.1 April 2023

Official Journal of the
Korean Society of Peripheral Nervous System

www.thenerve.net

eISSN 2465-891X

The Nerve

Vol.9, No.1 April 2023

Aims and Scope

The Nerve is the official journal of the Korean Society of Peripheral Nervous System, and published twice a year (30th April, 31st October). This Journal publishes important issues covering all aspects of the peripheral and central nervous systems. Laboratorial investigations, original research articles, studies on valuable cases, technical notes of special surgical tactics or editorials in the field of neurosurgery, neurology and neuroscience are acceptable. All submitted manuscripts are peer-reviewed and review articles can only be published upon specific request of the editorial board.

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Open Access

Publisher The Korean Society of Peripheral Nervous System
Editor-in-Chief Young Jin Kim, M.D.,Ph.D.

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Published on April 30, 2023

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The Nerve

Review Article

The Nerve 2023;9(1):1-8
https://doi.org/10.21129/nerve.2022.00199
eISSN 2465-891X

Thoracic Outlet Syndrome

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OPEN ACCESS

Received: September 13, 2022
Revised: October 30, 2022
Accepted: November 14, 2022

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Thoracic outlet syndrome (TOS) is a constellation of symptoms caused by the compression of neurovascular structures at the superior aperture of the thorax, properly referred to as the thoracic inlet. However, there is no consistent clinical presentation or definition. Based on a comprehensive literature review, this article presents the etiology, epidemiology, and clinical diagnostics of TOS, as well as the possibilities and outcomes of surgical treatment. The diagnosis and treatment are contentious, and some even question the existence of TOS. Its symptoms are often confused with those of distal compression neuropathies or cervical radiculopathies. The various surgical approaches for this syndrome are evaluated according to their ability to facilitate wide exposure, their potential morbidity, and their beneficial results. Most patients suffering from any form of TOS can benefit from surgical treatment. The duration of symptoms, socioeconomic factors and most notably, a stringent diagnostic workup and an adequate operative approach are important.

Keywords: Brachial plexus neuritis; Clavicle; Ribs; Thoracic outlet syndrome

INTRODUCTION

Pain, weakness, and discomfort in the upper limbs are common. Diagnosis of these symptoms is often difficult because of the various pain-sensitive structures in the neck, the upper thoracic aperture, and the upper limbs. If other causes such as a cervical degenerative disease, rotator cuff rupture, tumors, peripheral nerve entrapment, and other neurologic diseases have been excluded, and the symptoms can be provoked during examination, the case is often classed under thoracic outlet syndrome (TOS). The term "thoracic outlet syndrome" was coined by Peet et al.[19] in 1956 to describe several disorders attributed to mechanical compression of neural and/or vascular structures between the base of the neck and the axilla. TOS involves compression that results in injury or irritation of neurovascular structures as it passes through three narrow passages from base of the neck through the armpits to the arms. The most important of these is the interscalene triangle. The borders are the anterior scalene muscle anteriorly, the middle scalene muscle posteriorly and the medial surface of the first rib inferiorly. The triangle is small at rest but can be made smaller with certain provocative maneuvers. It can be further constricted by other structures such as fibrous bands, cervical ribs and abnormal muscles. The second passage is the costoclavicular triangle. The borders are the clavicle anteriorly, the first

rib posteromedially and the upper border of the scapula posterolaterally. The third passage is the subcoracoid space beneath the coracoid process deep to the pectoralis minor tendon[21].

ANATOMY

The thoracic outlet refers to the communication between the thoracic cavity and root of the neck. Three areas within the thoracic outlet where neurovascular compression can occur have been described: the interscalene triangle, the costoclavicular space, and the subpectoral tunnel. The most clinical important passage is the interscalene triangle, which is bordered by the anterior scalene muscle anteriorly, the middle scalene muscle posteriorly and the medial surface of the first rib inferiorly. This triangle includes the trunks of the brachial plexus and the subclavian artery. It should be noted that the subclavian vein flows anterior to the anterior scalene muscle. Immediately distal to the interscalene triangle, the neurovascular bundle enters the costoclavicular triangle, which is bordered anteriorly by the middle third of the clavicle, posteromedially by the first rib, and posterolaterally by the upper border of the scapula (Fig. 1). The neurovascular bundle then enters the subcoracoid space, also referred to as the retropectoralis minor space, beneath the coracoid process deep to the pectoralis minor tendon. Compression or irritation of the brachial plexus, or both, have been described within these spaces[10].

PATHOANATOMY

1. First Rib Anomalies

These include bifurcation, synostosis with the second rib, and hypoplasia or absence of the first rib. First, rib hypoplasia is often associated with a postfixed plexus, which can be entrapped against a fibrous band representing the remnants of the rib (Fig. 2).

2. Vertebral Abnormalities

The elongated transverse process of the seventh cervical vertebra was described by Raaf[20] to have an anomalous vertical fibrous band extending to the first rib. The band is located posterior to the brachial plexus, causing its compression. Other bony abnormalities associated with TOS include

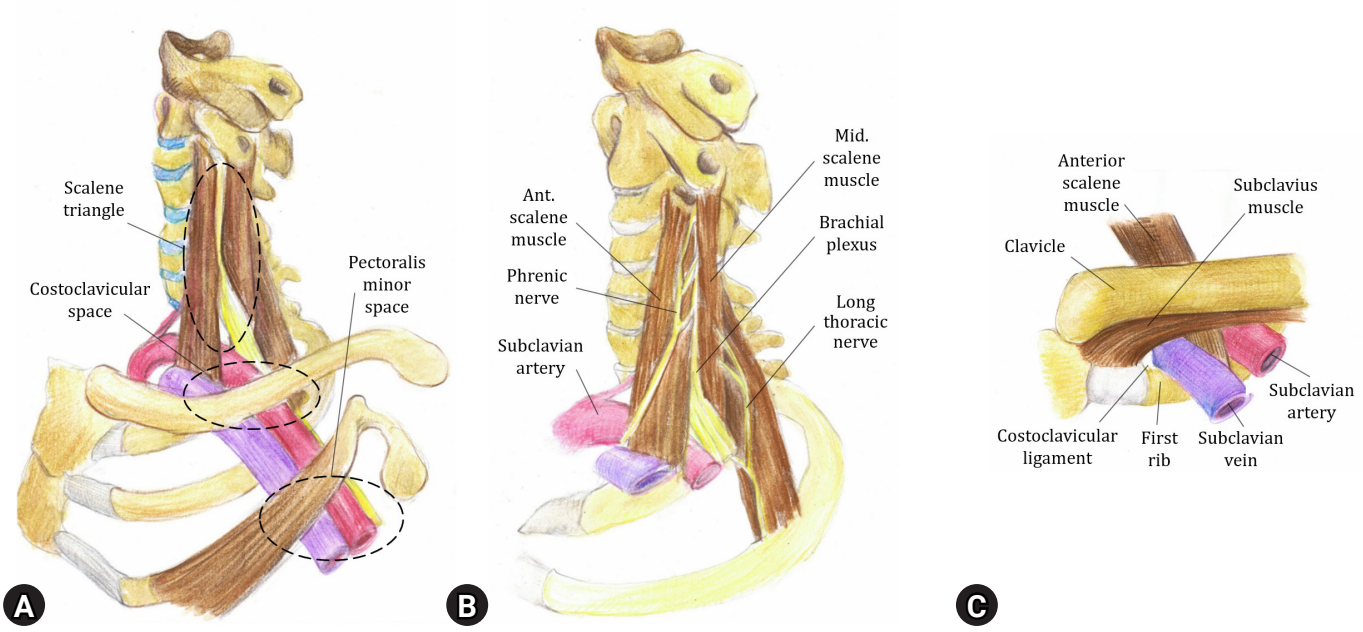

Fig. 1. (A) An overall view of the left thoracic outlet, examined from the thoracic outlet area, showing that it is made up of several distinct spaces. Nerve (yellow) compression can occur at the scalene triangle or pectoralis minor space, whereas venous compression most often occurs at the costoclavicular space. Arterial injury is most often due to bone trauma at the scalene triangle. (B) Detailed view of the scalene triangle on the patient's left side. (C) Anatomy of the subclavian vein at the costoclavicular space. [Modified from "Thoracic outlet syndrome: A common sequela of neckinjuries.", by Sanders RJ, Haug CE, 1991, Lippincott, pp. 34, 236. Copyright 1991 by the Lippincott. Reprinted with permission].

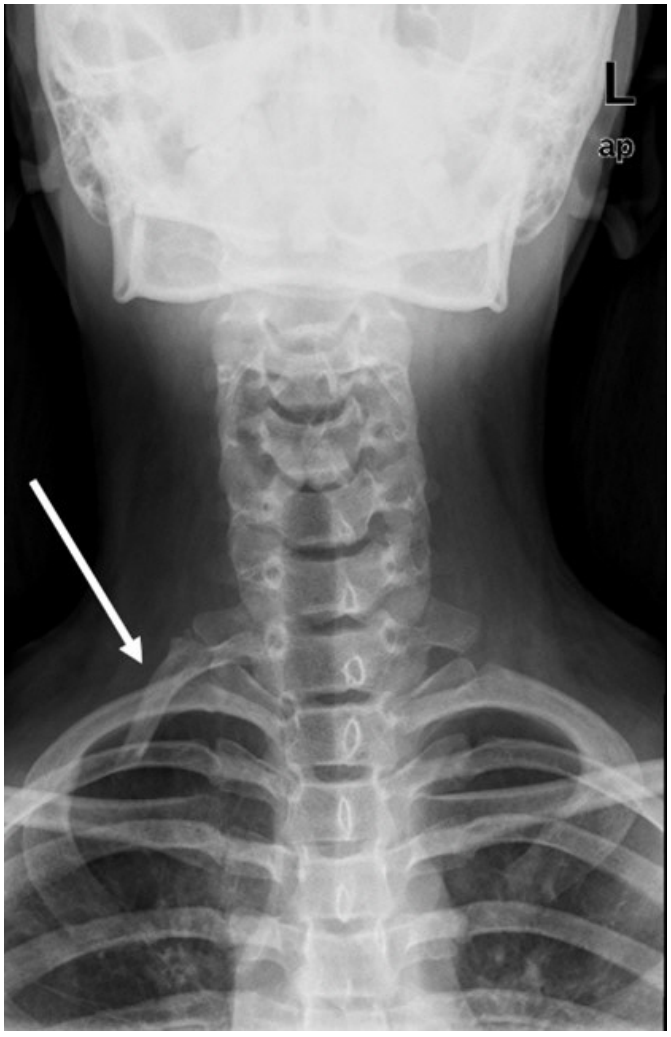

Fig. 2. The cervical rib is a possible pathoanatomical factor of thoracic outlet syndrome (TOS). This anteroposterior cervical radiograph demonstrates a cervical rib that caused TOS in a 22-year-old female patient (white arrow).

congenital pseudoarthrosis of the clavicle.

3. Cervical Muscles

The scalenus minimus muscle may cause neurovascular compression. The omohyoid muscle may also play a role in compressing the brachial plexus[1]. Telford and Mottershead[29] described neurovascular compression caused by anomalous insertion of the scalenus anticus, medius muscles, or both. They restricted the term "scalenus anticus syndrome" to lesions in which this muscle is the sole etiologic factor. Based on anatomic dissections, they described two types of sharp tendinous insertions of the scalenus anticus that may contribute to neurovascular compression.

4. Fibrous or Muscular Bands

These soft tissue structures irritate or cause pressure on the brachial plexus but not the subclavian artery. Although very important in the cause of TOS, these fibromuscular bands are not detected with radiography but are often encountered at surgery[24].

CLASSIFICATION AND SUBTYPES

1. Neurogenic TOS (NTOS)

Neurogenic types, accounting for more than 90% of TOS cases, were subdivided into "true" NTOS, and more common "disputed" NTOS. Both types are secondary to compression or traction injury to the lower trunk of the brachial plexus. True NTOS has named "true" because of the anatomical and electrodiagnostic evidence supporting the diagnosis. In contrast, the "disputed" NTOS, also known as nonspecific TOS, is believed by many to be an ambiguous clinical entity without objective clinical findings[33]. The classical form of true NTOS is called Gilliatt-Summer Hand[8]. This syndrome was first described in 1970 as thenar, hypothenar, and interossei weakness and/or atrophy, plus ulnar and medial antebrachial cutaneous hypoesthesia. Patients with true NTOS may report symptoms associated with pain, numbness, and weakness of the upper extremity. Overhead arm maneuvers or lift of heavy objects may aggravate the symptoms. However, approximately 85% of patients diagnosed with TOS have the disputed type. This form of TOS is associated with poorly defined and inconsistent symptomatology without objective evidence. As such, it has been embroiled in controversy, with many medical doctors questioning its very existence[10]. Patients with disputed NTOS will show similar symptoms of paresthesia and weakness with NTOS. But, usually there are more complaints of pain.

2. Vascular TOS (VTOS)

VTOS can be either arterial or venous. Venous compression can cause edema or cyanosis of the upper limb. It can also appear suddenly in the form of phlebitis occurring after varying degrees of effort. The patient can sometimes present only in the sequelae stage with thoracic collateral venous circulation. Arterial manifestations consist of upper extremity exertional ischemia or positional vasomotor dysfunction.

Signs of vertebrobasilar insufficiency or Raynaud's phenomenon can be observed due to compression of the origin of the vertebral artery[22]. The diagnosis of TOS is relatively simple when there are vascular symptoms in the upper limb when the arms are raised, but the vascular type is so rare that the venous type accounts for 2% to 3% of TOS and arterial type accounts for about 1%[25]. However, having vascular signs can help to guide the diagnosis in the presence of a predominantly neurological form of TOS.

DIAGNOSIS

1. Physical Examinations

1.1. Adson's Test

The patient's radial pulse is palpated (Fig. 3A), then the arm is externally rotated, extended and slightly abducted. The patient is asked to look towards the side being examined and to take a deep breath in (Fig. 3B). Abolition or a reduction in the radial pulse is a positive test.

1.2. Wright's Test (the hyper-abduction test)

The patient's arm is abducted to 90 degrees in external rotation while palpating the radial pulse. Again abolition of the pulse suggests a positive test but there is a high false positive rate.

1.3. Roos' Test

The patient's shoulder is abducted and the elbow is flexed to 90 degrees. In this position the patient is asked to open and close their hands for three minutes (Fig. 4). Inability to complete this exercise pain-free or reproduction of presenting symptoms constitutes a positive result.

1.4. The Military Brace Test

With both arms at the side, the patient moves the shoulder downward and backward to draw the clavicle closer to the first rib (Fig. 5). Diminution or obliteration of the radial pulse constitutes a positive test.

2. Electro Diagnostic Studies

Diagnostic criteria for electro-diagnostic tests are clearly established in electrophysiological tests, particularly in true neurologic TOS, altered ulnar sensory conduction (low amplitude sensory nerve action potentials) and motor median

Fig. 3. (A, B) Adson's test.

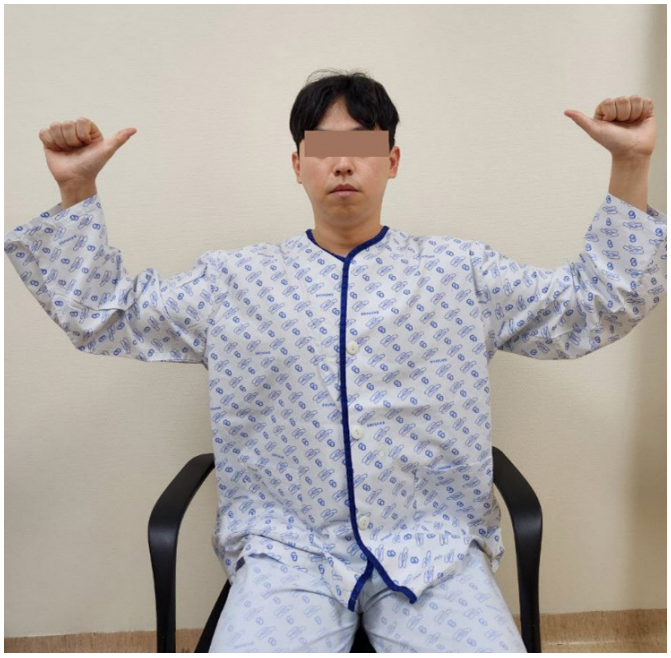

Fig. 4. Roos'test.

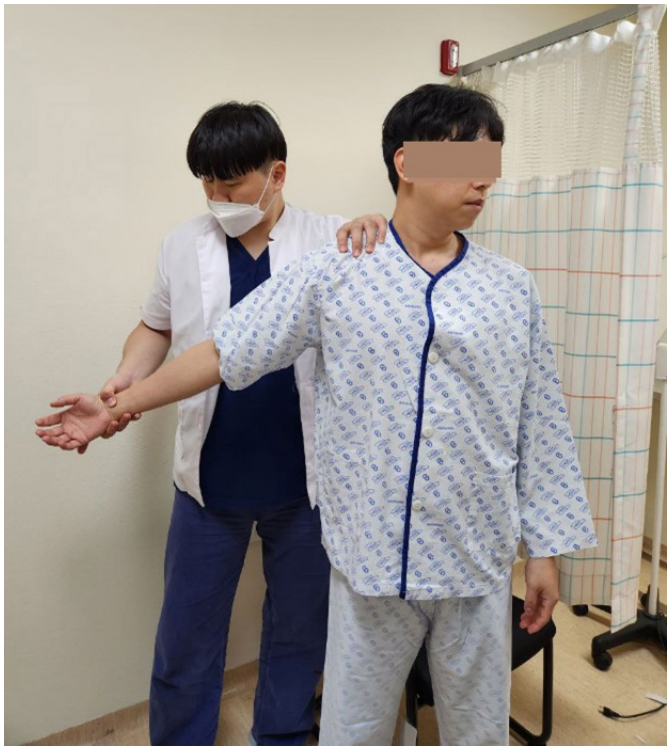

Fig. 5. Military brace test.

conduction (low amplitude compound muscle action potential). Routine electro-diagnostic studies can sometimes yield normal results but when there is strong clinical suspicion of a NTOS and the classical electro-diagnostic abnormalities are not found, F waves may be used at rest and in provocative positions to help support the diagnosis[11].

3. Other Diagnostic Tests

Scalene muscle block has been one of the most useful tests to confirm a diagnosis of NTOS. Although the response is subjective, a good response to the block has a high correlation with good responses to surgery for NTOS. Performed by the injection of a few mL of local anesthetic into the belly of the anterior scalene muscle, the test can be performed with electromyographic guidance or without it[12,27]. A neck X-ray is indicated to detect cervical ribs. Cervical magnetic resonance imaging or computed tomography scan is used to detect cervical spine disorders related to NTOS or may be a part of the differential diagnosis. Variations of magnetic resonance imaging are also being investigated for objective evidence of scalene muscle abnormalities or muscle compression of the brachial plexus. Magnetic resonance neurography is another recent imaging technique that shows deviations from the normal pathway by injecting a dye around the plexus[6].

Arteriography is not indicated in NTOS. As with the Adson test, demonstrating arterial compression is using an arterial sign to diagnose a neurologic condition. It is useless on NTOS. The only indication of arteriography is in ATOS, and then it is only necessary to plan the operation[6]. Venography is not indicated in NTOS. Venography is important in venous TOS and is indicated in patients with arm swelling and cyanosis. For VTOS, venography is more reliable than ultrasound[3].

DIFFERENTIAL DIAGNOSIS

Clinical aspects of TOS are very wide, ranging from mild discomfort to severe symptoms[14]. Patients may also exhibit unilateral or bilateral signs or symptoms associated with a combination of nerve and vascular components[9]. Isolated vascular forms of TOS are more easily diagnosed but are also rare. So, the examiner must distinguish which symptoms are related to brachial plexus compression, which are vascular, and which are unrelated to the pathology of the thoracic outlet[5]. Cervical problems are more often charac-

terized by persistent neck and shoulder pain, which may worsen depending on the position of the neck[14]. Distal compression neuropathy, such as carpal tunnel syndrome, is symptomatic alone and is predictable in relation to nerve distribution and exacerbated by wrist and elbow positions rather than shoulder or neck positions. The differential diagnoses important for the neurogenic form of TOS include musculoskeletal disease (such as arthritis or tendinitis) of the cervical column, shoulder girdle or arm, cervical radiculopathy or nerve compression of the upper extremities, idiopathic inflammation of the brachial plexus (also known as Parsonage-turner syndrome) and compression of the brachial plexus due to an infiltrative process or mass such as pulmonary apex Pancoast tumor[7,16].

CONSERVATIVE MANAGEMENT

Preventive measures are essential to correct or eliminate identified hazards, particularly in the workplace, as discussed below[18]. The use of orthoses has also provided useful results for distal symptoms in some patients[17]. Rehabilitation has been performed for many years according to Peet's protocol[19], although a slightly modified protocol has often been used in recent years, consisting of an initial phase of analgesics and muscle relaxants, which appears to provide better results (particularly in painful neurological form). Correctly performed rehabilitation can provide long-term relief of symptoms in about two-thirds of patients. It is particularly effective for proximal pain[28]. In refractory forms, multidisciplinary management is essential along with evaluating the various factors participating in the maintenance of chronic pain and a retraining program such as those proposed for chronic low back pain[15].

SURGICAL MANAGEMENT

Surgical intervention is considered in patients with vascular compression or NTOS that do not respond to conservative management. The three major surgical approaches to decompression of the thoracic outlet are transaxillary, supraclavicular, and posterior, although there are many variations and preferences that are surgeon dependent.

1. Transaxillary

First described by Roos[23] in 1966, the transaxillary approach is the most commonly performed approach today. Proponents claim that it provides superior exposure for first rib resection, as well as for the removal of cervical ribs and fibrous bands, with a more cosmetic scar. In a review of TOS over 50 years, Urschel and Razzuk[32], describe the transaxillary approach as an initial surgical approach through which they perform first rib and costoclavicular ligament resection, splenectomy, and C7, C8, and T1 neurolysis. They argue that while first rib resection can be accomplished via the supraclavicular approach, visualization is poor and requires retraction of the neurovascular structures.

2. Supraclavicular

The supraclavicular approach provides a more favorable exposure of the upper brachial plexus, the neck of the first

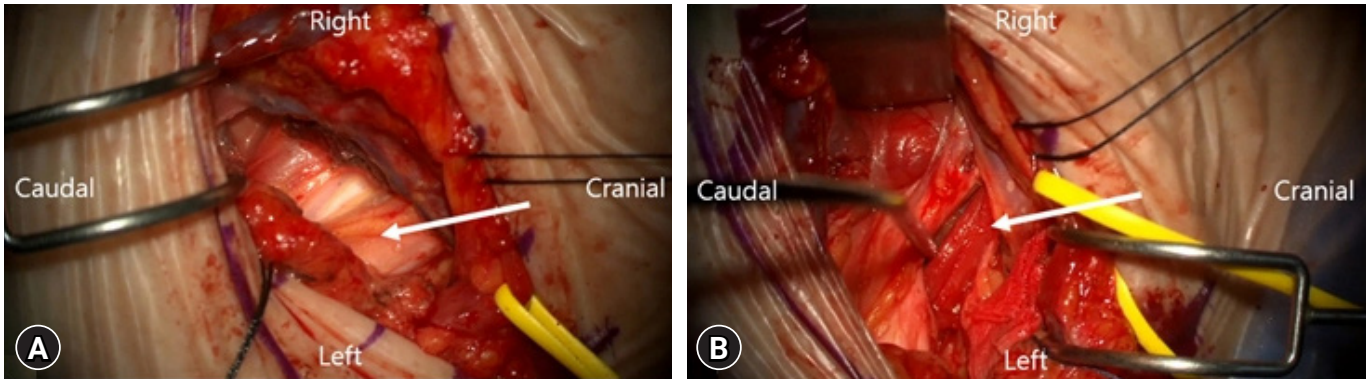

Fig. 6. Left supraclavicular approach for anterior and middle scalene muscle resection for treatment of neurogenic thoracic outlet syndrome. (A) The exposed subclavian artery and brachial plexus (white arrow) after resection of anterior scalene muscle. (B) The middle scalene muscle (white arrow) behind the brachial plexus.

rib, and the neurovascular structures. This approach is preferred by surgeons who perform isolated scalenectomies and removal of cervical ribs for NTOS[13]. Scalenectomy may be considered in patients with upper plexus-type NTOS, patients with TOS symptoms in the absence of abnormal bony architecture, patients who are excessively muscular or obese, or patients with recurrent TOS following prior first rib resection[2]. Although the supraclavicular approach may provide poorer exposure of the first rib compared with the transaxillary approach, Terzis and Kokkalis[31] reported good outcomes and fewer complications with the supraclavicular approach for first rib resection. If arterial reconstruction is necessary, the supraclavicular approach is preferred[30] (Fig. 6).

3. Posterior

The posterior approach, first described by Clagett[4] in 1962, allows better exposure of the proximal component of the brachial plexus for neurolysis; however, the approach is more invasive and it can lead to postoperative shoulder morbidity and scapular winging[26]. Urschel and Razzuk[32] reserve the posterior approach for removing rib remnants and performing brachial plexus neurolysis for patients with recurrent TOS.

CONCLUSION

A meticulous history and thorough physical examination are the most important factors for establishing a diagnosis of TOS. When indicated, radiographic and laboratory tests can improve diagnostic yield. Provocative positional maneuvers should be evaluated for vascular and neurological response. These maneuvers cannot make the diagnosis but can be a useful adjunct for confirming the diagnosis. VTOS is less common and often requires surgical treatment. NTOS is very common but less frequently requires surgical treatment. The selection of surgical approach and procedure must be determined by the nature of the pathologic condition and compression site.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Adson AW: Cervical ribs: symptoms, differential diagnosis and indications for section of the insertion of the scalenus anticus muscle. J Int Coll Surg 16:546–559, 1951
2. Atasoy E: A hand surgeon's further experience with thoracic outlet compression syndrome. J Hand Surg Am 35:1528–1538, 2010
3. Brantigan CO, Roos DB: Diagnosing thoracic outlet syndrome. Hand Clin 20:27–36, 2004
4. Clagett OT: Research and prosearch. J Thorac Cardiovasc Surg 44:153–166, 1962
5. Czihal M, Banafsche R, Hoffmann U, Koeppel T: Vascular compression syndromes. Vasa 44:419–434, 2015
6. Filler AG, Maravilla KR, Tsuruda JS: MR neurography and muscle MR imaging for image diagnosis of disorders affecting the peripheral nerves and musculature. Neurol Clin 22:643–682, vii-vii, 2004
7. Franklin GM: Work-related neurogenic thoracic outlet syndrome: Diagnosis and treatment. Phys Med Rehabil Clin N Am 26:551–561, 2015
8. Gilliatt RW: Thoracic outlet syndrome. Br Med J (Clin Res Ed) 287:764, 1983
9. Grunebach H, Arnold MW, Lum YW: Thoracic outlet syndrome. Vasc Med 20:493–495, 2015
10. Huang JH, Zager EL: Thoracic outlet syndrome. Neurosurgery 55:897–902, discussion 902-3. 2004
11. Jerrett SA, Cuzzone LJ, Pasternak BM: Thoracic outlet syndrome. Electrophysiologic reappraisal. Arch Neurol 41:960–963, 1984
12. Jordan SE, Machleder HI: Diagnosis of thoracic outlet syndrome using electrophysiologically guided anterior scalene blocks. Ann Vasc Surg 12:260–264, 1998
13. Klaassen Z, Sorenson E, Tubbs RS, Arya R, Meloy P, Shah R, et al.: Thoracic outlet syndrome: a neurological and vascular disorder. Clin Anat 27:724–732, 2014
14. Kuhn JE, Lebus VG, Bible JE: Thoracic outlet syndrome. J Am Acad Orthop Surg 23:222–232, 2015
15. Laulan J, Fouquet B, Rodaix C, Jauffret P, Roquelaure Y, Descatha A: Thoracic outlet syndrome: definition, aetiological factors, diagnosis, management and occupational impact. J Occup Rehabil 21:366–373, 2011
16. Masocatto NO, Da-Matta T, Prozzo TG, Couto WJ, Porfirio G: Thoracic outlet syndrome: a narrative review. Rev Col Bras Cir 46:e20192243, 2019
17. Nakatsuchi Y, Saitoh S, Hosaka M, Matsuda S: Conservative treatment of thoracic outlet syndrome using an orthosis. J Hand

Surg Br 20:34–39, 1995
18. Novak CB, Mackinnon SE, Patterson GA: Evaluation of patients with thoracic outlet syndrome. J Hand Surg Am 18:292–299, 1993
19. Peet RM, Henriksen JD, Anderson TP, Martin GM: Thoracic-outlet syndrome: evaluation of a therapeutic exercise program. Proc Staff Meet Mayo Clin 31:281–287, 1956
20. Raaf J: Surgery for cervical rib and scalenus anticus syndrome. J Am Med Assoc 157:219–223, 1955
21. Ranney D: Thoracic outlet: an anatomical redefinition that makes clinical sense. Clin Anat 9:50–52, 1996
22. Riddell DH, Smith BM: Thoracic and vascular aspects of thoracic outlet syndrome. 1986 update. Clin Orthop Relat Res: 31-36, 1986.
23. Roos DB: Transaxillary approach for first rib resection to relieve thoracic outlet syndrome. Ann Surg 163:354–358, 1966
24. Roos DB: Congenital anomalies associated with thoracic outlet syndrome. Anatomy, symptoms, diagnosis, and treatment. Am J Surg 132:771–778, 1976
25. Roos DB: Edgar J. Poth Lecture. Thoracic outlet syndromes: update 1987. Am J Surg 154:568–573, 1987
26. Roos DB: Historical perspectives and anatomic considerations. Thoracic outlet syndrome. Semin Thorac Cardiovasc Surg 8:183–189, 1996
27. Sanders RJ, Hammond SL, Rao NM: Diagnosis of thoracic outlet syndrome. J Vasc Surg 46:601–604, 2007
28. Smith TM, Sawyer SF, Sizer PS, Brismée JM: The double crush syndrome: a common occurrence in cyclists with ulnar nerve neuropathy-a case-control study. Clin J Sport Med 18:55–61, 2008
29. Telford ED, Mottershead S: Pressure at the cervico-brachial junction; an operative and anatomical study. J Bone Joint Surg Br 30b:249–265, 1948
30. Tender GC, Kline DG: Posterior subscapular approach to the brachial plexus. Neurosurgery 57:377–381, discussion 377-81. 2005
31. Terzis JK, Kokkalis ZT: Supraclavicular approach for thoracic outlet syndrome. Hand (N Y) 5:326–337, 2010
32. Urschel HC, Razzuk MA: Neurovascular compression in the thoracic outlet: changing management over 50 years. Ann Surg 228:609–617, 1998
33. Wilbourn AJ: Thoracic outlet syndrome is overdiagnosed. Muscle Nerve 22:130–136, discussion 136-137. 1999

The Nerve

Clinical Article

The Nerve 2023;9(1):9-17
https://doi.org/10.21129/nerve.2022.00213
eISSN 2465-891X

Characteristics of Cervical Spine Injuries Caused by Industrial Accidents: The Experience of a Single Regional Trauma Center in South Korea

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Received: October 12, 2022
Revised: October 27, 2022
Accepted: October 31, 2022

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Objective: This study examined the characteristics of patients with cervical spine injuries caused by industrial accidents and analyzed the factors related to mortality.
Methods: In total, 424 patients with cervical spine injuries who visited our hospital from 2016 to 2020 were divided into an industrial accident and non-industrial accident groups. Age, sex, fracture severity, facet injury, high cervical injury, spinal epidural hematoma, spinal cord injury, shock, arrival route, Injury Severity Score (ISS), Glasgow Coma Scale (GCS), mortality, and trauma mechanism were compared between the two groups. Regression analysis was performed to determine the factors affecting mortality.
Results: Industrial accident patients significantly differed from the rest of the study population in terms of the sex ratio (male ratio, 95.1% vs. 77.8%; p<0.001), arrival route (direct transport, 61.2% vs. 50.9%; p=0.017), and trauma mechanism (p<0.001). Among the trauma mechanisms, falls had the largest difference between industrial accident patients and all patients (55.3% and 28.1%, respectively). Significant associations with mortality were found for falls (odds ratio [OR], 22.330; p=0.015), ISS (OR, 1.056; p=0.008), GCS <9 (OR, 0.014; p<0.001), and shock (OR, 7.290; p<0.001).
Conclusion: Falls were the most frequent trauma mechanism of cervical spine injuries in patients who experienced industrial accidents. The factors significantly correlated with mortality were falls, ISS, GCS <9, and shock.

Keywords: Accidents, occupational; Spinal injuries; Trauma centers

INTRODUCTION

Cervical spine injuries are not typically accompanied by other injuries, compared to thoracolumbar spinal injuries[18]. Therefore, it is relatively easy to isolate and evaluate the impact of cervical spine injuries on the patient's prognosis as the impact of injuries in other organs is minimal[27]. Due to the highly mobile nature of the cervical spine, serious injuries, such as spinal cord injuries, can occur even with low-energy forces that do not cause fractures[14,27]. Despite a small degree of damage, upper spinal cord injury due to cervical spine injury can significantly affect the neurological

symptoms and functional prognosis of the patient across the whole body.

The prevalence of spine injury and accompanying spinal cord injury differs across countries and regions[6,28]. In the case of spinal cord injury, in developed nations, it has been reported variably as 11.5 to 53.4 persons per million persons and 13.0 to 220.0 persons per million[2,7,17,23].

There have been limited investigations on the prevalence of spinal injuries in South Korea. Despite the limited studies on spinal cord injury, those using the Health Insurance Review and Assessment Service data have recently been reported, but patients in industrial and traffic accidents were not included[5].

Our trauma center is near petrochemical and heavy industry complexes such as oil refineries and large shipyards, so we manage patients from various industrial accidents. In addition, cervical trauma caused by industrial accidents is estimated to have poor outcomes due to the severity of the trauma mechanism.

Therefore, this is the study to examine the characteristics of patients with cervical spine injuries caused by industrial accidents and analyze the factors related to mortality.

MATERIALS AND METHODS

This study was approved by our Institutional Review Board, and the requirement for informed consent was waived due to the retrospective nature of this study. (2021-04-039)

This retrospective, the single-centered study enrolled 45,586 patients who visited our emergency room due to trauma from January 2016 to May 2020. Among them, 424 patients with cervical spine injuries were included. Patients with cervical spine injury patients were classified as industrial accident patients (n=103) and the total patients (n=424). Industrial accident patients were defined as patients who had injuries that occurred during work hours according to the emergency room medical record review. For each patient group, age, sex, fracture severity, facet injury, high cervical injury, spinal cord injury, level of spinal injury, spinal epidural hematoma, traumatic brain injury (TBI), trauma mechanism, Injury Severity Score (ISS), Glasgow Coma Scale (GCS), shock, visit route, hospital stay, intensive care unit stay, and mortality were analyzed. Trauma mechanisms were classified as driver traffic accidents (TAs), passenger TA, pedestrian TA, motorcycle accidents, bicycle accidents, falls, slips, heavy equipment accidents, and others.

The fracture severity was classified into grade 0 to 3 as indicated by the AO Spine Subaxial Cervical Spine Injury classification system[25] (Grade 0: No fracture or AO spine subaxial classification A0; Grade 1: AO spine upper cervical classification type A, AO spine subaxial classification A1 to A4; Grade 2: AO spine upper cervical classification type B, AO spine subaxial classification type B; Grade 3: AO spine upper cervical classification type C, AO spine subaxial classification type C). The injury level was divided into upper (C2 or higher) and lower cervical spine (C3 or lower). The shock was a systolic blood pressure of <90 mmHg in the emergency room. Facet injury, spinal cord injury, spinal epidural hematoma, TBI, and mortality were classified as present or absent.

Statistical Analysis

The SPSS software (version 24.0; IBM Corp., Armonk, NY, USA) was used for statistical analysis. Categorical variables were analyzed by performing the chi-square test, while continuous variables were by performing the independent sample *t*-test. In addition, multiple regression analysis was performed to confirm the relationship between each factor on mortality.

RESULTS

Of the 424 patients with cervical spine injuries, when comparing total patients and industrial accident patients, 330 (77.8%) and 98 (95.1%) were men. The male ratio was significantly higher in the industrial accident patients compared to the total patients ($p<0.001$). The mean age for the total and industry accident patients was 53.58 ± 15.91 and 53.94 ± 13.36, respectively, with no significant difference. There were no significant differences in fracture severity, facet injury, high cervical injury, spinal epidural hematoma, spinal cord injury, ISS, GCS, shock, TBI, hospital stay, and intensive care unit stay.

When compared based on the visit route, there was a significant difference in direct transport with 216 (50.9%) in the total patients and 63 (61.2%) in the industrial accident patients ($p=0.017$). There was also a significant difference in the trauma mechanisms ($p<0.001$). For the total patients, there were 70 driver TAs (16.5%), 42 passenger TAs (9.9%), 48 pedestrian TAs (11.3%), 35 motorcycle TAs (8.3%), 32 bicycle

TAs (7.5%), 119 incidents of fall (28.1%), 45 slips (10.6%), 8 heavy equipment accidents (1.9%), and others were 25 (5.9%). Meanwhile, for the industrial accident patients, the incidence of driver TA was 14 (13.6%), passenger TA was 1 (1.0%), pedestrian TA was 2 (1.9%), motorcycle TA was 1 (1.0%), bicycle TA was 0 (0.0%), fall was 57 (55.3%), slip was 5 (4.9%), heavy equipment accident was 8 (7.8%), and others were 15 (14.6%). Among the trauma mechanisms, there was a marked difference between the total patients and the industrial accident patients in the category of falls (Table 1).

Simple and multiple regression analyses were performed for each factor to elucidate the contributing factors of mortality in patients with cervical spine injuries.

In simple regression analysis, high cervical injury (p<0.001), spinal cord injury (p=0.002), ISS (p<0.001), GCS <9 (p<0.001), shock (p<0.001), and TBI (p<0.001) were statistically significant. In multiple regression analysis, fall injury mechanism (p=0.015; odds ratio [OR], 22.330; 1.812-275.180), ISS (p=0.008; OR, 1.056; 1.015-1.099), GCS <9 (p<0.001; OR, 0.014; 0.003-0.065), and shock (p=0.001; OR,

Table 1. Comparison of all patients and industrial accident patients with cervical spine injuries

	Total (n = 424)	Industrial accident (n = 103)	p-value
Sex (male)	330 (77.8)	98 (95.1)	<0.001*
Age (years)	53.58 ± 15.91	53.94 ± 13.36	0.770
Fracture severity			0.116
Grade 0	344 (81.1)	78 (75.7)	
Grade 1	38 (9.0)	12 (11.7)	
Grade 2	26 (6.1)	7 (6.8)	
Grade 3	16 (3.8)	6 (5.8)	
Facet injury	77 (18.2)	21 (20.4)	0.500
High cervical injury	105 (24.8)	24 (23.3)	0.693
Spinal epidural hematoma	16 (3.8)	6 (5.8)	0.209
Spinal cord injury	195 (46.0)	46 (44.7)	0.756
SCI level			0.780*
No injury	229 (54.7)	57 (55.9)	
High cervical	26 (6.5)	6 (5.9)	
Subaxial cervical	159 (37.9)	38 (37.3)	
CT junction	5 (1.2)	1 (1.0)	
ISS	19.76 ± 14.98	20.08 ± 14.08	0.803
GCS < 9	69 (16.3)	14 (13.6)	0.397
Shock (SBP < 90 mmHg)	62 (14.6)	11 (10.7)	0.193
Arrival route (direct transport)	216 (50.9)	63 (61.2)	0.017*
Trauma mechanism			<0.001*
Driver TA	70 (16.5)	14 (13.6)	
Passenger TA	42 (9.9)	1 (1.0)	
Pedestrian TA	48 (11.3)	2 (1.9)	
Motorcycle accident	35 (8.3)	1 (1.0)	
Bicycle accident	32 (7.5)	0 (0.0)	
Fall	119 (28.1)	57 (55.3)	
Slip	45 (10.6)	5 (4.9)	
Heavy equipment accident	8 (1.9)	8 (7.8)	
Others	25 (5.9)	15 (14.6)	
Traumatic brain injury	132 (31.1)	34 (33.0)	0.632
Hospital stay (days)	28.15 ± 39.14	27.09 ± 29.92	0.752
Intensive care unit stay (days)	9.63 ± 25.40	9.02 ± 18.60	0.779

The data is presented as number (%) or mean ± standard deviation.
SCI: spinal cord injury; CT junction: cervicothoracic junction; ISS: Injury Severity Score; GCS: Glasgow Coma Scale; SBP: systolic blood pressure; TA: traffic accident.
*Statistical significance.

7.290; 2.182-24.349) were statistically significant (Table 2).

The frequency of the anterior, posterior, and anteroposterior fusions was compared in patients who underwent fusion due to cervical spine injury, depending on whether they were industrially or non-industrially injured. For 74 patients with a non-industrial accident, anterior fusion was performed in 42 patients (56.8%), posterior fusion in 22 (29.7%), and anteroposterior fusion in 10 (13.5%). Furthermore. 10 (50.0%) out of 20 patients who had industrial accidents underwent anterior fusion, posterior fusion in 3 (15.0%), and anteroposterior fusion in 7 (35.0%). Moreover, the proportion of industrial accident patients who underwent anteroposterior fusion was higher than that of non-industrial accident patients, but there was no statistically significant result (p=0.066). The number of fusion segments was compared to whether the patient had an industrial or a non-industrial accident and underwent fusion due to cervical spine injury. In the case of non-industrial accident patients, 1- (n=21, 28.4%), 2- (n=35, 47.3%), 3- (n=11, 14.9%), and 4-segment fusions (n=7, 9.5%) were implemented. In addition, in the case of industrial injury patients, 1- (n=11, 55.0%), 2- (n=5, 25%), 3- (n=1, 5%), and 4- (n=3, 15.0%) were implemented.

Table 2. Contributing factors to mortality in patients with cervical spine injury

	Total (n = 424)	Mortality (n = 44)	Univariate	Multivariate	
			p-value	p-value	OR (95% CI)
Sex (male)	330 (77.8)	35 (79.5)	0.772		
Age (years)	53.58 ± 15.91	48.98 ± 19.21	0.093		
Fracture severity			0.886		
Grade 0	344 (81.1)	36 (81.8)			
Grade 1	38 (9.0)	3 (6.8)			
Grade 2	26 (6.1)	3 (6.8)			
Grade 3	16 (3.8)	2 (4.5)			
Facet injury	77 (18.2)	6 (13.6)	0.411		
High cervical injury	105 (24.8)	30 (68.2)	<0.001*		
Spinal epidural hematoma	16 (3.8)	1 (2.3)	0.581		
SCI level			0.002*		
No injury	229 (54.7)	14 (33.3)			
High cervical	26 (6.2)	20 (47.6)			
Subaxial cervical	159 (37.9)	8 (19.0)			
CT junction	5 (1.2)	0 (0.0)			
ISS	19.76 ± 14.98	44.69 ± 19.91	<0.001*	0.008*	1.056 (1.015–1.099)
GCS < 9	69 (16.3)	40 (90.9)	<0.001*	<0.001*	0.014 (0.003–0.065)
Shock (SBP < 90 mmHg)	62 (14.6)	32 (72.7)	<0.001*	0.001*	7.290 (2.182–24.349)
Industrial accident	103 (24.3)	10 (22.7)	0.798		
Arrival route (direct transport)	216 (50.9)	27 (61.4)	0.144		
Trauma mechanism			0.680		
Driver TA	70 (16.5)	3 (6.8)		0.198	reference
Passenger TA	42 (9.9)	2 (4.5)		0.084	15.558 (0.691–350.508)
Pedestrian TA	48 (11.3)	8 (18.2)		0.580	1.985 (0.174–22.587)
Motorcycle accident	35 (8.3)	6 (13.6)		0.596	1.967 (0.161–23.994)
Bicycle accident	32 (7.5)	3 (6.8)		0.411	4.412 (0.128–151.966)
Fall	119 (28.1)	20 (45.5)		0.015*	22.330 (1.812–275.180)
Slip	45 (10.6)	1 (2.3)		0.061	26.176 (0.858–798.632)
Heavy equipment accident	8 (1.9)	1 (2.3)		0.356	20.216 (0.034–12053.147)
Others	25 (5.9)	0 (0.0)		0.998	0 (0)
Traumatic brain injury	132 (31.1)	26 (59.1)	<0.001*		

The data is presented as number (%) or mean ± standard deviation.
OR: odds ratio; CI, confidence interval; SCI: spinal cord injury; CT junction: cervicothoracic junction; ISS: Injury Severity Score; GCS: Glasgow Coma Scale; SBP: systolic blood pressure; TA: traffic accident.
*Statistical significance.

There was no clear difference between the two groups and no statistical significance was observed (p=0.080). In the industrial accident patient group, whether the operation with spinal fusion was investigated based on the fall mechanism. Finally, in the non-fall group (n=46), fusion was performed in 5 patients (10.9%), while in the fall patient group (n=57), fusion was performed in 15 patients (26.3%). The difference between the two groups was statistically significant (p=0.049) (Table 3).

DISCUSSION

The ratio of men, direct transport, and fall trauma mechanism was higher in industrial accident patients than in the total patients. Regarding sex, the ratio of male workers tends to be high because our trauma center is located in heavy industry and chemical complexes. The direct transport rate is high in industrial accident patients because the patient transfer system is relatively capable in case of an accident in the workplace. In addition, it is considered that the falling ratio is high because there are many high-altitude work sites due to the nature of heavy industry work, such as shipyards[1].

Mortality was associated with ISS, GCS, and shock[8,13]. In the case of high cervical injury and TBI, the univariate analysis showed a significant correlation, but the multivariate analysis did not. This may be due to the confounding effect of falls, which is significantly related to the trauma mechanism[15]. For the trauma mechanism, it was confirmed that TBI (p=0.006, coefficient 0.137) and high cervical injury (p=0.005, coefficient 0.136) had a significant correlation from the Pearson correlation analysis results. This is due to the high energy mechanism of a fall, which has a high rate in the trauma mechanism of industrial accident patients.

As described above, it was confirmed that fall appears as a factor influencing mortality due to cervical spine injury, but its effect on mortality does not solely depend on its high energy mechanism. Falling from both high and low heights may cause spinal injuries[4]. Although not differentiated in this study, a fall from a relatively low height (approximately 1 m) can cause significant damage to the cervical spinal cord[4]. This is particularly significant for middle-aged and older populations with underlying cervical spondylosis[5,19,20,22]. In a study by Zhang et al.[29] with 1,858 patients with traumatic spinal injury, a fall from a low height occurred more frequently with older age. The incidence of associated injuries to other body parts was low but had more severe neurologic deficits, suggesting cervical or upper thoracic cord injury[29]. As the population of industrial workers is aging, more attention should be given to preventing fall (high and low heights) injuries.

Although the prevention of accidents in industrial sites is very important, whenever a cervical cord injury occurs, a quick initial evaluation should be done, and when neces-

Table 3. The operation type and the number of segments of spinal fusion in patients with industrial accidents

	Total (n = 94, 22.2%)	Industrial accident (n = 20, 19.4%)	p-value
Anterior approach			0.066*
1 level	25 (26.6)	9 (45.0)	0.080†
2 levels	25 (26.6)	1 (5.0)	
3 levels	2 (2.1)	0 (0.0)	
≥4 levels	0 (0.0)	0 (0.0)	
Posterior approach			
1 level	2 (2.1)	0 (0.0)	
2 levels	11 (11.7)	2 (10.0)	
3 levels	6 (6.4)	0 (0.0)	
≥4 levels	6 (6.4)	1 (5.0)	
Anteroposterior approach			
1 level	5 (5.3)	2 (10.0)	
2 levels	4 (4.3)	2 (10.0)	
3 levels	4 (4.3)	1 (5.0)	
≥4 levels	4 (4.3)	2 (10.0)	

*A linear-by-linear association value for comparison of all patients and the industrial accident group for operation type.
†A linear-by-linear association value of all patients and the industrial accident group for the number of segments of the spinal fusion.

sary, prompt intervention is required[24]. Fehlings et al.[9] conducted a multicenter, nonrandomized, prospective cohort study comparing the differences in neurological prognosis depending on whether early surgery was performed in 313 patients with cervical cord injury and showed that patients who underwent early decompression surgery showed a significantly higher rate of >2-point grade improvement in the American Spinal Injury Association Impairment Scale 6 months after receiving the treatment than the group without early decompression surgery (OR, 2.83; 95% confidence interval, 1.10–7.28). Thus, it is necessary to transport patients directly to a trauma center that can promptly manage these patients after being dispatched from the scene. In this study, the direct transport rate of patients with cervical spine injury due to industrial accidents was approximately 61.2%, higher than the total patients (50.9%). Therefore, it is necessary to strengthen coordination between industries and emergency transport authorities to improve the direct transport rate to trauma centers.

In the analysis of patients who underwent spinal fusion for a cervical spine injury, the proportion of industrial accident patients who underwent simultaneous anteroposterior fusion compared to non-industrial accident patients tended to be higher but was not statistically significant. In the subgroup analysis of the operation with spinal fusion, the spinal fusion frequency was significantly higher in patients with injuries caused by a fall. This may be due to the degree of instability caused by high-energy injuries being relatively higher in industrial accident patients, especially those in the fall group. In this study, the AO spine subaxial cervical spine injury classification system was used as a classification criterion for the degree of cervical spine injury. However, in the Allen and Ferguson classification, which was based on the mechanism of cervical spine injury, the prognosis may be particularly poor in the distractive extension injury due to the accompanying spinal cord distraction and brain stem injuries[11,26]. This study introduced the cases of distractive extension injury among cervical spine injury patients (Fig. 1, 2).

Finally, when cervical spinal cord injury is suspected in the workplace, additional damage prevention is required through a cervical collar application. Patients with cervical spinal cord injury have limited functional recovery and a low rate of return to work after the injury[10,12,16,21]. Therefore when a cervical spinal cord injury is suspected, it is important to prevent further damage by applying preemptive

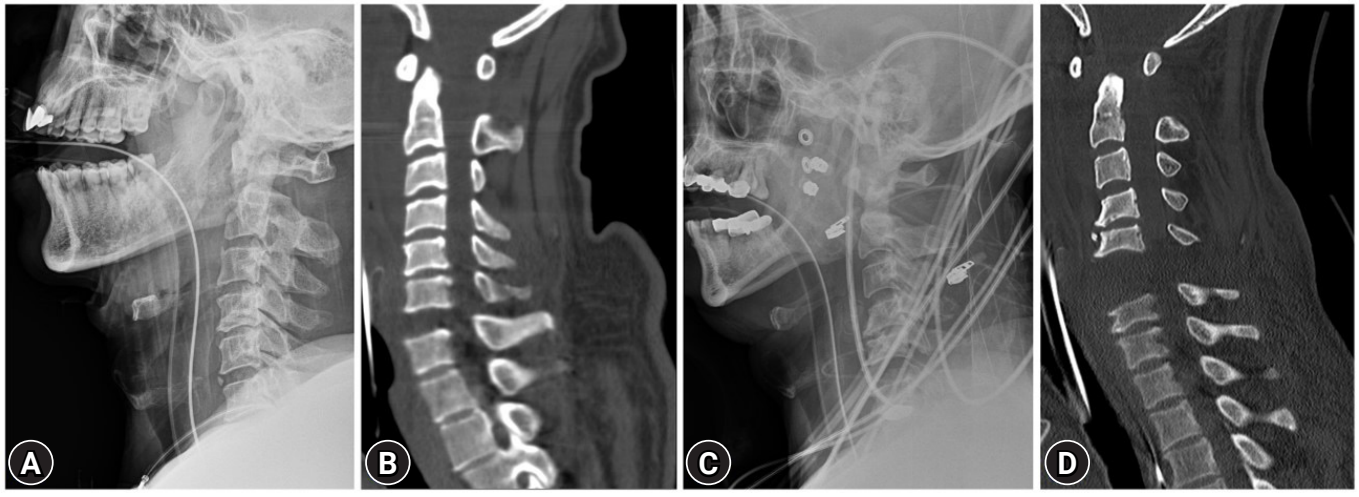

Fig. 1. Fatal cases of distractive extension injury-induced cervical dislocation. (A) A 58-year-old man was injured in a pedestrian traffic accident. Cardiopulmonary resuscitation (CPR) was performed during transport to the hospital. Cervical dislocation at C1/2 was confirmed, and no specific damage was confirmed in other body parts. He expired the day after admission. (B) A 55-year-old man was injured in a pedestrian traffic accident. CPR was performed on-site. Cervical dislocations at C1/2, C6/7 and traumatic subarachnoid hemorrhage were confirmed, and no other specific damage was confirmed in other body parts. He expired in the hospital on day 17 after admission. (C, D) A 60-year-old man was injured by falling from a 20-m height in a shipbuilding yard. CPR was performed while the patient was being transferred to our hospital after an initial evaluation at an external hospital. Cervical dislocations at C1/2 and C5/6 were confirmed, and emergency surgery was performed for thoracic and intra-abdominal bleeding. He expired on the third day of admission.

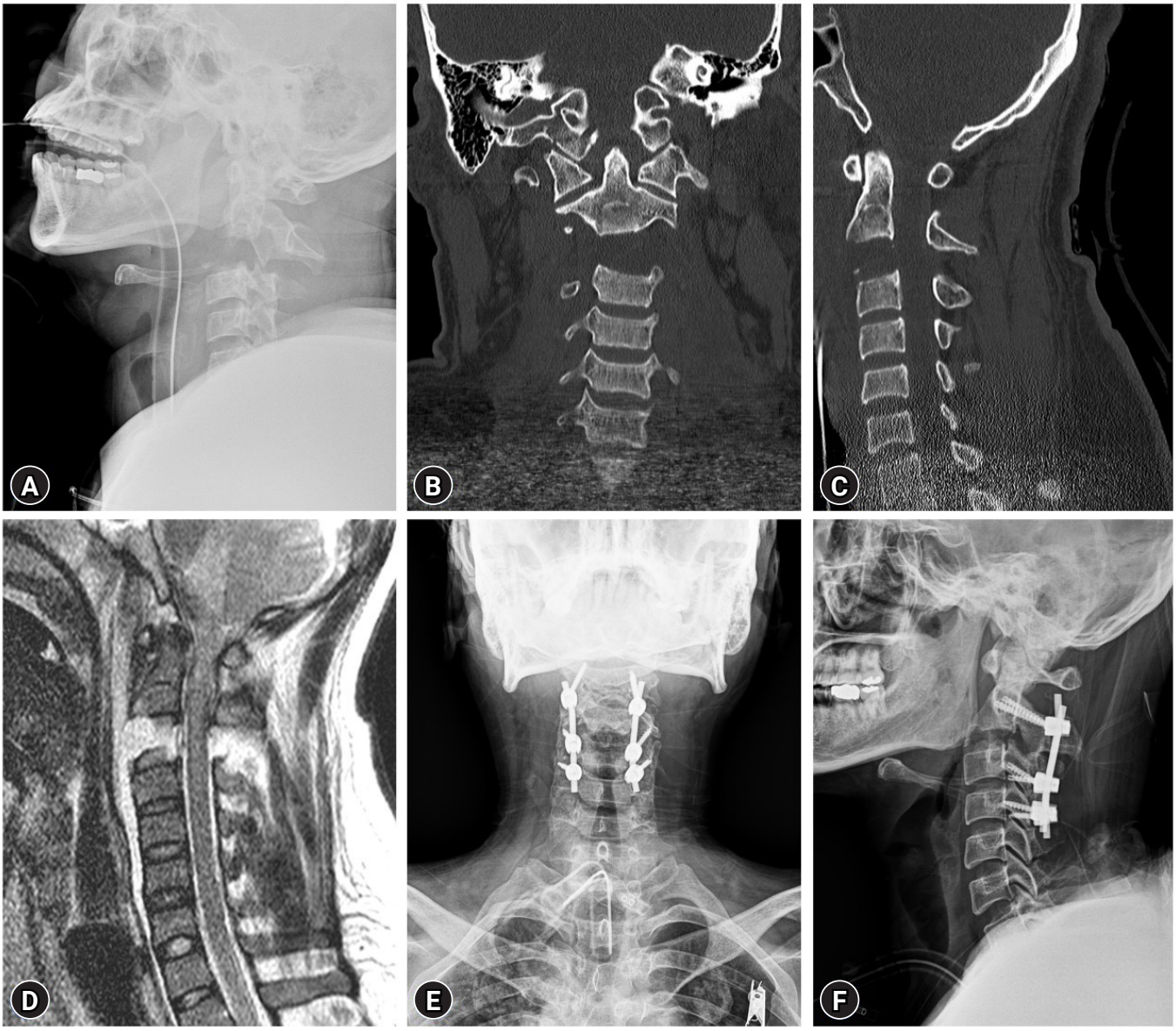

Fig. 2. Surviving case of distractive extension injury-induced cervical dislocation. A 30-year-old man, wearing a helmet, had his upper body caught and damaged by heavy equipment. Cardiopulmonary resuscitation was performed on-site. Cervical dislocation at C2/3 was confirmed, and multiple rib fractures and pneumothorax were confirmed. Due to the patient's poor general condition, surgical intervention for the cervical spine was performed on hospital day 35. He remained hospitalized for about a year due to treatment for bedsores and respiratory complications, and was then discharged with a tracheostomy using a portable ventilator. (A) Initial cervical spine X-ray. (B, C) Initial cervical spine computed tomography. (D) Sagittal plane of cervical spine magnetic resonance imaging. Brainstem signal intensity changes are confirmed. (E, F) Postoperative cervical spine X-ray.

cervical immobilization before transporting the patient[3]. In addition, educating field emergency personnel regarding these measures will improve patient outcomes. There are concerns about prophylactic cervical orthosis. In patients with reduced consciousness due to head injury, the cervical orthosis may cause an increase in intracranial pressure by inhibiting jugular venous return and may induce additional spinal cord injury by promoting cervical distraction in a cervical spine fracture accompanied by ankylosing spondylitis[25]. Therefore, caution is required in these circumstances.

This study has limitations. First, our study result may be biased due to its retrospective nature. Second, there was no direct association between industrial accidents and mortality. However, since the fall rate was high in patients with industrial accidents, and the trauma mechanism was significantly related to mortality, a relationship between industrial accidents and mortality may be assumed. Lastly, this study cannot represent all industrial accident patients. However, as our trauma center is the only tertiary general hospital and trauma center in the region that manages severe trauma patients, the characteristics of our industrial accident patients may be used as a reference.

However, as our trauma center is the only trauma center in the region that manages severe trauma patients, the characteristics of our industrial accident patients may be used as a reference. Third, in order to obtain accurate results, it is necessary to compare the non-industrial accident group and the industrial accident group directly. Although this study has a limitation in that the comparison between the total group and the industrial accident group is performed, it may be helpful to investigate the characteristics of the industrial accident group.

CONCLUSION

The most common mechanism of cervical spine injury in patients involved in industrial accidents is fall. Fall as the mechanism of injury, ISS, GCS <9, and shock had a significant correlation with mortality.

FUNDING

This research was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Science and ICT (2019R1I1A3A0106356314).

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Barlas B, Izci FB: Individual and workplace factors related to fatal occupational accidents among shipyard workers in Turkey. Saf Sci 101:173–179, 2018
2. Burney RE, Maio RF, Maynard F, Karunas R: Incidence, characteristics, and outcome of spinal cord injury at trauma centers in North America. Arch Surg 128:596–599, 1993
3. Chen HA, Hsu ST, Shin SD, Jamaluddin SF, Son DN, Hong KJ, et al.: A multicenter cohort study on the association between prehospital immobilization and functional outcome of patients following spinal injury in Asia. Sci Rep 12:3492, 2022
4. Chen Y, Tang Y, Vogel LC, Devivo MJ: Causes of spinal cord injury. Top Spinal Cord Inj Rehabil 19:1–8, 2013
5. Choi SH, Sung CH, Heo DR, Jeong SY, Kang CN: Incidence of acute spinal cord injury and associated complications of methylprednisolone therapy: a national population-based study in South Korea. Spinal Cord 58:232–237, 2020
6. Cripps RA, Lee BB, Wing P, Weerts E, Mackay J, Brown D: A global map for traumatic spinal cord injury epidemiology: towards a living data repository for injury prevention. Spinal Cord 49:493–501, 2011
7. DeVivo MJ, Vogel LC: Epidemiology of spinal cord injury in children and adolescents. J Spinal Cord Med 27 Suppl 1:S4–S10, 2004
8. Farzan N, Foroghi Ghomi SY, Mohammadi AR: A retrospective study on evaluating GAP, MGAP, RTS and ISS trauma scoring system for the prediction of mortality among multiple trauma patients. Ann Med Surg (Lond) 76:103536, 2022
9. Fehlings MG, Vaccaro A, Wilson JR, Singh A, D WC, Harrop JS, et al.: Early versus delayed decompression for traumatic cervical spinal cord injury: results of the Surgical Timing in Acute Spinal Cord Injury Study (STASCIS). PLoS One 7:e32037. 2012
10. Han ZA, Lee BS, Kim W, Lee SJ, Im HJ, Kim C, et al.: People with spinal cord injury in Korea. Am J Phys Med Rehabil 96:S83–S85, 2017
11. Kanagaraju V, Yelamarthy PKK, Chhabra HS, Shetty AP, Nanda A, Sangondimath GM, et al.: Reliability of allen ferguson classification versus subaxial injury classification and severity scale for subaxial cervical spine injuries: a psychometrics study. Spinal Cord 57:26–32, 2019
12. Khorasanizadeh M, Yousefifard M, Eskian M, Lu Y, Chalangari M, Harrop JS, et al.: Neurological recovery following traumatic spinal cord injury: a systematic review and meta-analysis. J Neurosurg Spine:1–17, 2019
13. Kondo Y, Abe T, Kohshi K, Tokuda Y, Cook EF, Kukita I: Revised trauma scoring system to predict in-hospital mortality in the emergency department: Glasgow Coma Scale, Age, and Systolic

Blood Pressure score. Crit Care 15:R191, 2011
14. Koyanagi I, Iwasaki Y, Hida K, Akino M, Imamura H, Abe H: Acute cervical cord injury without fracture or dislocation of the spinal column. J Neurosurg 93:15–20, 2000
15. Lee JH, Chough CK, Lee JI: Trauma patterns of drowning after falling from bridges over han river. Korean J Neurotrauma 13:85–89, 2017
16. Lidal IB, Huynh TK, Biering-Sørensen F: Return to work following spinal cord injury: a review. Disabil Rehabil 29:1341–1375, 2007
17. Löfvenmark I, Norrbrink C, Nilsson-Wikmar L, Hultling C, Chakandinakira S, Hasselberg M: Traumatic spinal cord injury in Botswana: characteristics, aetiology and mortality. Spinal Cord 53:150–154, 2015
18. Miller CP, Brubacher JW, Biswas D, Lawrence BD, Whang PG, Grauer JN: The incidence of noncontiguous spinal fractures and other traumatic injuries associated with cervical spine fractures: a 10-year experience at an academic medical center. Spine (Phila Pa 1976) 36:1532–1540, 2011
19. Moon BJ, Choi SK, Shin DA, Yi S, Kim KN, Yoon DH, et al.: Prevalence, incidence, comorbidity, and mortality rates of ossification of posterior longitudinal ligament in the cervical spine: A nested case-control cohort study. World Neurosurg 117:e323–e328, 2018
20. Nadhim EA, Hon C, Xia B, Stewart I, Fang D: Falls from height in the construction industry: A critical review of the scientific literature. Int J Environ Res Public Health 13:638, 2016
21. Post MW, Reinhardt JD, Avellanet M, Escorpizo R, Engkasan JP, Schwegler U, et al.: Employment among people with spinal cord injury in 22 countries across the world: Results From the international spinal cord injury community survey. Arch Phys Med Rehabil 101:2157–2166, 2020
22. Rivara FP, Thompson DC: Prevention of falls in the construction industry: evidence for program effectiveness. Am J Prev Med 18:23–26, 2000
23. Sabre L, Remmer S, Adams A, Väli M, Rekand T, Asser T, et al.: Impact of fatal cases on the epidemiology of traumatic spinal cord injury in Estonia. Eur J Neurol 22:768–772, 2015
24. Sánchez JAS, Sharif S, Costa F, Rangel J, Anania CD, Zileli M: Early management of spinal cord injury: WFNS spine committee recommendations. Neurospine 17:759–784, 2020
25. Sundstrøm T, Asbjørnsen H, Habiba S, Sunde GA, Wester K: Prehospital use of cervical collars in trauma patients: a critical review. J Neurotrauma 31:531–540, 2014
26. Urrutia J, Zamora T, Campos M, Yurac R, Palma J, Mobarec S, et al.: A comparative agreement evaluation of two subaxial cervical spine injury classification systems: the AOSpine and the Allen and Ferguson schemes. Eur Spine J 25:2185–2192, 2016
27. Wick J, Le H, Wick K, Peddada K, Bacon A, Han G, et al.: Patient characteristics, injury types, and costs associated with secondary over-triage of isolated cervical spine fractures. Spine (Phila Pa 1976) 47:414–422, 2022
28. Wyndaele M, Wyndaele JJ: Incidence, prevalence and epidemiology of spinal cord injury: what learns a worldwide literature survey? Spinal Cord 44:523–529, 2006
29. Zhang ZR, Wu Y, Wang FY, Wang WJ: Traumatic spinal cord injury caused by low falls and high falls: a comparative study. J Orthop Surg Res 16:222, 2021

The Nerve

Clinical Article

The Nerve 2023;9(1):18-26
https://doi.org/10.21129/nerve.2022.00227
eISSN 2465-891X

Advantages of Posterior Indirect Decompression Surgery in Thoracolumbar Burst Fractures with Neurologic Symptoms

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OPEN ACCESS

Received: November 4, 2022
Revised: January 4, 2023
Accepted: February 3, 2023

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Objective: Approximately 90% of spinal fractures occur at the thoracolumbar (T-L) junction and may be accompanied by neurological symptoms, in which decompression and post-fixation are generally performed. However, decompression surgery can aggravate patients' symptoms due to adverse incidents, such as developing postoperative hematomas or iatrogenic spinal cord injury. This study compared the surgical and radiographic outcomes of patients with T-L junction burst fractures and neurological deficits who underwent direct or indirect decompression.

Methods: We retrospectively reviewed all patients who had undergone posterior surgical treatment for T-L junction burst fractures with neurologic deficits. Patients were classified according to the procedure: indirect decompression (group 1) or spinal decompression through laminectomy and facetectomy (group 2). Clinical results and radiologic findings were compared between the two groups for 2 years.

Results: Among 57 patients who met the inclusion criteria, 29 were categorized into group 1, and 28 were categorized into group 2. Group 1 had a statistically significantly lower Oswestry Disability Index score than group 2 at the final follow-up visit (p=0.03). In group 1, both the T-L junction angle and wedge angle of the injured vertebrae improved significantly, both immediately after surgery (p=0.02 and p=0.01, respectively) and at the final follow-up visit (p=0.01 and p=0.01, respectively). In group 2, the difference between the pelvic incidence and lumbar lordosis was significantly greater than in group 1 at the final follow-up visit (p=0.02).

Conclusion: This study confirmed that symptoms could be sufficiently improved with indirect decompression, which should be kept in mind for cases where it is difficult to perform direct decompression,

Keywords: Spinal fractures; Thoracic vertebrae; Visual analog scale

INTRODUCTION

Approximately 90% of spinal fractures occur at the thoracolumbar (T-L) junction[7,15,28], including burst fractures and T-L vertebral collapse. T-L burst fracture is defined according to the presence of fractures or comminutions in both the anterior and middle columns, with the bony fragments retracted into the spinal canal[5]. A T-L burst fracture with a fractured and reverse-oscillating posterior vertebral wall can cause neurological deficits when bone fragments persist in the spinal canal during or after trauma[19,27]. Without appropriate treatment, these complications substantially affect physical health, occupational daily activities, and overall quality of life[18].

Surgery is primarily indicated to relieve spinal cord compression and restore neural function[4,20,26]. In patients diagnosed with fractures of the vertebral bodies and posterior elements with some degree of misalignment of the spine or those with T-L junction fractures presenting with spinal canal injuries and neurological symptoms, timely decompression and internal immobilization should be performed to restore vertebral body height and vertebral canal volume. The goal is to restore spinal stability as soon as possible in accordance with current medical guidelines[14,21].

Various surgical options are available for the management of T-L burst fractures, including posterior fixation and decompression, as well as direct anterior decompression through vertebral resection[6,10,12,22]. Posterior decompression and fixation are the most commonly implemented methods. However, decompression can aggravate neurologic symptoms, with postoperative hematomas or spinal cord injury commonly presenting in patients who have difficulty coagulating[13]. In contrast, indirect decompression can decompress nerve tissue without excising the compressed tissue. This method is primarily performed through distraction between the two vertebrae, which opens the neural foramen and increases the epidural space. Therefore, this technique allows for nerve tissue decompression without excision of the compression fragment. Distraction and ligamentotaxis indirectly lead to reduced fracture fragments, resulting in restoration of corpus height, kyphosis correction, and canal widening[16,30].

We ought to establish the surgical outcomes of indirect decompression in patients with T-L junction burst fractures presenting with neurological deficits. Toward this goal, we retrospectively evaluated the surgical outcomes of patients who underwent indirect decompression surgery and compared these outcomes to patients who underwent posterior fixation after laminectomy.

MATERIALS AND METHODS

1. Demographic Evaluation

The institutional review board at the participating medical center approved this study. Patients who underwent surgery at our tertiary medical center between August 2013 and January 2020 for traumatic T-L junction fractures with neurological deficits were retrospectively reviewed.

We included patients who (1) underwent posterior fusion surgery for a single-level burst fracture of the T-L junction from the T11 to L2 level with traumatic spinal cord injury; (2) had no prior history of spinal surgery; (3) had received surgical treatment within 48 hr after trauma; (4) only had radiating pain without motor function impairment; and (5) had a minimum follow-up of 24 months.

We excluded patients who (1) had a follow-up period shorter than 24 months; (2) presented with multi-level spinal fractures; (3) had a history of previous posterior spinal surgery; (4) had severe comorbidities (e.g., cancer metastasis, infectious diseases) that may adversely affect bone healing; and (5) experienced neurological defects such as motor weakness or cauda equina syndrome. Indirect decompression surgery was performed in patients for whom direct decompression surgery could not be performed due to age, underlying disease, and medications. Direct decompression and post-fixation surgery were performed in all other patients.

Demographic data were collected through questionnaires administered to all patients, including data on age, sex, underlying disease, injured vertebra level, smoking history, body mass index (BMI), surgical details, a range of follow-up information, data abstracted from electronic medical records, estimated blood loss during surgery, and operative times. We did not obtain consent for participation from the enrolled patients owing to the retrospective nature of the study. Thus, the normal requirement for informed consent was waived during the ethics review process.

2. Pain and Quality of Life Evaluation

Patient-reported questionnaires were administered before

surgery during outpatient clinic visits. Pain levels were quantified using a visual analog scale (VAS) with respect to back and leg pain both pre- and post- operatively (immediate, 12-month, and 24-month follow-up). The effects on disability and quality of life were measured using the Oswestry Disability Index (ODI) questionnaire at the same time points. A satisfaction questionnaire evaluating the received treatment was also administered. In cases where it was difficult for patients to complete a questionnaire, results were verified by a telephonic interview conducted with a member of the study staff.

3. Operative Technique

All patients were placed in a prone position with a Wilson frame adjoining the thoracic and iliac spines, thus straining the anterior columns of the spine to reset the spinal curvature. A midline skin incision was made, and the paravertebral muscles were separated bilaterally from the spinous process to expose the lamina and facet joint. The pedicle of the fractured vertebral body was evaluated using C-arm fluoroscopy. Segmental screws were inserted into one or two vertebrae above and one vertebra below the level of the fracture via the freehand technique. Six to eight pedicle screws were inserted into the pedicle. Polyaxial pedicle screws were inserted into the upper and lower normal vertebrae, and axial pedicle screws were inserted into the fractured vertebrae.

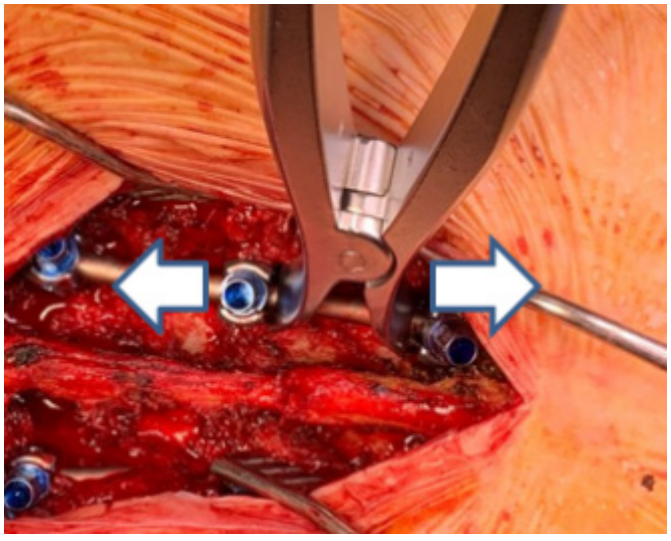

Fig. 1. A T12–L1 rod was distracted for the purpose of L1 indirect vertebral body decompression in patients with L1 burst fractures.

A screw 5 to 10 mm shorter than the vertebra was inserted into the pedicle screw of the upper and lower normal vertebrae. The connecting rod was then inserted and fixed with a cap.

In group 1 (the indirect decompression group), indirect decompression can be achieved through distraction by identifying areas with burst fractures, dura compression, and segmental kyphosis with a C-arm and performing distraction between the posterior segmental instruments above and below the area (Fig. 1).

In group 2 (the direct decompression group), we performed posterior decompression, including laminectomy and facetectomy, to widen the spinal canal when cord compression was observed following a fracture.

4. Radiographic Evaluation

We performed magnetic resonance imaging (MRI) and multi-slice computed tomography imaging of the T-L spine in all patients. Using sagittal MRI images, we calculated dural sac compression due to epidural hematoma or bone fragments. The dural compression ratio presents the ratio of compressed to supposedly normal dura at the level of the injury. This ratio was calculated using the following equation: $(1 - C/[(A + B)/2]) \times 100$[11] (Fig. 2).

We measured the angle of the T-L junction, thus evaluating kyphosis according to the Cobb method[9]. The Cobb angle was measured from the upper-end plate of T10 and the lower-end plate of L2. We also measured spinal parameters. These parameters included thoracic kyphosis (TK; T5-12), lumbar lordosis (LL; L1-S1), and pelvic incidence (PI)-LL mismatch. In addition, we recorded the wedge angle (WA) of the injured vertebral body. All radiological parameters were checked preoperatively, immediately postoperatively, and at the final (24-month) follow-up visit.

5. Statistical Analyses

Continuous variables were described as the mean ± standard deviation, and categorical variables were expressed as frequencies or percentages. Additionally, Student's t-test, χ^2, and Fisher's exact tests were used to determine statistically significant differences in radiological and clinical outcomes between the two groups. All statistical analyses were performed using SPSS Statistics for Windows, Version 17.0 (IBM Corp., Armonk, NY, USA). A p-value of less than 0.05 was considered statistically significant.

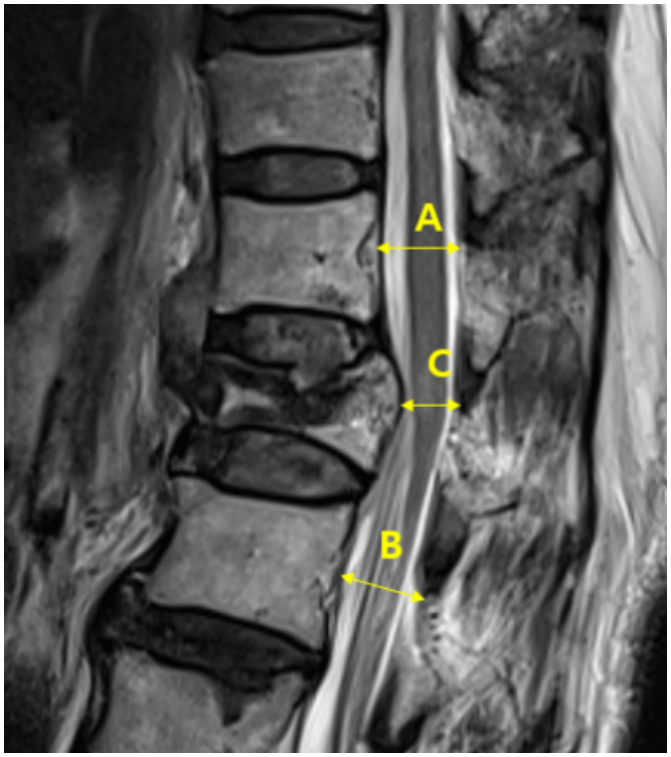

Fig. 2. Dural compression ratios were calculated using the following equation: (1−C/[A+B]/2)×100. We evaluated (A) the dura mater at the cephalad non-compressed level, (B) the dura mater at the caudal non-compressed level, and (C) the dura mater at the injury level.

RESULTS

1. Demographic Analysis

A total of 57 patients were enrolled in this study. Among these patients, 29 were categorized into group 1, and 28 were categorized into group 2. Among those in group 1, 19 were taking anticoagulants, 7 were ≥80 years old, and 3 had a hematologic disease. Serious complications, such as nerve root and spinal cord injuries, screw malposition, broken screws, and rods, hematomas pressing on the spinal cord, or wound infections, were not observed in enrolled patients. Age, sex, underlying disease, fractured vertebra level, bone marrow density, BMI, and smoking history distributions did not significantly differ between the two groups (Table 1).

2. Comparative Analysis of Surgical Information

Intraoperative bleeding volume was lower in group 1 vs. group 2; however, this difference was not statistically significant. In addition, there were no significant differences in the surgical level at which fixation was performed or the preoperative dura compression ratio. However, the indirect decompression group had a significantly shorter mean operative time than the direct decompression group (31 min, p=0.03; Table 2).

Table 1. Comparative descriptive statistics with respect to medical and demographic variables

Group	Group 1 (indirect decompression)	Group 2 (direct decompression)	p-value
Age	62.15 ± 9.50	60.52 ± 10.41	0.61
Sex			0.47
Male	17	19	
Female	12	9	
Hypertension (%)	34.3	37.1	0.81
Diabetes mellitus (%)	12.5	25.7	0.21
Smoking (%)	34.3	34.2	0.97
BMI	24.00 ± 3.24	24.58 ± 3.48	0.48
BMD	-1.38 ± 1.69	-1.49 ± 1.72	0.81
Injured vertebra			0.61
T11	4	6	
T12	11	3	
L1	8	8	
L2	6	11	

The data is presented as number or mean ± standard deviation.
BMI: body mass index; BMD: bone marrow density.

Table 2. Comparison of surgical time, intraoperative bleeding, and surgical factors between the 2 groups

Group (surgical method)	Group 1 (indirect decompression)	Group 2 (direct decompression)	p-value
Operation time (min)	126.06 ± 44.92	157.39 ± 61.26	0.03
Intraoperative blood loss (mL)	427.58 ± 239.63	603.57 ± 515.12	0.11
Fusion level	3.41 ± 0.50	3.32 ± 0.47	0.47
Dural compression ratio	0.27 ± 0.14	0.29 ± 0.10	0.55

Table 3. Clinical outcomes during the study follow-up period of both groups

Group (surgical method)	Group 1 (indirect decompression)	Group 2 (direct decompression)	p-value
VAS (back)			
Preoperative	8.37 ± 0.67	8.50 ± 0.96	0.58
Immediately postoperative	5.58 ± 1.99	5.10 ± 1.91	0.35
Final follow-up	3.00 ± 2.03	3.64 ± 2.02	0.23
VAS (leg)			
Preoperative	7.86 ± 1.12	7.03 ± 2.25	0.08
Immediately postoperative	3.51 ± 1.74	4.10 ± 2.49	0.30
Final follow-up	2.82 ± 1.53	3.25 ± 2.35	0.42
ODI score			
Preoperative	38.06 ± 5.30	39.71 ± 5.53	0.25
Immediately postoperative	22.86 ± 5.33	22.82 ± 9.34	0.98
Final follow-up	9.86 ± 3.93	14.85 ± 9.37	0.03

VAS: visual analog scale; ODI: Oswestry Disability Index.

3. Clinical Outcome

We found that the VAS and ODI scores before surgery as well as immediately after surgery were lower in group 1 than in group 2, with no significant differences between the two. However, at the final follow-up, patients in group 1 had significantly lower ODI scores compared with those in group 2 (p=0.03; Table 3).

4. Comparative Radiological Results

No significant between-group differences were observed for any of the pre-surgical radiologic parameters. Regarding the WA of the injured vertebral body, it was confirmed that the kyphotic angle was significantly smaller in group 1 compared to that in group 2 immediately after surgery (p=0.01) and at the last follow-up (p=0.01). In the angle of T-L junction, a statistically significantly smaller kyphotic angle was observed in group 1 immediately after surgery (p = 0.02), which was also confirmed at the final follow-up (p=0.01) (Fig. 3, Table 4). No significant differences in TK or LL were observed between the two groups. Group 2 had a larger PI-LL discrepancy than Group 1 at the final follow-up visit (p=0.02; Table 4).

DISCUSSION

This is the first study to compare the clinical and radiological features of patients with T-L junction burst fractures presenting with neurological symptoms who underwent indirect decompression surgery with those of patients who underwent direct decompression surgery.

The T-L junction segment is located at the physiological stress concentration points of the spinal cord[15]. Burst fractures typically lead to various symptoms caused by spinal cord compression due to the presence of bone fragments and epidural hematomas. Decompression and post-fixation are normally performed in the presence of neurological symptoms. However, direct decompression of the spinal cord area can aggravate hematomas or spinal cord injuries and cause dural tearing[29]. Moreover, older age, anticoagulant use, and many risk factors during surgery have been identified as causes of postoperative spinal epidural hematoma[3,8,13,25]. Therefore, we performed indirect decompres-

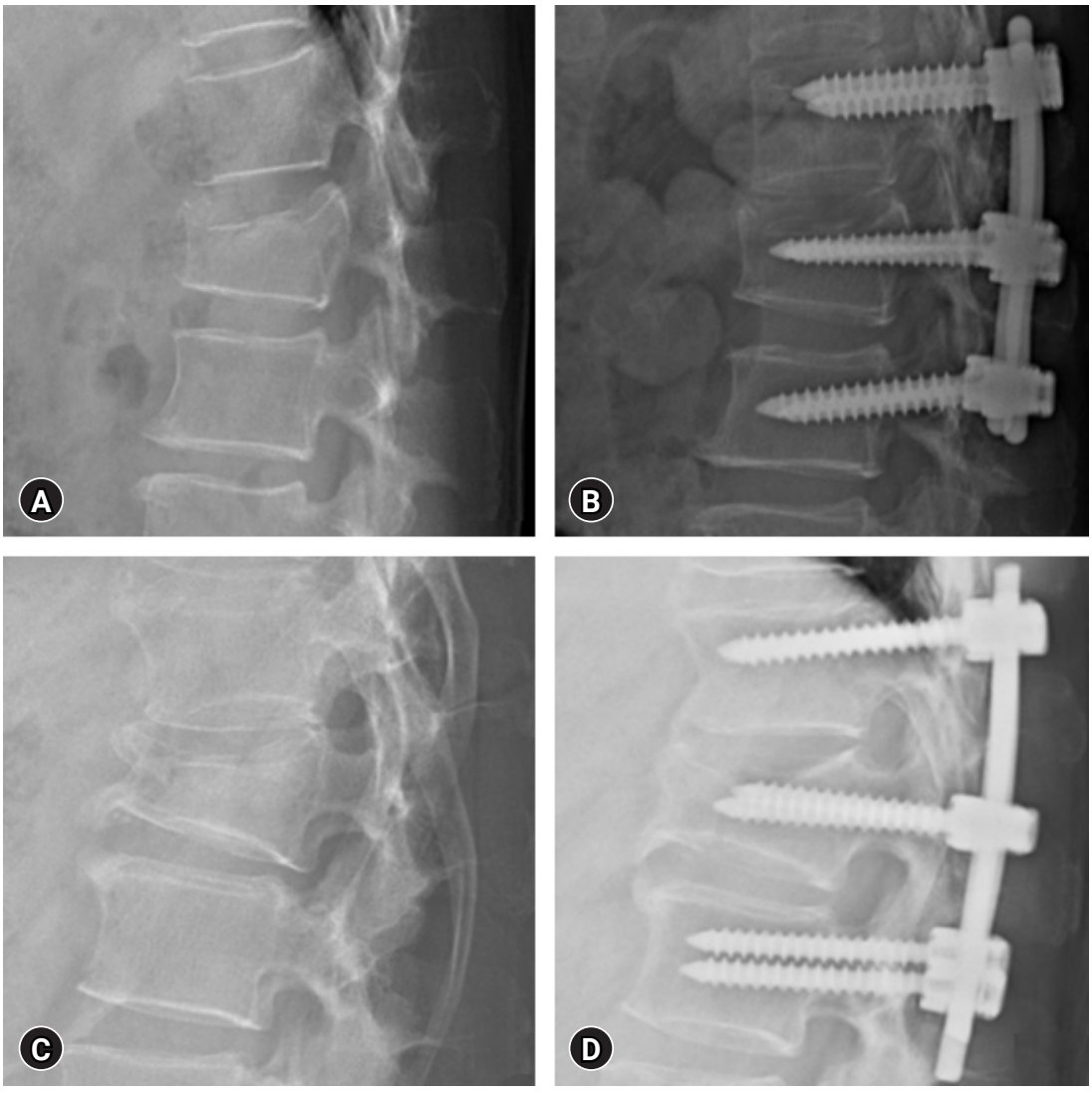

Fig. 3. Comparison of the vertebral body and thoracolumbar junction before and after surgery (24 months). Comparison of angular changes between the direct decompression surgery group using lateral X-ray (A, preoperative; B, 24 months postoperative) and the indirect decompression surgery group (C, preoperative; D, 24 months postoperative).

sion surgery for these at-risk patients.

Many studies have been conducted on partial lordosis and total spinal alignment correction using indirect decompression with a posterior approach[1,2,17]. In our study, the indirect decompression group showed lower WA and T-L junction angles. However, no significant differences were observed with respect to TK and LL. Future studies performing surgeries involving larger numbers of patients and more levels of the spine are needed.

In terms of PI-LL mismatch, we found a significant difference in the direct decompression group immediately after surgery. Schwab et al.[23] viewed PI-LL mismatch as a key parameter related to postoperative patient disability and health-related quality of life. Seo et al.[24] reported that a T-L junction Cobb angle larger than 10.5° immediately after surgery was associated with unfavorable radiological outcomes, which, in turn, were associated with poor clinical outcomes. In the current study, we confirmed that ODI scores were worse in the direct vs. indirect decompression group. The T-L kyphotic angle in the direct decompression group was 10.5° or higher. Consequently, we confirmed that clinical radiological results improved in the indirect vs. direct decom-

Table 4. Comparative radiologic parameters between the surgical groups

Group (surgery method)	Group 1 (indirect decompression)	Group 2 (direct decompression)	p-value
Angle of the thoracolumbar junction			
Preoperative	17.82 ± 10.05	17.28 ± 8.24	0.81
Immediately postoperative	6.85 ± 4.17	10.51 ± 7.33	0.02
2 years (final follow-up)	8.89 ± 5.39	13.51 ± 5.72	0.01
Thoracic kyphosis			
Preoperative	30.75 ± 10.92	30.21 ± 10.65	0.85
Immediately postoperative	17.68 ± 7.68	19.57 ± 8.69	0.39
2 years (final follow-up)	24.62 ± 8.97	25.53 ± 9.48	0.39
Lumbar lordosis			
Preoperative	35.79 ± 8.85	37.28 ± 11.42	0.58
Immediately postoperative	44.34 ± 6.01	43.27 ± 9.63	0.58
2 years (final follow-up)	39.08 ± 8.21	41.10 ± 6.29	0.31
PI-LL mismatch			
Preoperative	27.83 ± 10.10	27.52 ± 10.55	0.58
Immediately postoperative	20.75 ± 11.02	22.81 ± 10.87	0.44
2 years (final follow-up)	20.84 ± 11.01	26.51 ± 11.13	0.02
Wedge angle of injured vertebral body			
Preoperative	19.55 ± 8.21	19.46 ± 6.97	0.96
Immediately postoperative	7.53 ± 4.79	12.17 ± 8.71	0.01
2 years (final follow-up)	8.24 ± 7.00	12.60 ± 4.69	0.01

PI: pelvic incidence; LL: lumbar lordosis.

pression group. Furthermore, there was less improvement in kyphotic angle in the direct vs. indirect decompression group, resulting in a larger T-L junction kyphosis and whole spine malalignment, which consequently adversely affected ODI score improvements.

In addition to the substantial strengths of this study, we acknowledge several limitations. First, we enrolled a small sample size selected from a single medical center. Moreover, comparative study groups were lacking in the current study design. In particular, comparisons were not made according to various fracture shapes, e.g., pedicle fractures. Further comparative studies involving larger case series and fractures of various shapes are needed to confirm our findings in patients with T-L junction vertebral fractures. Second, the follow-up period was relatively short. Additional studies with longer follow-up periods are required to validate the neurological changes observed in this study.

CONCLUSION

In this study, the clinical and radiological results of direct and indirect decompression were compared. We sought to confirm the usefulness of indirect decompression in patients with T-L junction tear fractures and neurological symptoms when direct decompression was difficult. Indirect decompression was associated with better clinical outcomes and improved radiographic alignment compared to direct decompression. Further studies with more patients and longer duration are needed. However, our findings will serve as a reference to guide future research and provide direct information for medical guidelines and clinical decision-making.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Abumi K, Shono Y, Taneichi H, Ito M, Kaneda K: Correction of cervical kyphosis using pedicle screw fixation systems. Spine (Phila Pa 1976) 24:2389-2396, 1999
2. Ando K, Imagama S, Ito Z, Kobayashi K, Ukai J, Muramoto A, et al.: Ponte Osteotomy During Dekyphosis for Indirect Posterior

Decompression With Ossification of the Posterior Longitudinal Ligament of the Thoracic Spine. Clin Spine Surg 30:E358–E362, 2017
3. Awad JN, Kebaish KM, Donigan J, Cohen DB, Kostuik JP: Analysis of the risk factors for the development of post-operative spinal epidural haematoma. J Bone Joint Surg Br 87:1248–1252, 2005
4. Chen SL, Huang YH, Wei TY, Huang KM, Ho SH, Bih LI: Motor and bladder dysfunctions in patients with vertebral fractures at the thoracolumbar junction. Eur Spine J 21:844–849, 2012
5. Denis F: The three column spine and its significance in the classification of acute thoracolumbar spinal injuries. Spine (Phila Pa 1976) 8:817–831, 1983
6. Dobran M, Nasi D, Brunozzi D, di Somma L, Gladi M, Iacoangeli M, et al.: Treatment of unstable thoracolumbar junction fractures: short-segment pedicle fixation with inclusion of the fracture level versus long-segment instrumentation. Acta Neurochir (Wien) 158:1883–1889, 2016
7. Esses SI, Botsford DJ, Kostuik JP: Evaluation of surgical treatment for burst fractures. Spine (Phila Pa 1976) 15:667–673, 1990
8. Fraser S, Roberts L, Murphy E: Cauda equina syndrome: a literature review of its definition and clinical presentation. Arch Phys Med Rehabil 90:1964–1968, 2009
9. Harrison DE, Cailliet R, Harrison DD, Janik TJ, Holland B: Reliability of centroid, Cobb, and Harrison posterior tangent methods: which to choose for analysis of thoracic kyphosis. Spine (Phila Pa 1976) 26:E227–E234, 2001
10. Kaneda K, Taneichi H, Abumi K, Hashimoto T, Satoh S, Fujiya M: Anterior decompression and stabilization with the Kaneda device for thoracolumbar burst fractures associated with neurological deficits. J Bone Joint Surg Am 79:69–83, 1997
11. Kawano O, Ueta T, Shiba K, Iwamoto Y: Outcome of decompression surgery for cervical spinal cord injury without bone and disc injury in patients with spinal cord compression: a multicenter prospective study. Spinal Cord 48:548–553, 2010
12. Keys HM, Bundy BN, Stehman FB, Muderspach LI, Chafe WE, Suggs CL, et al.: Cisplatin, radiation, and adjuvant hysterectomy compared with radiation and adjuvant hysterectomy for bulky stage IB cervical carcinoma. N Engl J Med 340:1154–1161, 1999
13. Kou J, Fischgrund J, Biddinger A, Herkowitz H: Risk factors for spinal epidural hematoma after spinal surgery. Spine (Phila Pa 1976) 27:1670–1673, 2002
14. Leferink VJ, Nijboer JM, Zimmerman KW, Veldhuis EF, ten Vergert EM, ten Duis HJ: Burst fractures of the thoracolumbar spine: changes of the spinal canal during operative treatment and follow-up. Eur Spine J 12:255–260, 2003
15. Lin B, Chen ZW, Guo ZM, Liu H, Yi ZK: Anterior Approach Versus Posterior Approach With Subtotal Corpectomy, Decompression, and Reconstruction of Spine in the Treatment of Thoracolumbar Burst Fractures: A Prospective Randomized Controlled Study. J Spinal Disord Tech 25:309–317, 2012
16. Malham GM, Parker RM, Goss B, Blecher CM, Ballok ZE: Indirect foraminal decompression is independent of metabolically active facet arthropathy in extreme lateral interbody fusion. Spine (Phila Pa 1976) 39:E1303–E1310, 2014
17. Matsuyama Y, Sakai Y, Katayama Y, Imagama S, Ito Z, Wakao N, et al.: Indirect posterior decompression with corrective fusion for ossification of the posterior longitudinal ligament of the thoracic spine: is it possible to predict the surgical results? Eur Spine J 18:943–948, 2009
18. McLain RF: Functional outcomes after surgery for spinal fractures: return to work and activity. Spine (Phila Pa 1976) 29:470–477, discussion Z6. 2004
19. Meves R, Avanzi O: Correlation among canal compromise, neurologic deficit, and injury severity in thoracolumbar burst fractures. Spine (Phila Pa 1976) 31:2137–2141, 2006
20. Park SR, Na HY, Kim JM, Eun DC, Son EY: More than 5-Year Follow-up Results of Two-Level and Three-Level Posterior Fixations of Thoracolumbar Burst Fractures with Load-Sharing Scores of Seven and Eight Points. Clin Orthop Surg 8:71–77, 2016
21. Rabie A, Ibrahim AM, Lee BT, Lin SJ: Use of intraoperative computed tomography in complex facial fracture reduction and fixation. J Craniofac Surg 22:1466–1467, 2011
22. Sasso RC, Best NM, Reilly TM, McGuire RA Jr: Anterior-only stabilization of three-column thoracolumbar injuries. J Spinal Disord Tech 18 Suppl:S7–S14, 2005
23. Schwab FJ, Blondel B, Bess S, Hostin R, Shaffrey CI, Smith JS, et al.: Radiographical spinopelvic parameters and disability in the setting of adult spinal deformity: a prospective multicenter analysis. Spine (Phila Pa 1976) 38:E803–E812, 2013
24. Seo DK, Kim CH, Jung SK, Kim MK, Choi SJ, Park JH: Analysis of the Risk Factors for Unfavorable Radiologic Outcomes after Fusion Surgery in Thoracolumbar Burst Fracture : What Amount of Postoperative Thoracolumbar Kyphosis Correction is Reasonable? J Korean Neurosurg Soc 62:96–105, 2019
25. Sokolowski MJ, Garvey TA, Perl J, Sokolowski MS, Cho W, Mehbod AA, et al.: Prospective study of postoperative lumbar epidural hematoma: incidence and risk factors. Spine (Phila Pa 1976) 33:108–113, 2008
26. Wang F, Zhu Y: Treatment of complete fracture-dislocation of

thoracolumbar spine. J Spinal Disord Tech 26:421–426, 2013
27. Whang PG, Vaccaro AR: Thoracolumbar fracture: posterior instrumentation using distraction and ligamentotaxis reduction. J Am Acad Orthop Surg 15:695–701, 2007
28. Wood KB, Bohn D, Mehbod A: Anterior versus posterior treatment of stable thoracolumbar burst fractures without neurologic deficit: a prospective, randomized study. J Spinal Disord Tech 18 Suppl:S15–S23, 2005
29. Xu N, Yu M, Liu X, Sun C, Chen Z, Liu Z: A systematic review of complications in thoracic spine surgery for ossification of the posterior longitudinal ligament. Eur Spine J 26:1803–1809, 2017
30. Yoshihara H: Indirect decompression in spinal surgery. J Clin Neurosci 44:63–68, 2017

The Nerve

Clinical Article

The Nerve 2023;9(1):27-33
https://doi.org/10.21129/nerve.2022.00248
eISSN 2465-891X

Association of Acute Myocardial Infarction with Ossification of the Posterior Longitudinal Ligament in Korea: A Nationwide Longitudinal Cohort Study

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OPEN ACCESS

Received: December 16, 2022
Revised: January 8, 2023
Accepted: February 3, 2023

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Objective: This nationally matched longitudinal study aimed to investigate the relationship between acute myocardial infarction (AMI) and ossification of the posterior longitudinal ligament (OPLL) in Korea.

Methods: We collected patient data from January 1, 2004 to December 31, 2015 from the National Health Insurance Service Health Screening Cohort. Patients with OPLL were defined as patients with the International Classification of Diseases, Tenth Revision code M48.8 (other specified spondylopathies) and were newly diagnosed through computed tomography imaging. The OPLL group had a total of 1,289 patients. The control group included 6,445 people. Utilizing the Kaplan-Meier technique, The incidence of AMI in both groups was estimated. A Cox proportional-hazards regression analysis was used to compute the AMI hazard ratio.

Results: After controlling for age and sex, the hazard ratio of AMI in the OPLL group was 2.065 (95% confidence interval [CI], 1.228–3.474). The adjusted hazard ratio in the OPLL group was 2.209 after restricting the sample for demographics and concomitant medical conditions (95% CI, 1.311–3.721). In a subgroup analysis, the incidence of AMI was substantially greater in the OPLL group, which included women younger than 65 years and without hypertension, diabetes, or dyslipidemia.

Conclusion: This nationwide longitudinal study found that patients with OPLL were at higher risk of AMI.

Keywords: Epidemiology; Longitudinal ligaments; Myocardial Infarction; Population; Risk factors

INTRODUCTION

Ossification of the posterior longitudinal ligament (OPLL) is a rare pathologic process of lamellar bone deposition that can result in spinal cord compression[2]. The prevalence of OPLL has been estimated to be 0.6% to 4.6% in South Korea[14,16,29]. OPLL is a multifactorial disease caused by genetic and environmental factors[20], but the pathogenesis remains poorly understood. OPLL is often found on multiple levels rather than on a single level, and in many cases, it occurs together with ossification of the anterior longitudinal ligament, ossification of the ligamentum flavum[30], or diffuse idiopathic skeletal hyperostosis (DISH)[28]. Therefore, it may be considered as part of a systemic disease rather than a disease of a single lesion[27].

In previous studies, the incidence of acute myocardial infarction (AMI) was higher in patients with acute infections[17,26], and another study found that patients with pyogenic spondylitis had a higher risk of developing AMI[13]. We considered the possibility of a relationship between AMI and other spinal diseases, and OPLL was selected as the target.

Given the paucity of studies demonstrating an association between OPLL and AMI, we conducted a national longitudinal study to investigate whether there were significant changes in the incidence of AMI in patients with OPLL.

MATERIALS AND METHODS

1. Data Source

We conducted the study based on data from the National Health Insurance Service-Health Screening Cohort (NHIS-HEALS) between 2004 and 2015. South Korea provides a single-payer health insurance system supervised and managed by the NHIS. The NHIS conducts health examinations every 2 years for citizens aged 40 and older and annually for non-office workers. The NHIS collects data on sociodemographic parameters (age, sex, average insurance premium, residential area, and presence of disability), clinical information (comorbidities, number of outpatient visits, and hospitalization records), and the results from a national health screening program. This collected information is stored in the National Health Information Database (NHID)[10,24], and the data is accessible to the public for research purposes.

The study protocol conformed to the ethical guidelines of the World Medical Association Declaration of Helsinki and was approved by the Institutional Review Board of our study (IRB No. 2020-01-011).

2. Study Design and Establishment

This sex-/age-matched cohort study aimed to determine the potential risk of AMI in individuals with OPLL. The study population included an OPLL group and a control group. For the OPLL group, patients corresponding to the International Classification of Diseases, Tenth Revision (ICD-10) codes 'M48.8' and 'M48.80' to 'M48.83' and those newly diagnosed by computed tomography were selected. The NHIS-HEALS cohort population consisted of the total number of patients enrolled between January 1, 2002, and December 31, 2003, which was 514,557; This accounts for about 10% of Koreans over 40 who underwent national examinations during this period. The selected population was followed up for 12 years from January 2004 to December 2015.

From the NHIS-HEALS cohort population of 514,557 individuals, we screened 3,405 individuals corresponding to ICD-10 codes 'M48.8' and 'M48.80' to 'M48.83'. Excluding 1,977 patients who had not undergone CT imaging, 1,428 patients diagnosed with OPLL according to a CT scan were selected. After excluding 139 patients diagnosed with OPLL before January 1, 2004, 1,289 patients were finally selected for the study (Fig. 1). Through 1:5 age- and sex-stratified matching (without replacement) using a greedy-matching algorithm with the R package 'MatchIT' software, 6,445 individuals were chosen as controls[7,8].

The criteria for the selection of the patients with AMI are as follows: (1) ICD-10 codes (I21, I22); (2) brain CT or MRI; and (3) hospitalization, as used in the previous studies[15,22,23]. The NHIS-HEALS database was used to obtain information about underlying comorbidities, such as hypertension, diabetes, and dyslipidemia. Patients in this study were followed from the first episode of AMI until death or the end of the follow-up period.

3. Statistical Analysis

Mean differences in demographic variables between the OPLL and control groups were investigated using the χ^2 and Student's *t*-test. The Kaplan-Meier technique was used to evaluate the survival rate without AMI in both groups. The differences in the rates of surviving disease-free between the groups were compared using the Wilcoxon's log-rank test.

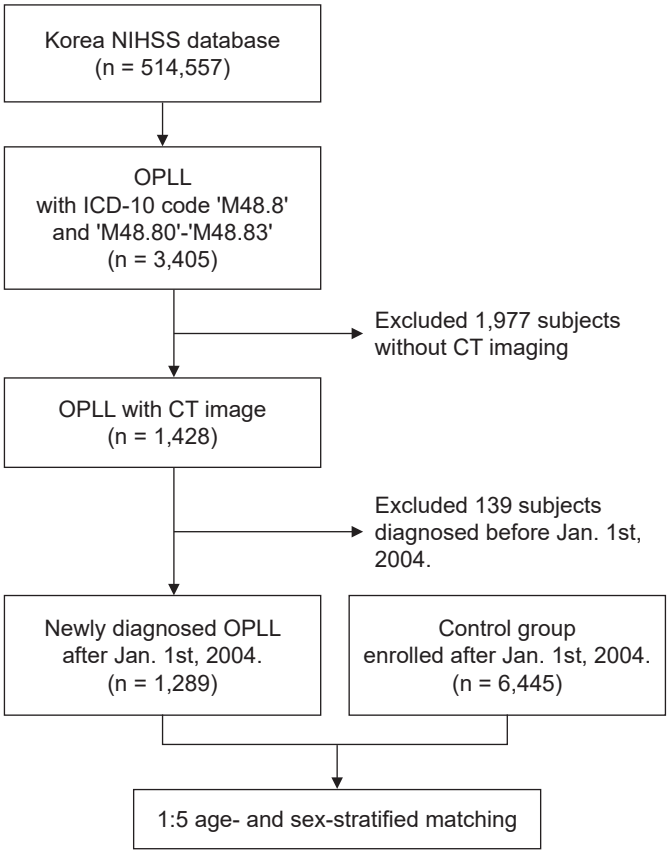

Fig. 1. A flow diagram depicting the cohort formation process. The National Health Insurance Service-Health Screening Cohort (NHIS-HEALS) was used in this 12-year longitudinal cohort study. NIHSS: the National Institutes of Health Stroke Scale; OPLL: ossification of the posterior longitudinal ligament; ICD-10: International Classification of Diseases, Tenth Revision; CT: computed tomography.

Multivariate studies employing a Cox proportional hazard regression model were used to evaluate the impact of OPLL on the subsequent occurrence of each event. Two Cox proportional hazards regression models were employed; Model 1 was adjusted for age and sex, and Model 2 was adjusted for the lowest quintile of income, age, sex, and accompanying comorbidities. Subgroup analyses were also performed using Cox proportional hazards regression models to estimate the effects of OPLL on the risk of each event. Data analysis was performed using R software (version 3.3.3; The R Foundation for Statistical Computing, Vienna, Austria).

Table 1. Characteristics of the OPLL and control groups

Variables	OPLL (n = 1,289)	Control (n = 6,445)	p-value
Sex (male)	623 (48.33%)	3,115 (48.33%)	
Age	57.4 ± 9.65	57.4 ± 9.65	
Age ≥ 65	339 (26.30%)	1.695 (26.30%)	
Low income	314 (24.36%)	1,687 (26.18%)	0.186
Diabetes	127 (9.85%)	841 (13.05%)	0.002
Hypertension	470 (36.46%)	2,691 (41.75%)	<0.001
Dyslipidemia	187 (14.51%)	1,122 (17.41%)	0.013

The data is presented as number (%) or mean ± standard deviation.
OPLL: ossification of the posterior longitudinal ligament.

RESULTS

1. Characteristics of the OPLL and Control Groups

During the study period, 1,289 patients were newly diagnosed with OPLL. Males accounted for 48.33%. The average age was 57.4±9.65 years, and the population aged 65 years or older accounted for 26.30%. Among the patients with OPLL, 314 (24.36%) were in the low-income quintile. In addition, 127 (9.85%), 470 (36.46%), and 187 (14.51%) patients had comorbidities such as diabetes, hypertension, and dyslipidemia, respectively (Table 1).

2. AMI in the OPLL and Control Groups

The OPLL group had a significantly higher incidence of AMI than the control group (p<0.01). The Kaplan-Meier curve of the cumulative incidence of AMI indicated that the risk of developing AMI was higher in the OPLL group than in the control group (Fig. 2). In multivariate analyses using the Cox proportional hazards regression model, the risks of AMI was higher in the OPLL group compared to the control group; The hazard ratio of AMI in the OPLL group was 2.065 (95% confidence interval [CI], 1.228–3.474) in Model 1, while it was 2.209 (95% CI, 1.311–3.721) in Model 2 (Table 2).

3. Subgroup Analysis of AMI Incidence Rate

When analyzing the subgroups of the OPLL group and the control group, the incidence rate of AMI was substantially higher in females in both the OPLL group and the control group (95% CI, 1.620–7.317; Table 3). The incidence rate of AMI showed a significant increase in both the OPLL group and the control in the under-age-65 subgroup (95% CI, 1.486–5.252; Table 3), the non-diabetic subgroup (95% CI, 1.116–3.639; Table 3), the non-hypertensive subgroup (95%

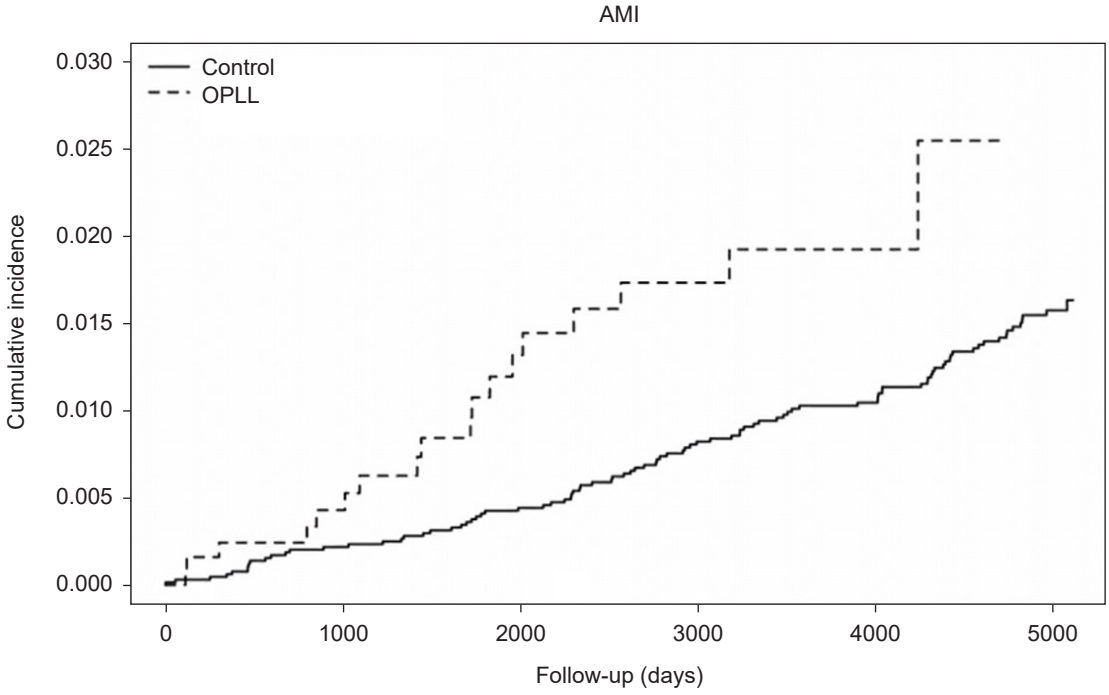

Fig. 2. The cumulative incidence rates of acute myocardial infarction (AMI) in the ossification of the posterior longitudinal ligament (OPLL) and control groups were compared. The Kaplan-Meier curves for increasing AMI risk were contrasted between the OPLL and control groups.

Table 2. Adjusted hazard ratio for AMI in the OPLL and control groups

Group	n	Event	Duration (days)	Duration (years)	Incidence rate (%)	HR (95% CI)	
						Model 1*	Model 2†
AMI							
Control	6,445	92	29,585,869	81,057.175	1.135	1	1
OPLL	1,289	18	3,215,056	8,808.373	2.044	2.065 (1.228, 3.474)	2.209 (1.311, 3.721)

P-values were 0.006 and 0.003 for model 1 and model 2, respectively.
AMI: acute myocardial infarction; OPLL: ossification of the posterior longitudinal ligament; HR: hazard ratio; CI: confidence interval.
*Model 1: adjusted for age and sex.
†Model 2: adjusted for age, sex, income, diabetes, hypertension, and dyslipidemia.

CI, 1.089–4.523; Table 3), and the non-dyslipidemia subgroup (95% CI, 1.556-4.583; Table 3).

DISCUSSION

Our findings show a higher incidence of AMI in patients with OPLL. This was a significant result in several models that were adjusted considering not only sex and age but also the patient's economic status and comorbidities, in this case hypertension, diabetes, and dyslipidemia; The hazard ratio of AMI occurrence was 2.065 in model 1 and 2.209 in model 2 (Table 2).

There are no known studies of the association between OPLL and AMI, and there is no definitively established theory of the pathophysiology of OPLL. In addition, given that OPLL is known to be an idiopathic or multifactorial disease determined by environmental factors, it is difficult to identify a clear pathological cause. However, relatively recent human leukocyte antigen haplotype analyses and genetic studies have revealed that several genetic loci affect OPLL susceptibility[12,18,19,33]. Genes for collagen, nucleotide pyrophosphatase, transforming growth factors (TGF), and the vitamin

Table 3. Subgroup analyses between the OPLL and control groups

Variables	OPLL		Control		HR (95% CI)
	n	Incidence rate (%)	n	Incidence rate (%)	
Sex					
Male	8	20.412	66	1.752	1.460 (0.688, 3.096)
Female	10	2.049	26	0.599	**3.443 (1.620, 7.317)**
Age					
<65	13	2.036	53	0.868	**2.793 (1.486, 5.252)**
≥65	5	2.062	39	1.953	1.175 (0.456, 3.025)
Diabetes					
N	14	1.755	70	0.990	**2.015 (1.116, 3.639)**
Y	4	4.807	22	2.130	2.733 (0.913, 8.186)
Hypertension					
N	10	1.783	43	0.899	**2.219 (1.089, 4.523)**
Y	8	2.500	49	1.474	1.992 (0.926, 4.286)
Dyslipidemia					
vN	18	2.392	65	0.973	**2.671 (1.556, 4.583)**
Y	0	0.000	27	1.891	-

OPLL: ossification of the posterior longitudinal ligament; HR: hazard ratio; CI: confidence interval.

D receptor have all been implicated[31], and mutations in collagen genes and the TGF-β superfamily genes have been proposed as genetic markers for OPLL[9,11,12,33]. Myocardial infarction is associated with the induction of several members of the superfamily, including TGF-β1, TGF-β2, TGF-β3, bone morphogenetic protein (BMP)-2, BMP-4, BMP-10, growth differentiation factor (GDF)-8, GDF-11 and activin A[5,6]. In addition, the TGF-β superfamily is involved in the regulation of cardiac fibrosis after cardiac fibrosis following myocardial infarction, and researchers are examining myocardial infarction treatments using this signaling pathway[3,4,34]. Bai et al.[1] induced myocardial infarction in rats by inhibiting the TGF-β1 gene through RNA manipulation. Therefore, if studies of OPLL and various genes (especially the TGF-β superfamily) are conducted, similarities with AMI may be found based on genetics.

According to subgroup analyses, the association between OPLL and AMI was more likely in women younger than 65 without hypertension, diabetes, or dyslipidemia (Table 3). Hypertension and diabetes are widely recognized as strong risk factors for AMI and are also risk factors for OPLL. Shin et al.[25] found through a nationwide population-based case-control study that hypertension, diabetes, ischemic stroke, hypothyroidism, and osteoporosis were risk factors for OPLL. Oshima et al.[21] showed that carotid arteriosclerosis is a risk factor for OPLL. Therefore, the risks of both OPLL and AMI may be increased in patients with underlying diseases. This suggests that the association between OPLL and AMI can be maximized in patients without underlying diseases such as hypertension, diabetes, and dyslipidemia, which is consistent with the subgroup analyses in this study.

The limitations of this study, which we considered, include the following. First, The severity and trend of the diseases were not considered in this study. Clinically, AMI is diagnosed with elevated cardiac enzyme, new electrocardiographic change, symptoms of ischemia, and angiographic evidence of thrombus. Given the inability to access individual patient's data in the NHIS database, many researchers including cardiologists used "ICD code (I21, I22) and hospitalization ≥1" as the definition of AMI in South Korea. In addition, initially, our study plan included studying the change in association according to affected areas and the number of levels of involvement, but this was not possible due to data access limitations. Second, as is widely known, the causes of AMI are various, such as carotid artery occlusive disease, arrhythmia, and embolism. In the data we collected, none of these comorbidities were utilized, and heterogeneous patient populations could have negatively affected our results. Third, when explaining the association between OPLL and AMI in the genetic background, non-atherosclerotic AMI was not considered. Atherosclerosis has the most important pathological role of AMI, but non-atherosclerotic processes

are also contributors to AMI[32]. In this study, there were limitations in distinguishing the pathogenesis of AMI. This may have negatively impacted study results when comparing associations from a genetic perspective.

Despite some limitations, this nationwide cohort study is the first to demonstrate a higher incidence of AMI in patients with OPLL. This study suggests the potential contribution of OPLL to the incidence of AMI.

CONCLUSION

Our nationwide longitudinal cohort analysis shows that patients with OPLL have an elevated risk of AMI.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

ACKNOWLEDGEMENTS

This work was supported by Basic Science Research Program through the National Research Foundation of Korea (NRF) funded by the Ministry of Education (NRF-2020R1I1A1A01072258). This work was also supported by a grant of Basic Science Research Program through the NRF funded by the Ministry of Science, ICT and future Planning (NRF-2020R1F1A1069875).

REFERENCES

1. Bai M, Pan CL, Jiang GX, Zhang YM: CircRNA 010567 improves myocardial infarction rats through inhibiting TGF-β1. Eur Rev Med Pharmacol Sci 24:369–375, 2020
2. Boody BS, Lendner M, Vaccaro AR: Ossification of the posterior longitudinal ligament in the cervical spine: a review. Int Orthop 43:797–805, 2019
3. Cheng X, Wang L, Wen X, Gao L, Li G, Chang G, et al.: TNAP is a novel regulator of cardiac fibrosis after myocardial infarction by mediating TGF-β/Smads and ERK1/2 signaling pathways. EBioMedicine 67:103370, 2021
4. Gao L, Wang LY, Liu ZQ, Jiang D, Wu SY, Guo YQ, et al.: TNAP inhibition attenuates cardiac fibrosis induced by myocardial infarction through deactivating TGF-β1/Smads and activating P53 signaling pathways. Cell Death Dis 11:44, 2020
5. Gordon KJ, Blobe GC: Role of transforming growth factor-beta superfamily signaling pathways in human disease. Biochim Biophys Acta 1782:197–228, 2008
6. Hanna A, Frangogiannis NG: The Role of the TGF-β Superfamily in Myocardial Infarction. Front Cardiovasc Med 6:140, 2019
7. Ho D, Imai K, King G, Stuart EA: MatchIt: Nonparametric preprocessing for parametric causal inference. J Stat Softw 42:1–28, 2011
8. Ho DE, Imai K, King G, Stuart EA: Matching as nonparametric preprocessing for reducing model dependence in parametric causal inference. Polit Anal 15:199–236, 2007
9. Inamasu J, Guiot BH, Sachs DC: Ossification of the posterior longitudinal ligament: an update on its biology, epidemiology, and natural history. Neurosurgery 58:1027–1039, 2006
10. Kang SH, Choi EK, Han KD, Lee SR, Lim WH, Cha MJ, et al.: Underweight is a risk factor for atrial fibrillation: A nationwide population-based study. Int J Cardiol 215:449–456, 2016
11. Kawaguchi H, Kurokawa T, Hoshino Y, Kawahara H, Ogata E, Matsumoto T: Immunohistochemical demonstration of bone morphogenetic protein-2 and transforming growth factor-beta in the ossification of the posterior longitudinal ligament of the cervical spine. Spine (Phila Pa 1976) 17:S33–S36, 1992
12. Kawaguchi Y, Furushima K, Sugimori K, Inoue I, Kimura T: Association between polymorphism of the transforming growth factor-beta1 gene with the radiologic characteristic and ossification of the posterior longitudinal ligament. Spine (Phila Pa 1976) 28:1424–1426, 2003
13. Kim SB, Kim H, Kim J, Kim WY, Hong JB, Lee JK, et al.: The association of acute myocardial infarction with pyogenic spondylitis in Korea: A nationwide longitudinal cohort study. Nerve 8:71–76, 2022
14. Kim TJ, Bae KW, Uhm WS, Kim TH, Joo KB, Jun JB: Prevalence of ossification of the posterior longitudinal ligament of the cervical spine. Joint Bone Spine 75:471–474, 2008
15. Lee JK, Kim H, Hong JB, Sheen SH, Han IB, Sohn S: Association of acute myocardial infarction with seropositive rheumatoid arthritis in Korea: A nationwide longitudinal cohort study. J Clin Neurosci 78:97–101, 2020
16. Moon BJ, Choi SK, Shin DA, Yi S, Kim KN, Yoon DH, et al.: Prevalence, incidence, comorbidity, and mortality rates of ossification of posterior longitudinal ligament in the cervical spine: A nested case-control cohort study. World Neurosurg 117:e323–e328, 2018
17. Musher DM, Abers MS, Corrales-Medina VF: Acute infection and myocardial infarction. N Engl J Med 380:171–176, 2019

18. Nakajima H, Watanabe S, Honjoh K, Okawa A, Matsumoto M, Matsumine A: Expression analysis of susceptibility genes for ossification of the posterior longitudinal ligament of the cervical spine in human OPLL-related tissues and a spinal hyperostotic mouse (ttw/ttw). Spine (Phila Pa 1976) 45:E1460–E1468, 2020
19. Nakajima M, Takahashi A, Tsuji T, Karasugi T, Baba H, Uchida K, et al.: A genome-wide association study identifies susceptibility loci for ossification of the posterior longitudinal ligament of the spine. Nat Genet 46:1012–1016, 2014
20. Nam DC, Lee HJ, Lee CJ, Hwang SC: Molecular pathophysiology of ossification of the posterior longitudinal ligament (OPLL). Biomol Ther (Seoul) 27:342–348, 2019
21. Oshima Y, Doi T, Kato S, Taniguchi Y, Matsubayashi Y, Nakajima K, et al.: Association between ossification of the longitudinal ligament of the cervical spine and arteriosclerosis in the carotid artery. Sci Rep 10:3369, 2020
22. Park CJ, Choi YJ, Kim JG, Han IB, Do Han K, Choi JM, et al.: Association of acute myocardial infarction with ankylosing spondylitis: A nationwide longitudinal cohort study. J Clin Neurosci 56:34–37, 2018
23. Park CS, Choi EK, Han KD, Lee HJ, Rhee TM, Lee SR, et al.: Association between adult height, myocardial infarction, heart failure, stroke and death: a Korean nationwide population-based study. Int J Epidemiol 47:289–298, 2018
24. Seong SC, Kim YY, Park SK, Khang YH, Kim HC, Park JH, et al.: Cohort profile: the national health insurance service-national health screening cohort (NHIS-HEALS) in Korea. BMJ Open 7:e016640. 2017
25. Shin J, Choi JY, Kim YW, Chang JS, Yoon SY: Quantification of risk factors for cervical ossification of the posterior longitudinal ligament in Korean populations: A nationwide population-based case-control study. Spine (Phila Pa 1976) 44:E957–E964, 2019
26. Smeeth L, Thomas SL, Hall AJ, Hubbard R, Farrington P, Vallance P: Risk of myocardial infarction and stroke after acute infection or vaccination. N Engl J Med 351:2611–2618, 2004
27. Sohn S, Chung CK: Increased bone mineral density and decreased prevalence of osteoporosis in cervical ossification of the posterior longitudinal ligament: a case-control study. Calcif Tissue Int 92:28–34, 2013
28. Sohn S, Chung CK, Han I, Park SB, Kim H: Increased bone mineral density in cervical or thoracic diffuse idiopathic skeletal hyperostosis (DISH): A case-control study. J Clin Densitom 21:68–74, 2018
29. Sohn S, Chung CK, Yun TJ, Sohn CH: Epidemiological survey of ossification of the posterior longitudinal ligament in an adult Korean population: three-dimensional computed tomographic observation of 3,240 cases. Calcif Tissue Int 94:613–620, 2014
30. Sohn S, Yoon JW, Chung CK: Increased bone mineral density in patients with ossification of the ligamentum flavum: a case-control study. J Clin Densitom 17:195–199, 2014
31. Stetler WR, La Marca F, Park P: The genetics of ossification of the posterior longitudinal ligament. Neurosurg Focus 30:E7, 2011
32. Waterbury TM, Tarantini G, Vogel B, Mehran R, Gersh BJ, Gulati R: Non-atherosclerotic causes of acute coronary syndromes. Nat Rev Cardiol 17:229–241, 2020
33. Yan L, Gao R, Liu Y, He B, Lv S, Hao D: The pathogenesis of ossification of the posterior longitudinal ligament. Aging Dis 8:570–582, 2017
34. Zhang Q, Wang L, Wang S, Cheng H, Xu L, Pei G, et al.: Signaling pathways and targeted therapy for myocardial infarction. Signal Transduct Target Ther 7:78, 2022

The Nerve

Case Report

The Nerve 2023;9(1):34-39
https://doi.org/10.21129/nerve.2022.00192
eISSN 2465-891X

Atypical Heterotopic Bone Formation Rear to the Functioning Cervical Artificial Disc Prosthesis Causing Cervical Spondylotic Myelopathy

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OPEN ACCESS

Received: September 6, 2022
Revised: October 21, 2022
Accepted: October 31, 2022

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Although heterotopic ossification (HO) might occur in a substantial proportion of cervical disc arthroplasty-switched spinal segments, it is predominantly discovered at the anterior vertebral edges of the treated interspace. Herein, we present the case of a 63-year-old woman who presented with clinical signs of myelopathy almost 5 years after the implantation of a Mobi-C disc prosthesis for C6-7 soft disc herniation. As shown by magnetic resonance imaging and computed tomography, spinal cord compression and a consequent signal change inside the cord were attributed to bony spurs from HO posterior to the still-moving prosthesis. Initial full posterior decompression through C6-7 bilateral laminectomy added to posterior stabilization almost fully relieved the patient's functional and sensory changes from myelopathy. However, the device, as well as the ectopic bone deposits, had to be removed, and switching to anterior arthrodesis was necessary due to the imminent aggravation and progression of cervical kyphotic curvature from the still-functioning device. To the authors' knowledge, such extensive bone accumulation posterior to a functional Mobi-C cervical prosthesis causing myelopathy has not yet been reported in the literature. Conversion to solid fusion would be preferred to posterior decompression for the sake of maintaining cervical curvature.

Keywords: Arthroplasty; Cervical vertebrae; Ossification, heterotopic

INTRODUCTION

Cervical disc arthroplasty (CDA) is a viable and effective treatment of cervical degenerative disc diseases and has been proposed as an alternative to the conventional anterior cervical discectomy and fusion. The formation of heterotopic ossification (HO) is considered one of the major complications after CDA, which, in the setting of CDA, specifically refers to the undesirable ectopic osteogenesis anterior, posterior, or lateral to the implant and subsequently plays a contradictory role against the fundamental goal of CDA by impeding the range of motion (ROM) of the implanted devices[2].

While the majority of studies have focused on the identifications of etiology, risk factors of HO as well as their feasible prevention measures, the question that might be a crucial

concern to all surgeons is whether the presence of HO would pose a significant impact on the clinical outcomes has not been properly addressed currently. Moreover, scarce reference could be searched among the past published literatures reporting the accumulation of this HO rear to the previously inserted, moving implant and consequently incurring an unexpected cervical spondylotic myelopathy (CSM)[16]. This case report describes a patient presented with clinical signs of cervical myelopathy caused by the atypical HO rear to the still functioning cervical artificial disc implant.

CASE REPORT

This 63-year-old female presented with the clinical signs of myelopathy almost 5 years after the initial implantation of a Mobi-C disc prosthesis (Zimmer Biomet, Warsaw, IN, USA) at the C6-7 level due to the left side upper extremity radiculopathy affected with both spinal canal and foraminal stenosis from a local hospital (Fig. 1). Started from approximately a month prior to the referral, an intractable, lancinating pain combined with electricity like paresthesia, especially at the region of the left elbow as well as both palm and fingertips hindered her from the indoor activity at the kitchen, which later rapidly prevailed to refrain her from the outdoor activity due to gait disturbance by paraparesis progression. She showed the dominant radiculopathy and paresthesia at the left C6 and C7 dermatome exaggerated response of both the biceps and triceps brachial reflex, and grade 4 weakness of both lower extremities. The new magnetic resonance imaging on admission surprisingly demonstrated another severe spinal cord compression and consequent swelling and signal change inside the cord at the previously addressed level of C6-7, which was attributed to the bony spurs collections rear to the Mobi-C disc prosthesis as manifested on the concomitant computed tomography scan (Fig. 2).

1. Initial Surgery and Its Consequence

In order to fully decompress the affected spinal cord as well as to offer initial stabilization to the still functioning prosthesis, a posterior full decompressive laminectomy added with C6 lateral mass and C7 pedicle screw fixation was performed. This was originally schemed to avoid any untoward complication occurring during the revision approach or manipulation to resect off the HO that might stick to the ventral aspect of the dura. Upon gentle retraction of the lateral margin of the dura at the axillar portion of the exiting C7 root, the surgeon could directly encounter the expected aberrant, discolored but protruded bony spur mass ventrally affecting the cervical spinal cord (Fig. 3). Dorsal cortical bone over the left side C6 lateral mass had breakage violation during the screw insertion due to simple technical error, which eventually obliged the surgeon to shift the fixation level to the cranial level of C5, unfortunately (Fig. 4A).

Fortunately, the patient showed prompt recovery from her original neurological defect upon initial procedure, with a trace of neuropathic component remnant at the distal part of the upper limb such as fingertip.

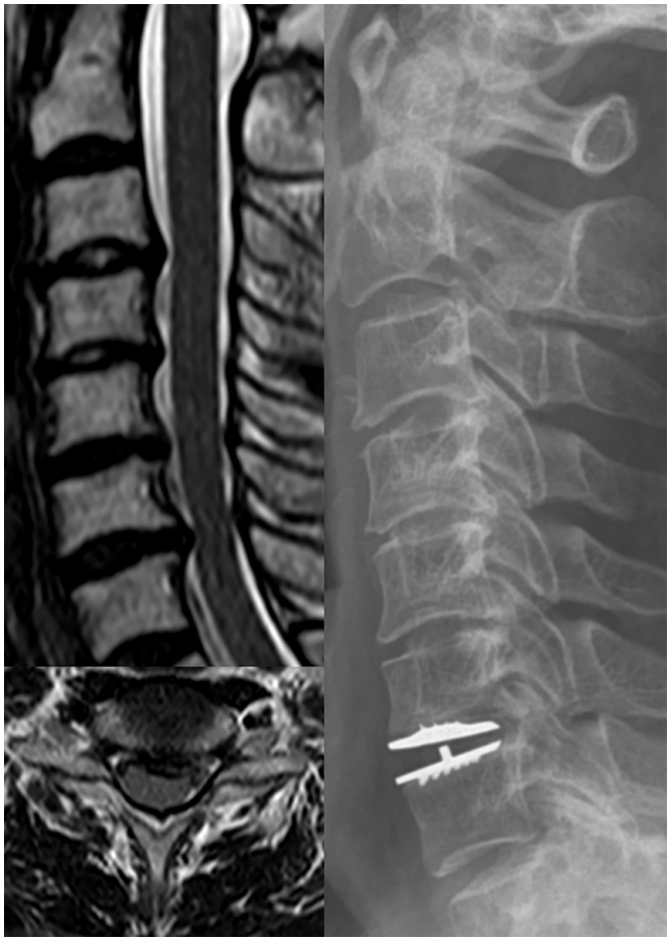

Fig. 1. T2-weighted sagittal (left upper) and axial (left lower) images from magnetic resonance imaging performed before the initial operation 5 years ago show cervical spondylotic stenosis at C6-7. A postoperative lateral-view radiograph (right) shows a Mobi-C artificial disc placed at the corresponding cervical level.

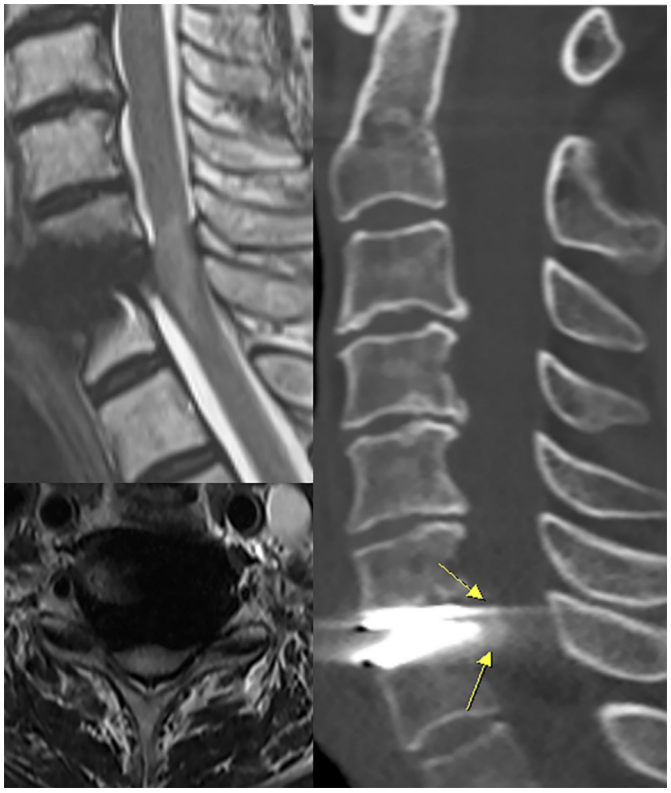

Fig. 2. T2-weighted sagittal (left upper) and axial (left lower) images from magnetic resonance imaging demonstrate severe spinal cord swelling as well as intramedullary high-signal edematous changes corresponding to the previously addressed level of C6-7. A concomitant computed tomography sagittal-view scan (right) reveals a collection of bony spurs rear to the Mobi-C disc prosthesis (arrow).

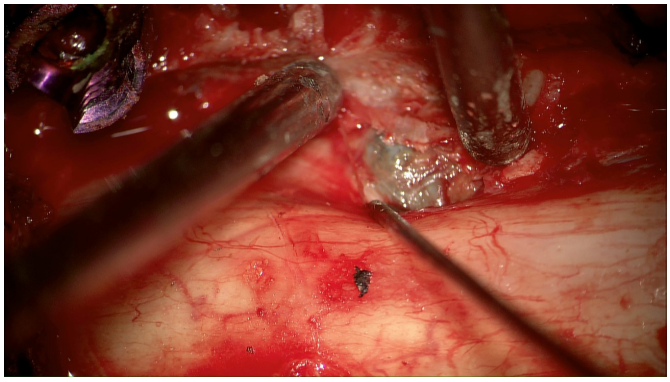

Fig. 3. Intraoperative findings during the initial posterior decompression and fixation procedure. A protruding, dark, discolored, friable bony spur mass impinged the cervical spinal cord ventrally.

2. Second Surgical Procedure and Postoperative Course

The patient managed to be in fair condition, clinically and radiologically, up to two months after the initial procedure till she started to appeal the involuntarily, 'forwardly tilted neck' condition on the second visit to the outpatient office. The additional radiograph on lateral posture featured the well-maintained posterior fixation constructs while a concomitantly veered, exaggeratedly flexed but not dislocated moving core inside the Mobi-C artificial disc even during the neutral standing posture with the sagittal vertical axis distance exceeding more than 28 mm (Fig. 4B). Due to the constant discomfort caused by elongated, curved neck posture with subsequent incapability to maintain the proper horizontal gaze, she asked for another surgical corrective measure to overcome this unexpected, deformed status of twice treated neck. The flexed but still functioning prosthesis, as well as the ectopic bone deposited rear to the device for the sake of additional direct decompression of the spinal cord, had to be removed and switched to a firm anterior fusion arthrodesis to provide an immediate correction to the cervical kyphotic curvature change (Fig. 4C).

She also managed to recover fairly even after this second revision surgery and was discharged a few days later leaving a specific expression that describes her condition; she can now 'look up' her family without the necessity of rigid external orthosis.

DISCUSSION

HO is defined as the formation of bone outside the skeletal system. It is a well-known phenomenon that might disable patients in total hip or knee joint replacement[5,8], but it has also been repeatedly detected in spinal patients after the wide acceptance of CDA. Intraoperative measures to deter the delayed HO development after cervical artificial disc implantation involve a gentle surgical technique, avoidance of muscle trauma, and repetitive rinsing of the surgical field[14]. Selection of the largest possible caliber for the contacting plate part of the CDA device that might be capable to cover the majority of the surface area for the opened endplates (adequacy of the endplate coverage) could also play a deterrent role against this HO progression by minimizing the unnoticeable discharges from the both above and below vertebral body components[11-13]. Despite all these efforts, the meta-analysis pooled data from the Kong present the 53.6%

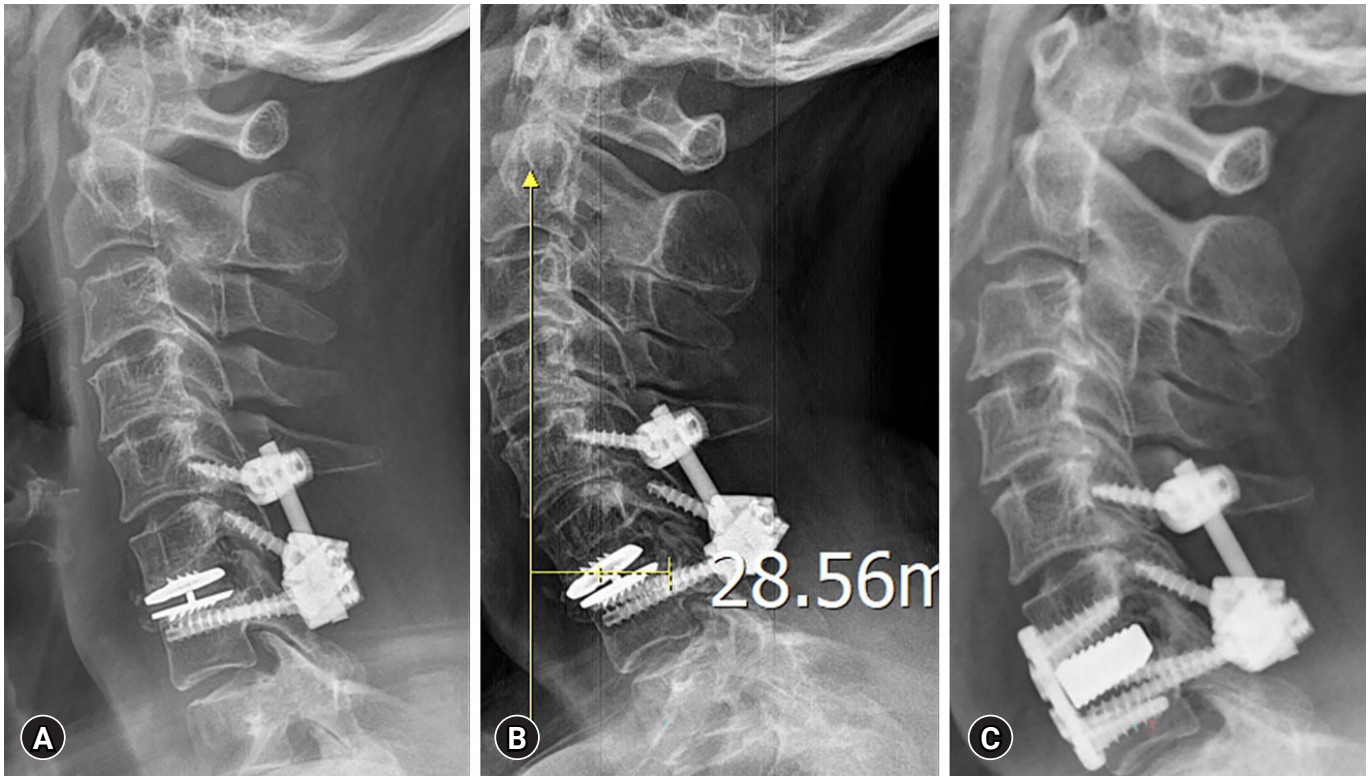

Fig. 4. An immediate postoperative radiograph after the initial posterior decompression and fixation procedure (A). Due to the dorsal cortical bone manipulative violation during the screw insertion over the left side of the C6 lateral mass, the surgeon was obliged to shift the fixation level to the cranial level. The progression of kyphotic cervical alignment propagating from the flexed conformation of the Mobi-C device was manifested prominently on a lateral radiograph from follow-up a couple of months after initial surgery. The sagittal vertical axis distance exceeded 28 mm (B). A plain lateral-view after the secondary conversion to solid anterior cervical fusion with full removal of the causative mobile device revealed an immediate correction of the cervical kyphotic curvature (C).

and 47.5% prevalence of HO and severe HO respectively within 5 to 10 years after CDA with its positive correlation with the length of follow-up period[6].

Although the HO might occur in a substantial proportion of CDA switched spinal segments, but does not appear to lead to a decline in clinical outcomes. Its incidence, progression, clinical Implications, and risk factors based on the long-term outcomes up to seven years have been reported after the usage of Mobi-C device and the trial results have been consistent with the continued non-inferiority of CDA for clinical outcomes and lower cumulative reoperation rates despite up to 26.6% of its incidence[3,7]. Solid bridging of spurs usually remains asymptomatic and is predominantly discovered at the anterior vertebral edges of the treated interspace merely through routine follow-up radiological examinations[1,7,13,15]. Some studies demonstrated that the changes in biomechanical factors were associated with the prevalence and/or severity of HO; however, a causal relationship between these factors remains unproven. Hu et al.[4] have iterated that a more than 5° increase in immediate post-operative disc space angle and less segmental ROM have conferred a negative effect on HO formation. Meanwhile, Shen et al.[10] have previously concluded that endplate coverage of less than 93.8% or intervertebral height change of more than 1.8 mm would exacerbate the non-uniform distribution of stress in the bone-implant interface and promote posterior HO development after cervical disc replacement. Further investigations are warranted to corroborate these risk factors, including multilevel calcified disc herniation, severe spondylosis, and suboptimal placement of the device during primary cervical disc replacement surgery.

Consequently, this unprecedented HO collection rear

to the device as well as into the spinal canal eventually incurring the clinical CSM neurologic feature might not have been discovered or anticipated neither by the surgeon or patient herself, although she has been followed up with regular functional radiographs after initial procedure. The authors might suggest the conventional hypothesis that permanent micro stress between the bony endplate and the device, which might have originated from the non-physiologic prosthesis motion, might have promoted osseous spur formation and its enlargement[2]. Probably an untoward synergy between the non-physiological motions created from the ventrally placed prosthesis with relatively smaller caliber along with the presumably insufficiently resected, remnant dorsal osteophytes might have triggered this appositional bone growth over the residual osteophytes, whose growths are well informed to be promoted by the untoward segmental motion. But there could be no clear elucidation regarding its isolated collection rear to the initial implant, sparing the preferential ventral aspect of the addressed cervical level. Moreover, this presumably consolidated, functionally deprived prosthesis after the secondary posterior fixation surgery was not fully immobilized, retaining its inherent mobility to be flexed. This post-surgical phenomenon suggests the lack of capability for both the posteriorly sealed HO as well as posterior stand-alone fixation to provide firm stability over the functionally deprived cervical motion segment after the untoward artificial disc insertion. As iterated above, a conversion to the solid anterior fusion after full removal of the causative mobile device as well as the ectopic bone deposits would be the preferred revision measure over the simple posterior decompression and fixation for the sake of cervical curvature maintenance.

Recently, there has been data emerging to suggest that the formation of HO might be affected by an increased preoperative signal intensity in the spinal cord, postoperative ROM at the surgical level, and the prosthesis vertebral ratio[9].

However, it should be noted that, despite these hypotheses, there has been a paucity of consistent evidence. Larger scale investigations are needed to further corroborate the risk factors on the genesis of HO, especially for those lobulated rear to the implant causing CSM as in our case, after CDA.

CONCLUSION

To the author's knowledge, such extensive bone accumulation posterior to a functional Mobi-C cervical prosthesis causing myelopathy has not yet been reported in the literature. Conversion to a solid anterior fusion after full removal of the causative device as well as the ectopic bone deposits would be preferred to simple posterior decompression for the sake of cervical curvature maintenance.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Aghayev E, Bärlocher C, Sgier F, Hasdemir M, Steinsiepe KF, Wernli F, et al.: Five-year results of cervical disc prostheses in the SWISSspine registry. Eur Spine J 22:1723–1730, 2013
2. Chang PY, Wu JC, Mayo BC, Massel DH, Wang MY: Heterotopic ossification in cervical disc arthroplasty. Contemp Spine Surg 18:1–5, 2017
3. Davis RJ, Nunley PD, Kim KD, Hisey MS, Jackson RJ, Bae HW, et al.: Two-level total disc replacement with Mobi-C cervical artificial disc versus anterior discectomy and fusion: a prospective, randomized, controlled multicenter clinical trial with 4-year follow-up results. J Neurosurg Spine 22:15–25, 2015
4. Hu L, Zhang J, Liu H, Meng Y, Yang Y, Li G, et al.: Heterotopic ossification is related to change in disc space angle after Prestige-LP cervical disc arthroplasty. Eur Spine J 28:2359–2370, 2019
5. Iorio R, Healy WL: Heterotopic ossification after hip and knee arthroplasty: risk factors, prevention, and treatment. J Am Acad Orthop Surg 10:409–416, 2002
6. Kong L, Ma Q, Meng F, Cao J, Yu K, Shen Y: The prevalence of heterotopic ossification among patients after cervical artificial disc replacement: A systematic review and meta-analysis. Medicine (Baltimore) 96:e7163, 2017
7. Nunley PD, Cavanaugh DA, Kerr EJ, Utter PA, Campbell PG, Frank KA, et al.: Heterotopic ossification after cervical total disc replacement at 7 years-prevalence, progression, clinical implications, and risk factors. Int J Spine Surg 12:352–361, 2018
8. Pohl F, Seufert J, Tauscher A, Lehmann H, Springorum HW, Flentje M, et al.: The influence of heterotopic ossification on functional status of hip joint following total hip arthroplasty. Strahlenther Onkol 181:529–533, 2005
9. Qi M, Chen H, Cao P, Tian Y, Yuan W: Incidence and risk factors

analysis of heterotopic ossification after cervical disc replacement. Chin Med J (Engl) 127:3871–3875, 2014
10. Shen YW, Yang Y, Liu H, Rong X, Ding C, Meng Y, et al.: Effects of endplate coverage and intervertebral height change on heterotopic ossification following cervical disc replacement. J Orthop Surg Res 16:693, 2021
11. Tu TH, Wu JC, Huang WC, Guo WY, Wu CL, Shih YH, et al.: Heterotopic ossification after cervical total disc replacement: determination by CT and effects on clinical outcomes. J Neurosurg Spine 14:457–465, 2011
12. Tu TH, Wu JC, Huang WC, Wu CL, Ko CC, Cheng H: The effects of carpentry on heterotopic ossification and mobility in cervical arthroplasty: determination by computed tomography with a minimum 2-year follow-up: Clinical article. J Neurosurg Spine 16:601–609, 2012
13. Wenger M, Hoonacker P, Zachee B, Lange R, Markwalder TM: Bryan cervical disc prostheses: preservation of function over time. J Clin Neurosci 16:220–225, 2009
14. Wenger M, Markwalder TM: Bryan total disc arthroplasty: a replacement disc for cervical disc disease. Med Devices (Auckl) 3:11–24, 2010
15. Wenger M, Markwalder TM: Posterior decompression salvages Bryan total disc arthroplasty in post-operatively recurrent uncoforaminal stenosis. J Clin Neurosci 21:741–744, 2014
16. Wenger M, Markwalder TM: Heterotopic ossification associated with myelopathy following cervical disc prosthesis implantation. J Clin Neurosci 26:154–156, 2016

The Nerve

Case Report

The Nerve 2023;9(1):40-47
https://doi.org/10.21129/nerve.2022.00220
eISSN 2465-891X

Paresthesia and Pain in Both Arms when Shampooing One's Hair: Symptoms of Neurogenic Thoracic Outlet Syndrome

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Received: October 18, 2022
Revised: November 11, 2022
Accepted: November 28, 2022

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Neurogenic thoracic outlet syndrome (TOS) is a clinical diagnosis based on the reproduction of a patient's symptoms with a provocation test (arm elevation) after excluding other conditions that might cause similar symptoms. Neurologic symptoms and signs can vary from mild paresthesia and numbness to intrinsic hand muscle atrophy. The main controversy in patients with neurogenic TOS involves neurologic-type complaints of paresthesia, numbness, and pain. However, there is no positive objective test to identify the cause. A 54-year-old female patient presented with numbness and radiating pain in her bilateral arms that occurred every time she bowed her head while shampooing. The patient had a history of two neck sprains due to slipping before the onset of symptoms. In addition to pain and numbness in both arms at arm elevation, pain in the suprascapular and occipital areas was also present. After excluding cervical nerve root lesions and other bone abnormalities, the patient's symptoms disappeared by brachial plexus decompression through a supraclavicular approach. It is difficult to diagnose neurogenic TOS with pain and paresthesia without muscle weakness in the upper extremities. If physicians do not consider the possibility of neurogenic TOS in patients with upper extremity paresthesia and pain, unnecessary multiple treatments may be performed, prolonging patients' suffering. The exacerbation of pain and paresthesia in both arms and hands can occur immediately after the head is lowered during shampooing. This can be interpreted as a characteristic symptom of a constricted interscalene triangle and brachial plexus compression caused by hyperabduction of the arm.

Keywords: Brachial plexus; Pain; Thoracic outlet syndrome

INTRODUCTION

Thoracic outlet syndrome (TOS) refers to compression of the subclavian vessels and brachial plexus in the region of the superior aperture of the chest, with the most common compression of these structures against the first rib[8]. Historically, the diagnosis and treatment of TOS have been difficult and controversial topics[4,8]. For example, even the term of *the thoracic outlet* is confusing[8]. Anatomically, the area between the scalene muscles and the first rib is termed *the thoracic inlet*[13]. Neurologic symptoms and signs can range from mild paresthesia and numbness to intrinsic hand mus-

cle atrophy[4,9]. In many cases, there might be concomitant distal peripheral nerve entrapment such as cubital or carpal tunnel syndrome[8]. In neurogenic TOS, there is no reliable objective test to identify the cause. Nerve conduction studies (NCS) are useful for detecting sites of concomitant distal nerve compression, such as the median nerve at the carpal tunnel and the ulnar nerve at the elbow[4,8,9]. However, neither NCS nor somatosensory-evoked potentials (SSEPs) are universally accepted as helpful in diagnosing neurogenic TOS[4,8,9]. In these cases, the diagnosis of TOS is suggested by physical examination and provocative test[4,8,9].

We want to report a very rare case of paresthesia accompanying arm elevation. It occurred on both arms as the main symptom whenever the head was bowed. A hyperabduction test of the arm on physical examination was helpful for the diagnosis. Subsequent decompression of the brachial plexus via the supraclavicular approach successfully relieved the pain and paresthesia of the neurogenic TOS.

CASE REPORT

A 54-year-old female patient presented with numbness and radiating pain in her bilateral arms every time she bowed (Fig. 1A). The patient slipped and fell two years ago, suffered neck pain, and underwent an anterior C5/6 cervical fusion surgery a month later. Her neck pain disappeared after the surgery. A year before her visit, she fell backward while sitting in a wheelchair with a cast on her foot due to an ankle sprain. Her back and right shoulder hit the ground, although no pain occurred. Three months later she fell backward again. From then on, she developed numbness and pain in her neck, shoulders and arms. When the patient stayed still, there was no pain. However, when the patient lowered her head, a momentary numbness occurred in both arms. The numbness in both arms and pain in the neck and shoulders occurred every time the patient bowed her head. There was no numbness when the patient moved her arms or shoulders.

In the early stages of pain, the pain that occurred momentarily disappeared immediately. Over time, the duration of pain and numbness accompanied by lowering the head increased. Sometimes, as the momentary pain lasted for more than 5 min, the patient had no choice but to stay still while waiting for the pain to go away. Sometimes numbness occurred in both arms and left upper back when the patient turned her head sideways. At night, numbness occurred in the arms according to the posture of the neck. Six months prior to her presentation, the pain intensified, making the patient's daily life difficult. In particular, when the patient bowed her head while shampooing, the pain in both arms lasted for more than two hours. Along with numbness in both arms when bowing the head, a tightening pain occurred in the left occipital area. Occipital pain was tightening and squeezing in nature. It lasted all day. It radiated to the left temporal and posterolateral neck (Fig. 1B). She was treated at a hospital where she underwent cervical surgery. She was told that there was no problem with the cervical spine surgery site and that there was no additional cervical disc herniation (Fig. 1C). Drug treatment and physical therapy were performed for 6 months. However, there was no improvement in symptoms. The occipital pain did not improve with nonsteroidal anti-inflammatory drugs (NSAIDs), including Ultracet®, gabapentin, pregabalin, muscle relaxants, and occipital nerve blocks.

On physical examination, no specific findings were observed except for the surgical scar for cervical fusion on the front neck. It was confirmed that immediate numbness occurred in both arms when the patient bowed her head. Numbness in both arms occurred even when the patient's head was turned to the side a lot. However, limitation of neck motion was not confirmed. Neurological examination revealed that both arms and hands had no motor weakness. Pinch and grip strengths were also found to be normal. The deep tendon reflex was normoactive. Mild hypesthesia was observed in the left supraclavicular region, shoulder, and upper lateral region of the left upper arm. A slight tenderness was found in the left supraclavicular region. However, no paresthesia was induced upon compression.

Percussion of the nerve (Tinel's sign) was negative in the common nerve entrapment site (carpal tunnel, median nerve forearm, cubital tunnel, and brachial plexus) of the upper extremity. However, hyperabduction of bilateral arm to 180 degrees while keeping wrists and elbows straight for 1 min produced mild paresthesia of bilateral arms and hands, and it was judged to be positive. The Wright hyperabduction and Adson tests were negative. The Spurling's test was also negative. There were no systemic diseases to cause pain. Laboratory findings showed no abnormalities. Electrodiagnostic tests including electromyography (EMG), nerve conduction test, and SSEP was all normal. Plain radiographs of

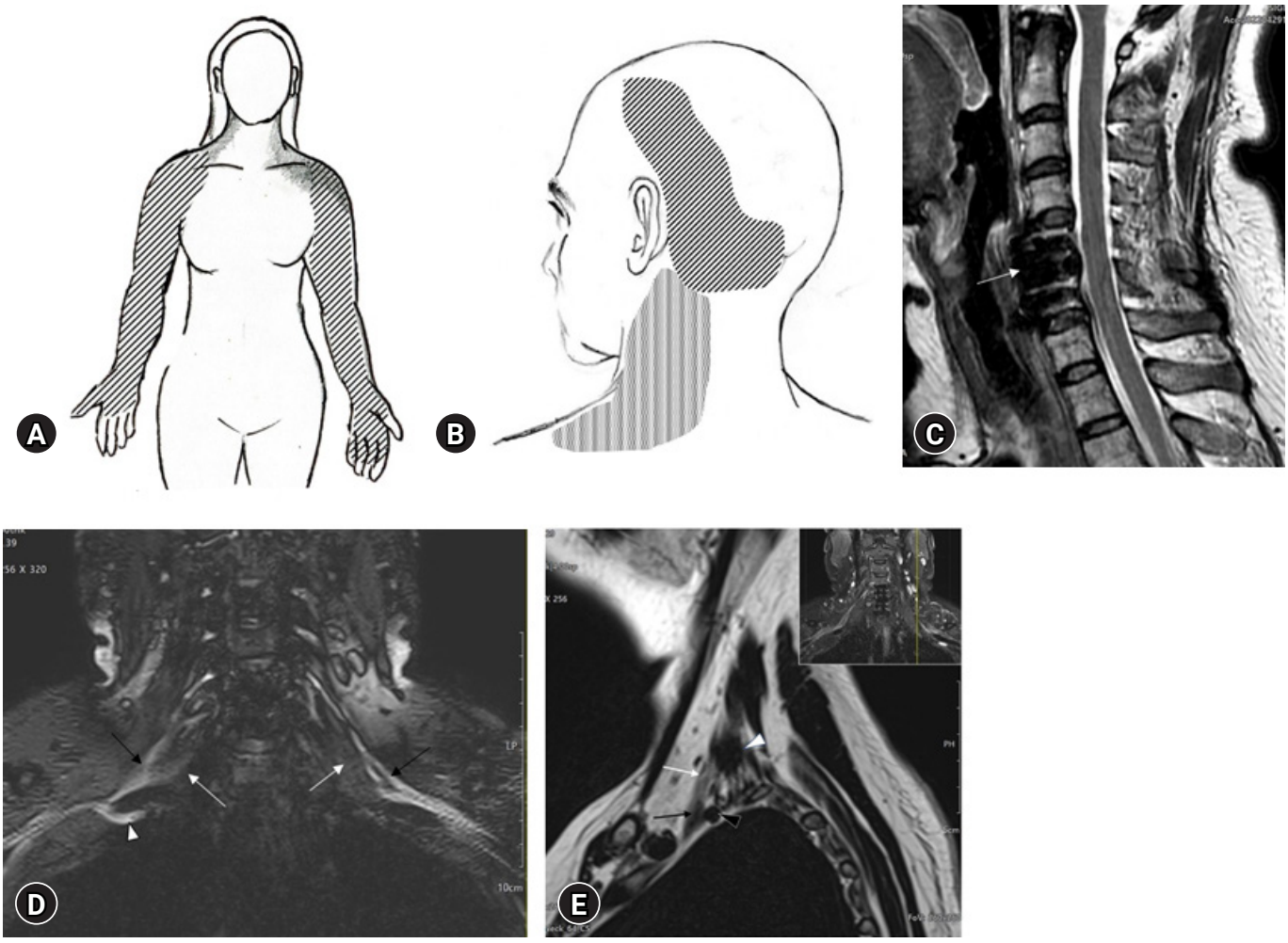

Fig. 1. Distribution of bilateral arm pain and radiologic findings. (A) Distribution of pain and paresthesia (hatched area) in the bilateral arms and hands. The gray area indicates the distribution of the aching pain associated with arm paresthesia. (B) Distribution of aching and tightening pain in the left occipital area. It radiated to the temporoparietal vertex and posterolateral neck. (C) Sagittal T2-weighted magnetic resonance imaging of the cervical spine showing no abnormality, except for prior C5/6 anterior cervical discectomy fusion (arrow). (D) A coronal T2-weighted, enhanced, short tau inversion recovery image of the brachial plexus showing suspected hypertrophy of the anterior scalene muscle (white arrows) and interdigitation of the contour of the brachial plexus (black arrows). Deviation in the course of the lower trunk of the right brachial plexus (white arrow) was noted. (E) A sagittal T2-weighted image of the left brachial plexus shows the left brachial plexus (white arrow) leaving the interscalene triangle between the anterior (black arrow) and middle (white arrowhead) scalene muscles. The back arrowhead indicates the subclavian artery.

the chest and cervical spine showed no cervical ribs or other bony abnormalities such as prominent transverse process or old clavicle fractures, or findings of degenerative arthritis, such as instability, osteophytes, or intervertebral disk space narrowing other than C5/6 anterior cervical fusion. Computed tomography (CT) and magnetic resonance imaging (MRI) of the cervical spine showed no evidence of residual stenosis or adjacent segment degeneration after cervical surgery. Hypertrophy of scalene muscles and irregularity of the brachial plexus contour was suspected on brachial plexus MRI (Fig. 1D). Decompression of the brachial plexus was proposed with a possibility of brachial plexus entrapment (i.e., neurogenic TOS) and medical intractability in mind.

The supraclavicular approach for decompression of the brachial plexus was performed first on the left side, where the pain was more severe. The operation was performed under general anesthesia and intraoperative neurophysiological monitoring according to the method suggested by Mack-

innon et al.[1,2,4]. The patient was supine with an underlying shoulder pump to extend the neck. After making an 8-cm linear skin incision about two centimeters above and paralleling the clavicle, supraclavicular nerves were identified and protected deep to the platysma muscle. Dissection was carried down by dividing the omohyoid muscles, elevating supraclavicular fat pad, and partially dividing the sternocleidomastoideus muscle. After securing the phrenic nerve in front of the anterior scalene muscle in the field of view, it was found that the upper trunk of the left brachial plexus was compressed and swollen between anterior and middle scalene muscles (Fig. 2A). The anterior scalene muscle was divided, taking care not to injure the phrenic nerve with bipolar cautery. Division of the anterior scalene muscle led to exposure of the middle trunk. The long thoracic nerve was isolated from the lateral and posterior part of the middle

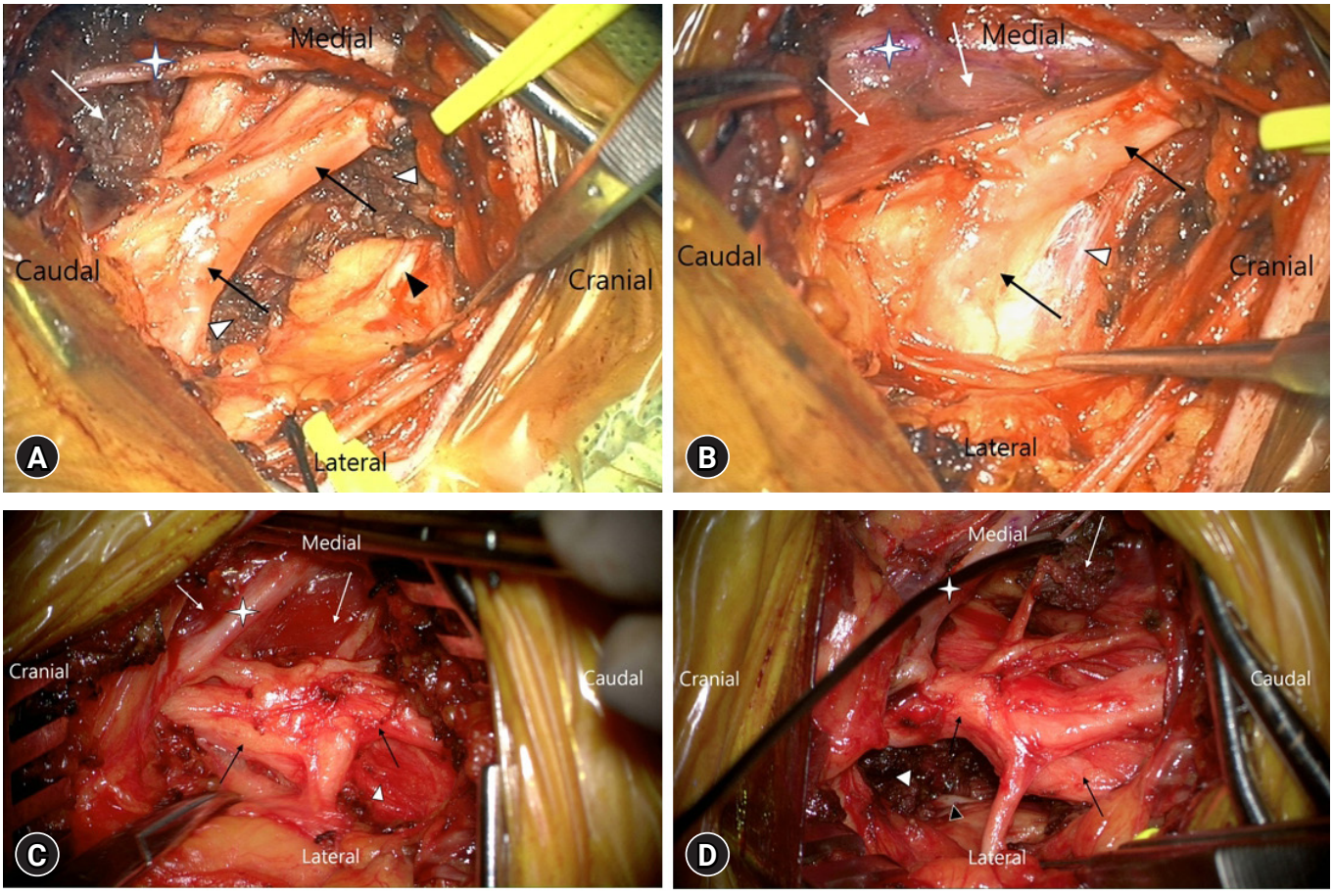

Fig. 2. Intraoperative photographic findings of neurogenic thoracic outlet syndrome during decompression surgery via the supraclavicular approach. (A) An intraoperative photograph showing the upper trunk (black arrows) of the left brachial plexus. The upper trunk was found to be impinged between the anterior (white arrows) and middle (white arrowhead) scalene muscles. The white star indicates the left phrenic nerve, branching from the upper trunk. (B) An intraoperative photograph showing decompression of the left brachial plexus. Indentation and distortion of the course of middle and lower trunks of the brachial plexus medial to the upper trunk (black arrows) were found between cut edges of the anterior (white arrow) and middle (white arrowhead) scalene muscles. The white star indicates the left phrenic nerve. The black arrowhead indicates the long thoracic nerve. (C) An intraoperative photograph showing the upper trunk (black arrows) of the right brachial plexus. The upper trunk was swollen and fixed between the tense anterior (white arrows) and posterior (white arrowhead) scalene muscles. The white star indicates the left phrenic nerve overlying the anterior scalene muscle. (D) An intraoperative photograph showing completed decompression of the right brachial plexus (black arrows). Indentations of the lower and middle trunks of the right brachial plexus were observed medial to the upper trunks (black arrows) between cut edges of the anterior (white arrow) and middle (white arrowhead) scalene muscles. The long thoracic nerve (black arrowhead) was isolated from the middle scalene muscle.

scalene muscle. Whether shoulder contraction was induced by intraoperative electrical stimulation was then checked. The middle scalene muscle inserted into the first rib was then divided to expose the lower trunk of the brachial plexus. All tendinous edges of scalene muscles around the plexus and fibrous sheath of the nerve, which could potentially entrap the nerve, were removed from view under a microscope (Fig. 2B). After securing hemostasis and applying an anti-adhesion gel and films, the overlying wound was closed in layers with closed suction drainage left in the wound. The postoperative course was uneventful. Gentle range of neck motion started with active ambulation permitted within two days after surgery.

In an interview two weeks after the surgery, no neurological abnormalities were observed in the left arm. The pain in the surgical site was minimal. The patient reported that the numbness in the left arm when the head was bowed no longer occurred, although it was still present in the right arm. The pain in the left occipital area along with the pain in the left arm completely disappeared. The patient requested an expedited surgical schedule for her right arm pain.

Decompression of the right brachial plexus was performed one and a half months after the operation on the left. It was performed in the same manner as in the first left surgery (Fig. 2C, D). The patient was discharged on the 5th day after surgery. After a month, it was confirmed that the numbness and pain in the right arm that had occurred when the patient bowed his head also disappeared. However, weakness was found in the abduction of the right shoulder. The largest abduction angle of the shoulder was only possible to 90 degrees. There were no restrictions on right shoulder flexion, extension, or adduction. No sensory disturbance or pain was identified. Abduction paralysis of the right shoulder improved to 120 degrees 3 months after the operation. It was no longer observed at six months. Twelve months after the operation, the patient's arm numbness due to neck flexion no longer occurred. There was no disturbance in daily life.

DISCUSSION

1. Neurogenic TOS

TOS is a constellation of clinical manifestations in the neck, shoulder, and upper extremities caused by compression of neurovascular structures in the thoracic outlet region[1,2,4]. Its debated history, pathophysiology, and even existence make TOS the most controversial topic in peripheral nerve surgery[4]. The lack of professional consensus, in combination with a wide variability of symptoms and lack of a gold standard for its diagnosis, can explain how a diagnosis for a patient with this condition is often overlooked[4]. In this context, it took more than a year for the numbness of the arm accompanying head bending in the current case to be diagnosed as neurogenic TOS. Thus, its diagnosis is difficult if a patient is not observed or examined with TOS in mind. Some experienced researchers have emphasized general principles of the cause and symptoms of TOS[4]. They believe that paresthesia and numbness experienced in hand with overhead activities are related to compression of the brachial plexus while the frequently more concerning problem of pain in the scapular, neck, and shoulder is related to muscle imbalance[4]. In this context, we could suspect TOS in the current case based on the fact that hair shampooing as an overhead activity exacerbated the numbness for more than two hours. However, in order to diagnose it, some processes were required to exclude other structural causes.

Neurogenic TOS is thought to result from a combination of a congenial anatomical predisposition and trauma to the neck[3,4,15]. Another common cause is a poor posture of the neck, upper back, and shoulders[4]. Obesity and a propensity for increased flexion of the neck and shoulders have been suggested as factors that increase the incidence of neurogenic TOS[4].

TOS typically occurs in young and middle-aged adults. It occurs in women three times more frequently than in man[2].

Patient symptoms may differ depending on which structure is compressed in the cervicoaxillary canal[4]. The subclavian vein, the subclavian artery, and the brachial plexus are three neurovascular elements involved in TOS. That is, symptoms of nerve compression are different from those of arterial or venous compression. Neurogenic TOS is much more common than arterial or venous TOS, accounting for up to 98% of cases[2,4]. Arterial TOS has symptoms such as cold extremities, easy fatigue, and Raynaud syndrome caused by ischemia in the upper extremity. Venous TOS is mostly related to axillary subclavian vein thrombosis[4]. Therefore, neurogenic TOS presented as numbness and pain in the upper extremity can be distinguished easily from vascular TOS based on symptoms. Although neurogenic TOS is more common than vascular TOS, it is typically more difficult to diagnose neurogenic TOS because its greater variability in

symptomatology. Fifteen percent of cases might have some concomitant arterial symptoms. However, arterial symptoms seldom exist alone[4]. Physicians who diagnose only vascular forms of TOS are misdiagnosing the vast majority of patients they see who have neurologic TOS[4].

2. Anatomy of TOS

The brachial plexus has a course between the anterior and middle scalene muscles. It continues distal deep to the clavicle and superior to the first rib. This opening is anatomically referred to as the thoracic inlet and clinically as the thoracic outlet[8,13]. Three different compartments in the cervicoaxillary canal are related to the genesis of neurovascular compression syndrome: the interscalene triangle, the costoclavicular space, and the pectoralis minor region[4-7,11]. The medial or proximal segment of the cervicoaxillary canal comprises the scalene triangle and costoclavicular space, where the majority of neurovascular compression occurs[4].

The anterior scalene muscle originates from the anterior tubercles of the transverse processes of the third through sixth cervical vertebrae. It inserts onto the scalene tubercle of the first rib. The middle scalene originates from the posterior tubercles of transverse processes of the second through seventh cervical vertebrae. It inserts onto a more posterior portion of the first rib. The subclavian artery and the brachial plexus pass through the space posterior to the anterior scalene muscle called scalene triangle or interscalene space. This space is bounded by the anterior scalene muscle anteriorly, the middle scalene muscle posteriorly, and the first rib inferiorly. It has some overlap with the posterior space of the costoclavicular space[4]. It has been acknowledged that significant distortions of the cervicoaxillary canal and its neurovascular contents can occur due to a wide range of shoulder and upper extremity motions[4]. The brachial plexus and subclavian artery become compressed when the scalene triangle is narrowed with hyperabduction of the arm[4]. When the superior aspect of the scalene triangle is narrowed, the upper components of the brachial plexus become compressed. When the floor of the triangle is elevated, the lower components of the brachial plexus and the subclavian artery become compressed[4].

3. Diagnosis of Neurogenic TOS

The diagnosis of TOS is based on findings of clinical evaluation, particularly if symptoms can be reproduced when various dynamic maneuvers including elevation of the arm are undertaken[3,9]. Therefore, clinical diagnosis of TOS is often difficult. Imaging tests such as CT and MRI that can confirm anatomical structures of the thoracic outlet are essential along with EMG[4,8,9].

The onset of symptoms of TOS may be insidious or follow trauma[4]. Neck and shoulder pain and stiffness might be early signs of muscle spasm and imbalance[4,8]. Pain and paresthesia associated with nerve dysfunction are present in up to 95% of cases. They typically occur in delayed fashion weeks or months later, often after acute musculoskeletal symptoms have resolved[3,4]. Numbness may present with or without tingling. Symptoms might be exacerbated following strenuous physical activity or prolonged arm elevation[4]. The occurrence of symptoms after activity can help us distinguish TOS from primary shoulder or cervical spine pathology when symptoms tend to occur during activity[4]. Symptoms of neurogenic TOS depend on which trunk of the brachial plexus is involved[4]. The lower trunk is known to be most commonly involved[4]. When isolated upper trunk symptoms occur, cervical spine pathology is often the causative agent[4]. When the upper trunk is involved in TOS, symptoms occur in the neck, deltoid area, and lateral ar. They may also radiate to the side of the face, the ear, the occiput, and in the median nerve distribution[4,8,9].

It is important to distinguish between the more common cervical spine diseases and TOS[4]. Common cervical spine diseases such as cervical disk disease and spondylosis causing nerve root compression are usually associated with neck pain, stiffness, radiating paresthesia, and weakness of involved cervical roots[4]. Generally, they are common in the C5-C6 or C6-C7 intervals, creating symptoms in the respective nerve root distribution. Because the lower trunk of the brachial plexus is most commonly involved in TOS, compression of the C8 or T1 nerve roots can more closely mimic TOS, with symptoms in an ulnar nerve distribution. However, cervical disk disease involving the C8 or T1 is much less common than compression of the fifth, sixth, or seventh roots[4].

Among several provocative maneuvers of neurogenic TOS, hyperabduction test described by Novak et al.[10,11] was positive in the current case. However, other physical tests such as the wright hyperabduction test, Adson test, Halstead test, and costoclavicular test were negative. Flexion of the neck typically induced characteristic pain and paresthesia in

bilateral arm in the current patient. Hair shampooing as an overhead activity characteristically exacerbated arm numbness for several hours. Narrowing of the scalene triangle due to hyperabduction of the arm is well acknowledged. At the same time, neck flexion was thought to increase the tension of hypertrophied anterior and middle scalene muscles, resulting in increased compression of the brachial plexus. In addition, overhead activities of bending the neck and raising the arms during hair shampooing are interpreted as conditions that can cause a narrowing of the cervical axillary canal, especially the scalene triangle.

Imaging tests such as CT and MRI are needed to investigate congenital or other organic causes of TOS such as tumors or other space-occupying soft tissue lesions[9]. Generally, these studies are not necessary for patients with TOS[9]. However, they may help us rule out the presence of cervical disk disease, spinal stenosis, or nerve root impingement[5-7]. Both MRI and ultrasound are thought to be useful when performed with provocative maneuvers such as hyperabduction of the arm. They can detect vascular TOS to a greater degree than detecting neurogenic TOS[5-7]. Therefore, unlike vascular TOS, imaging-based diagnosis has limitations in neurogenic TOS[4].

CT and MRI might be helpful in the identification of soft tissue abnormalities associated with TOS. Several anatomical variations of the scalene muscles have been suggested to be responsible for TOS[7]. They include hypertrophy of the anterior scalene muscle, origin of the anterior and middle scalene muscles from a common belly that divides in two distally, the passage of the brachial plexus through the substance of the anterior scalene muscle, a broad middle scalene muscle inserting more anteriorly on the first rib than what is normal, interdigitation between the anterior and middle scalene muscles, supernumerary muscle such as scalenus minimus muscle, and anomalous fibrous bands[5-7,12,14,17]. However, the clinical significance of these findings in TOS remains unclear.

Electrodiagnostic studies are typically normal in patients with TOS unless TOS is associated with cubital or carpal tunnel syndrome[4]. NCSs and EMG are controversial in diagnosing TOS[4,8,9]. They are helpful for identifying more peripheral nerve compression that may exist with TOS concomitantly[2]. EMG findings tend to become positive only late in pathology[4]. NCSs, especially ulnar nerve conduction velocities, have been suggested to be more useful for the earlier detection of TOS[13]. However, some authors remain pessimistic about its usefulness[4,8,9].

4. Management of Neurogenic TOS

It is known that 50% to 80% of patients with neurogenic TOS improve through physiopherapy[10]. The main goal of physical therapy is to decrease external nerve compression resulting from muscle imbalance[4,9]. Stretching and strengthening exercises focus on correcting abnormal posture while restoring muscle balance[4,9]. If TOS symptoms do not improve with physiotherapy, the release of any concomitant distal nerve compression such as a cubital tunnel or carpal tunnel syndrome is recommended[4,9]. Although the risk of surgical decompression of thoracic outlet by skilled operators is very low, surgery should be selected with caution due to the potential of serious morbidity of high nerve injury[4,9]. If there are no cervical ribs, decompression of the brachial plexus via scalenotomy is recommended[4,9]. Generally, first rib resection is recommended when there is a significant compressive element[17].

For thoracic outlet decompression, several surgical approaches have been proposed, including high posterior thoracoplasty, anterior approach, and transaxillary approach[4,8,9]. Scalenotomy alone is associated with a higher long-term recurrence rate of up to 65%[4,8,9]. We adopted the supraclvacular approach for the brachial plexus decompression suggested by Mackinnon et al.[8] It allows surgeons complete visualization of all the neurovascular elements and removal of the first rib[4]. During dissection, care should be taken to preserve the supraclavicular and long thoracic nerves. Gentle but early postoperative movement of the head, neck, and upper extremity is encouraged to minimize scar formation around the brachial plexus[8]. For neurogenic TOS, first rib resection is not necessary for satisfactory relief of symptoms[4,8]. In the present case, there was no bone pathology like a cervical rib. Sufficient decompression of the brachial plexus was possible without first rib resection. Intraoperative nerve stimulation was helpful for identifying the long thoracic nerve during dissection of the middle scalene muscle. Surgical failure and recurrence are known to be relatively common[2]. Repeated decompression is warranted for appropriately selected patients[16]. In case of reoperation, an alternative approach such as the posterior thoracoplasty approach is recommended to reduce dissection in a previously scarred bed and consequent risk of nerve or vessel

injury[8,9].

CONCLUSION

Diagnosis and treatment of TOS remain controversial and difficult, particularly in patients with neurogenic TOS without muscle atrophy. In these patients, the diagnosis of neurogenic TOS can be made by provocative testing after excluding other potentially causative conditions. Most patients improve with conservative management, including activity, posture modification, and physical therapy. Those with persistent significant symptoms are candidates for surgical decompression with a supraclavicular approach.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Atasoy E: Thoracic outlet syndrome: anatomy. Hand Clin 20:7–14, 2004
2. Brantigan CO, Roos DB: Diagnosing thoracic outlet syndrome. Hand Clin 20:27–36, 2004
3. Brantigan CO, Roos DB: Etiology of neurogenic thoracic outlet syndrome. Hand Clin 20:17–22, 2004
4. Colbert SH. Thoracic outlet syndrome. In: Mackinnon SE ed. Nerve surgery. New York, NY: Thieme Medical Publishers, 2015, pp310–337
5. Collins JD, Shaver ML, Disher AC, Miller TQ: Compromising abnormalities of the brachial plexus as displayed by magnetic resonance imaging. Clin Anat 8:1–16, 1995
6. Demondion X, Bacqueville E, Paul C, Duquesnoy B, Hachulla E, Cotten A: Thoracic outlet: assessment with MR imaging in asymptomatic and symptomatic populations. Radiology 227:461–468, 2003
7. Demondion X, Herbinet P, Van Sint Jan S, Boutry N, Chantelot C, Cotten A: Imaging assessment of thoracic outlet syndrome. Radiographics 26:1735–1750, 2006
8. Mackinnon S, Patterson GA, Colbert SH: Supraclavicular approach to first rib resection for thoracic outlet syndrome. Oper Tech Thorac Cardiovasc Surg 10:318–328, 2005
9. Mackinnon SE, Novak CB: Thoracic outlet syndrome. Curr Probl Surg 39:1070–1145, 2002
10. Novak CB, Collins ED, Mackinnon SE: Outcome following conservative management of thoracic outlet syndrome. J Hand Surg Am 20:542–548, 1995
11. Novak CB, Mackinnon SE, Patterson GA: Evaluation of patients with thoracic outlet syndrome. J Hand Surg Am 18:292–299, 1993
12. Ochsner A, Gage M, DeBakey M: Scalenus anticus (Naffziger) syndrome. Am J Surg 28:669–695, 1935
13. Ranney D: Thoracic outlet: an anatomical redefinition that makes clinical sense. Clin Anat 9:50–52, 1996
14. Roos DB: Congenital anomalies associated with thoracic outlet syndrome. Anatomy, symptoms, diagnosis, and treatment. Am J Surg 132:771–778, 1976
15. Sanders RJ, Jackson CG, Banchero N, Pearce WH: Scalene muscle abnormalities in traumatic thoracic outlet syndrome. Am J Surg 159:231–236, 1990
16. Urschel HC, Razzuk MA: The failed operation for thoracic outlet syndrome: the difficulty of diagnosis and management. Ann Thorac Surg 42:523–528, 1986
17. Urschel HC, Razzuk MA: Neurovascular compression in the thoracic outlet: changing management over 50 years. Ann Surg 228:609–617, 1998

The Nerve

Case Report

The Nerve 2023;9(1):48-50
https://doi.org/10.21129/nerve.2022.00234
eISSN 2465-891X

A Case of Subcutaneous Schwannoma of the Scalp

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OPEN ACCESS

Received: December 2, 2022
Revised: January 15, 2023
Accepted: January 31, 2023

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Schwannomas are benign neural tumors derived from Schwann cells, which surround the peripheral nerves. Here, we present a case of subcutaneous schwannoma of the scalp, with the goal of increasing awareness of the differential diagnosis of scalp masses. A 45-year-old woman was admitted with a palpable scalp mass on the occiput initially noticed 2 years prior. Palpation revealed a 1.5-cm round subcutaneous mass, which was soft and exhibited a movable tendency. The lesion margin was well-circumscribed and contained under the skin. Computed tomography showed a 6 × 12-mm soft-tissue density subcutaneous nodule in the right paramedian occipital region. Thus, an epidermal cyst or lipoma was suspected. The pathological diagnosis (hematoxylin and eosin staining) revealed evidence indicating a subcutaneous schwannoma of the scalp. We report a subcutaneous schwannoma of the scalp, demonstrating that schwannomas can also occur as subcutaneous scalp lesions. Therefore, we suggest that although the treatment of subcutaneous schwannomas does not differ from other soft-tissue masses, a pathological examination should be performed to establish an exact diagnosis in such cases.

Keywords: Neurilemmoma; Scalp; Subcutaneous tissue

INTRODUCTION

Schwannoma is a benign, rarely recurring tumor in the peripheral nerves. Schwann cells, which separate and insulate nerve cells, are glial cells of the peripheral nervous system. In the field of neurosurgery, schwannomas are noted for their specific locations, including the cerebellopontine angle and cranial nerve; however, they are uncommon in the cutaneous nerve. Cutaneous schwannomas develop in the major peripheral nerves and can be located superficially, although they most commonly occur in the subcutaneous layer or even deeper[5].

In this report, we present a case of subcutaneous schwannoma of the scalp and discuss its characteristics.

CASE REPORT

The patient was a 45-year-old woman admitted with a palpable scalp mass on the occiput initially noticed 2 years prior. The mass had grown gradually over the last year and has since stabilized at the current size. However, it caused her mild discomfort, particularly while lying down, but no noticeable pain. She reported no head trauma or injection in the scalp. Palpation examination revealed a 1.5 cm-sized

round subcutaneous mass, which was soft and exhibited a movable tendency. The margin of the lesion was well circumscribed and contained under the skin, with no signs of skin retraction, openings, or purulent drainage.

Computed tomography (CT) showed a 6 × 12-mm sized soft-tissue density subcutaneous nodule in the right paramedian occipital region. However, no abnormal density was detected in the brain parenchyma and skull (Fig. 1).

Considering all this evidence, we suspected this mass was an epidermal cyst or lipoma. Subsequently, under local anesthesia, the patient elected to undergo surgical excision of the mass. The mass was completely resected, with no postoperative complications. At 3 weeks after the surgery, the surgical wound had completely healed, and the patient's symptoms had all improved.

Pathology

At 1 week after the surgery, a pathological diagnosis was performed. Hematoxylin and eosin staining under a low power field (Original magnification, ×100) revealed that the mass was composed mostly of spindle cells (Fig. 2). Under a high power field (Original magnification, ×400), the staining demonstrated compact spindle cells with characteristic nuclear palisading (Verocay body, Antoni A; asterisk) and loose hypocellular (Antoni B; arrow) areas between the compact cell area, providing reasonable evidence of a schwannoma (Fig. 3).

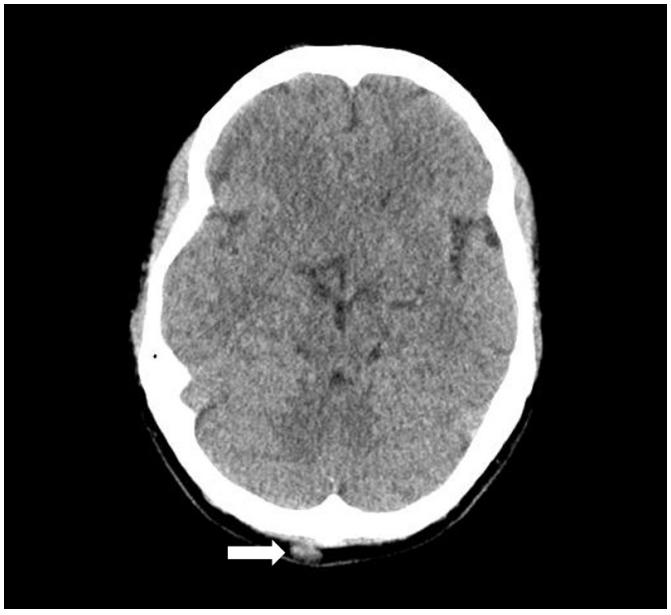

Fig. 1. Computed tomography shows a 6 × 12-mm soft-tissue density subcutaneous nodule in the right paramedian occipital region (arrow).

DISCUSSION

Soft-tissue nodules are common - about two-thirds of

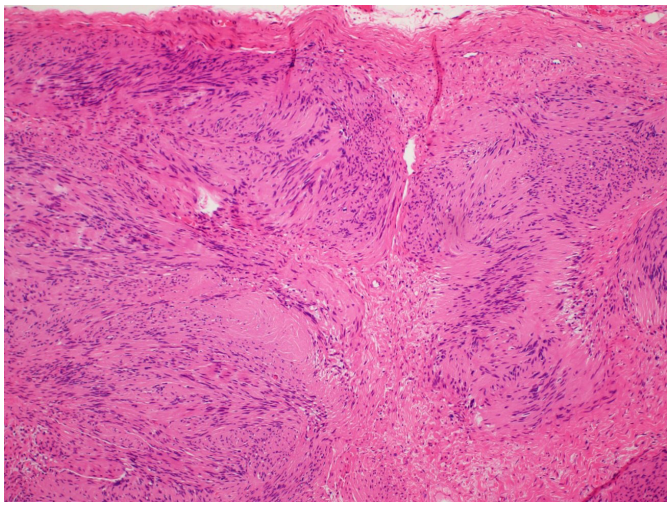

Fig. 2. The mass is composed of spindle cells (hematoxylin and eosin stain, ×100 magnification).

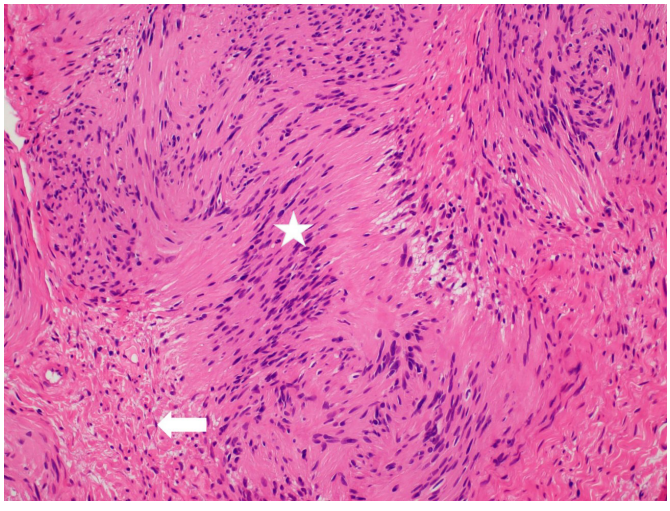

Fig. 3. A high-power view shows compact spindle cells with a characteristic nuclear palisading area (Verocay bodies, Antoni A) (asterisk) and loose hypocellular areas (Antoni B) (arrow) between compact cell areas (hematoxylin and eosin stain, ×400 magnification).

soft-tissue tumors are classified into seven diagnostic categories: lipoma and lipoma variants (16%), fibrous histiocytoma (13%), nodular fasciitis (11%), hemangioma (8%), fibromatosis (7%), neurofibroma (5%), and schwannoma (5%)[4].

Furthermore, peripheral nerve tumors have several classifications, such as nonneoplastic vs. neoplastic, benign vs. malignant, and sheath vs. non-sheath origins. Schwannoma is considered part of the neoplastic subset due to their growth; otherwise, they are classified as benign with a sheath origin. Compared to neurofibromas, benign schwannomas have a slower rate of progression, lower association with pain, and fewer neurologic symptoms[7].

Schwannoma is a neural tumor derived from Schwann cells surrounding the peripheral nerves. The neural sheath comprises three cell types: the fibroblast, Schwann cell, and perineural cell[6]. Among them, Schwann cells play the important role of developing into a schwannoma. Schwannomas are composed exclusively of Schwann cells located in the nerve sheath, whereas neurofibromas consist of all the different cell types that constitute a nerve[2].

Schwannomas are most commonly found in the retroperitoneum (32%), mediastinum (23%), head and neck (18%), and extremities (16%)[8]. Most schwannoma cases (about 90%) are sporadic, whereas 2% are related to neurofibromatosis type 2[3]. Clinically, these benign tumors are easily mistaken for other lesions, including lipomas and epidermal cysts. Considering that these two lesions account for a large proportion of scalp lesions, the preoperative diagnosis in our case was an epidermal cyst or subcutaneous lipoma. Unfortunately, no clear radiographic imaging was available for differential diagnosis. In our case, the patient underwent non-contrast brain CT scanning, and the lesion showed a high-density round mass similar to that observed in other epidermal/dermal cystic lesions.

Schwannomas are exclusively treated with excision, and they have a good prognosis and low recurrence rate. However, the recurrence rates for completely resected schwannomas of the scalp are unknown because only a few reports are available in the literature. Vestibular schwannomas, which are well known in the neurosurgery field, generally have recurrence rates of 2% to 3% in cases of total resection[1]. Thus, we believe that the recurrence rates of subcutaneous schwannomas of the scalp may be in this range.

CONCLUSION

Many neurosurgeons consider schwannomas to develop in the cranial nerve; however, our case shows that schwannomas can also present as subcutaneous scalp lesions. Although subcutaneous schwannomas are not different from other soft-tissue masses in terms of treatment, pathological examination should be performed to establish an exact diagnosis.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Ahmad RA, Sivalingam S, Topsakal V, Russo A, Taibah A, Sanna M: Rate of recurrent vestibular schwannoma after total removal via different surgical approaches. Ann Otol Rhinol Laryngol 121:156–161, 2012
2. Balzarotti R, Rondelli F, Barizzi J, Cartolari R: Symptomatic schwannoma of the abdominal wall: A case report and review of the literature. Oncol Lett 9:1095–1098, 2015
3. Goldblum JR, Folpe AL, Weiss SW. Benign tumors of peripheral nerves. In: Goldblum JR, Folpe AL, Weiss SW eds. Enzinger and Weiss's soft tissue tumors, ed 7th. Philadelphia, PA: Elsevier, 2020, pp885–958
4. Kransdorf MJ: Benign soft-tissue tumors in a large referral population: distribution of specific diagnoses by age, sex, and location. AJR Am J Roentgenol 164:395–402, 1995
5. Patel HA, Makhijani S: Cutaneous schwannoma presenting as a lower back mass. Int J Surg Case Rep 32:25–28, 2017
6. Patterson JW. Weedon's skin pathology, ed 4th. Philadelphia, PA: Elsevier, 2016
7. Valeyrie-Allanore L, Ismaïli N, Bastuji-Garin S, Zeller J, Wechsler J, Revuz J, et al.: Symptoms associated with malignancy of peripheral nerve sheath tumours: a retrospective study of 69 patients with neurofibromatosis 1. Br J Dermatol 153:79–82, 2005
8. White W, Shiu MH, Rosenblum MK, Erlandson RA, Woodruff JM: Cellular schwannoma. A clinicopathologic study of 57 patients and 58 tumors. Cancer 66:1266–1275, 1990

The Nerve

Case Report

The Nerve 2023;9(1):51-55
https://doi.org/10.21129/nerve.2022.00241
eISSN 2465-891X

Spontaneous Shrinkage of a Dumbbell-Shaped Schwannoma in the Cervical Spine: A Case Report

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OPEN ACCESS

Received: December 11, 2022
Revised: January 23, 2023
Accepted: January 31, 2023

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Cervical dumbbell-shaped schwannomas are uncommon and challenging; clinicians often face the choice between performing incomplete tumor resection and sacrificing nerve roots. Aggressive and total resection is the treatment of choice for this tumor, although surgical resection in asymptomatic patients remains a matter of debate. We present a case report of spontaneous shrinkage of a dumbbell-shaped schwannoma of the cervical spine. A 68-year-old female patient first presented in 2013 with a progressive history of pain in the lower back and both buttocks over the previous 10 years. A dumbbell-shaped cervical spine tumor that had a 30-mm maximum diameter with a foraminal obstruction was identified, along with multiple tiny intradural extramedullary tumors in the lumbar spine. The cervical tumor gradually decreased in size during annual follow-up visits through 2015. Magnetic resonance imaging conducted in November 2017 revealed that this dumbbell-shaped tumor had shrunk significantly, leaving only the paravertebral section with a maximal diameter of 14 mm. This case demonstrated a schwannoma that naturally decreased in size with no treatment. Clinicians should consider the possibility of a spontaneous reduction in schwannoma size when making treatment decisions in asymptomatic patients, in whom avoiding unnecessary surgery may prevent nerve root damage.

Keywords: Cervical vertebrae; Neoplasm regression, spontaneous; Neurilemmoma

INTRODUCTION

Spinal dumbbell-shaped tumors are located in the intervertebral foramina or dura mater and exhibit a dumbbell shape. Surgery to remove these tumors that are located in the cervical intervertebral foramina may damage nerve roots or lead to incomplete tumor resection, vertebral artery injury, or post-laminectomy kyphosis[2]. Therefore, the best treatments for asymptomatic patients with these tumors remain debated. In the case of intracranial schwannoma, spontaneous shrinkage has been reported in more than 21 studies[11]. there are only 2 cases reports of spontaneous shrinkage of the spinal schwannoma[7,8]. Both cases involved shrinkage due to cellular reactions or chemical reactions to drugs, but we will present regression that arose during simple follow-up. This is a case report of spontaneous shrinkage of a cervical dumbbell-shaped tumor referred to our institution between November 2015 and November 2017.

CASE REPORT

A 68-year-old female patient presented in 2013 with a progressive history of pain in the lower back and buttocks for the past 10 years. A radiological assessment that included spinal magnetic resonance imaging (MRI) was performed, multiple tiny neurogenic tumors around the lumbar spinal cord were observed, including a neurogenic tumor at the cervical 6/7 level. A 30-mm-sized tumor at the C6/7 level was compressing the spinal cord from the left and extended to the left C6/7 paravertebral space. There were few changes in tumor size in 2014, but an MRI obtained in November 2015 revealed that the dumbbell-shaped tumor had shrunk, leaving only the paravertebral component with a 24-mm maximal diameter from the axial view, and there were no new symptoms reported by the patient. Two years later, an MRI from November 2017 showed significant changes; the dumbbell-shaped tumor had decreased in size with a 14-mm maximal diameter (Fig. 1). In the annual follow-up, the tumor size did not decrease further from 2017 to 2019. The patient still had multiple suspicious schwannoma tumors in the lumbar region. There were no symptomatic changes or new symptoms after six years of follow-up visits (Fig. 2).

DISCUSSION

While generally uncommon overall, spinal schwannoma is the most common type of spinal extramedullary neurogenic tumor[4,12]. Spinal neurogenic tumors can be located anywhere in the intradural, epidural, and paravertebral space and can grow and compress the neural structures, causing pain or neurologic deficits. Symptoms may vary depending on the adjacent neural structure. The surgical approach should be selected according to the location of the lesion or adjacent neural structures. Although the surgical method varies depending on the location, surgical method may be complicated when it is located in both the extradural and paravertebral space[1,16]. Therefore, several classifications have been proposed accordingly[10].

To resolve neurological symptoms and encourage regrowth, total gross removal is preferred over subtotal removal[9]. However, depending on the location's complexity, a 2-stage procedure may be required for complex and large tumors; complications like a vertebral artery injury or

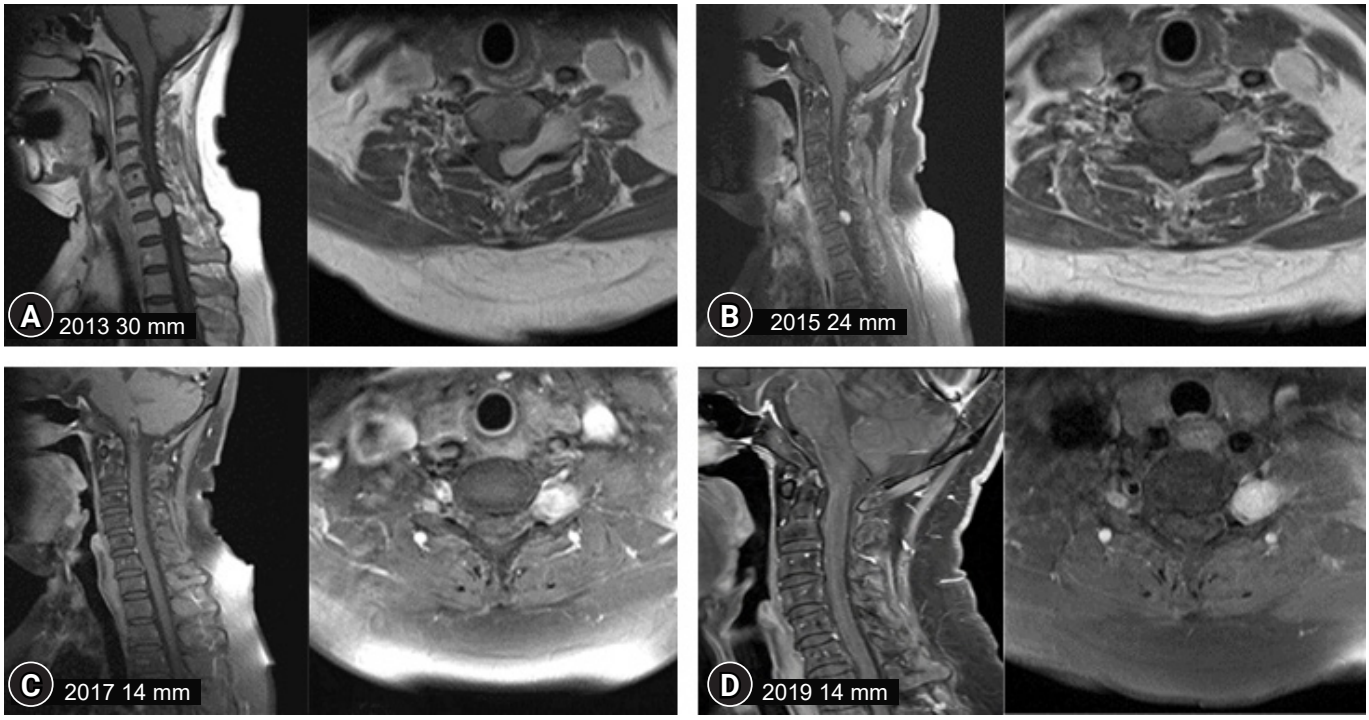

Fig. 1. A left C6/7 dumbbell-shaped schwannoma in a 68-year-old woman that decreased in size over time. The tumor shrank very little from 2013 to 2015 (A, B), but changed significantly from 2015 to 2017 (B, C). No further changes were observed from 2017 to 2019 (C, D).

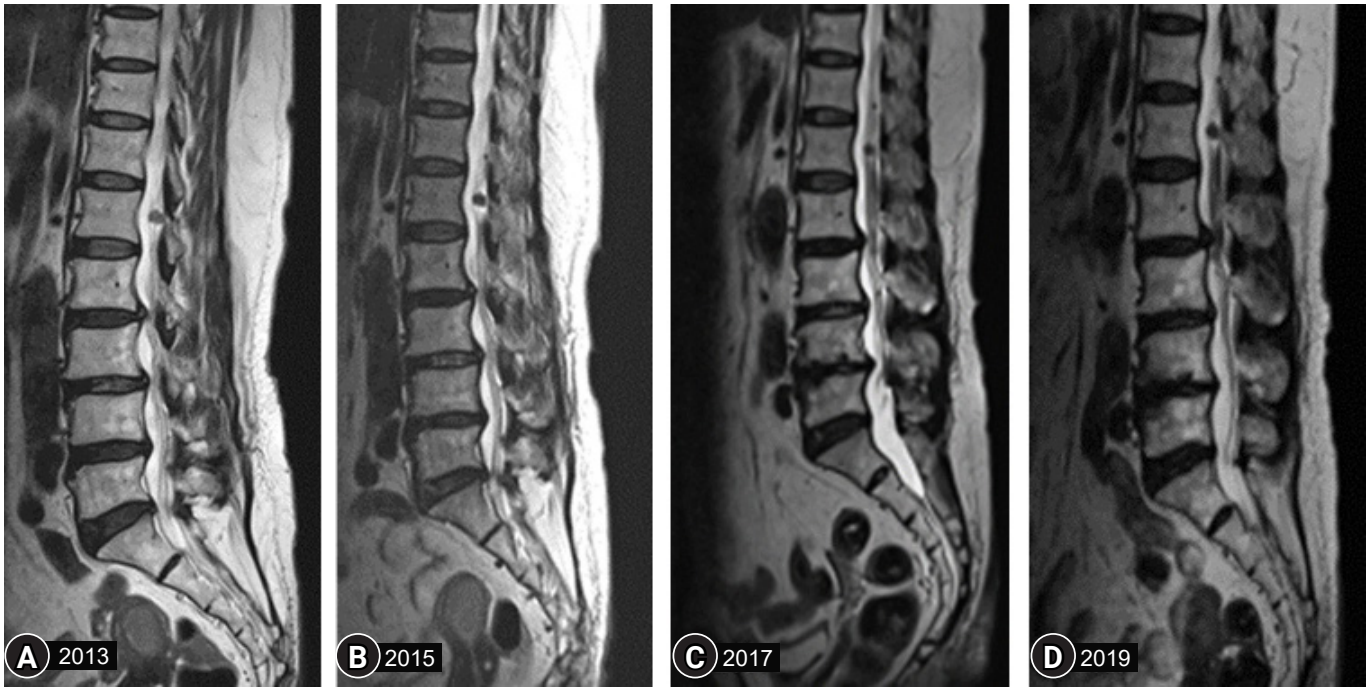

Fig. 2. Multiple schwannomas in the lumbar region with no size changes from 2013 to 2019 (A-D) that produced no symptoms.

Table 1. Cases of regression of spinal schwannoma without surgical resection

References	Year	Sex	Age (years)	Size of tumor (mm)	% of shrinkage	Follow-up period (years)	Special features
Ito et al.[7]	2019	F	58	NA	NA	2	Intramural hemorrhage
Kunnel Jomon et al.[8]	2020	F	77	10.4	18.7	10	Multiple myeloma treated with pomalidomide
This case	2023	F	68	30	53.3	6	None

F: female; NA: not available.

post-laminectomy kyphosis have also been documented[5,15]. Therefore, due to its slow-growing, pathologically benign nature, surgical treatments in asymptomatic patients remain under debate[3]. Since there are many cases of benign characteristics of spinal neurogenic tumor, previous authors have suggested that if the tumor size does not increase by 2.5% or more per year, it is not growing very quickly[6]. In these cases, they recommended serial follow-up monitoring.

In the case of vestibular schwannoma (VS) of World Health Organization Grade I, some patients have demonstrated natural shrinkage. Between 1988 and 2013, 21 studies[11]. reported shrinkage of these tumors that ranged from 1% to 29% during follow-up periods that lasted from 6 months–27 years. The degree of tumor shrinkage identified ranged from 5.38% to 100% during the same follow-up. In contrast, few reports have described the spontaneous regression of a spinal cord dumbbell-shaped schwannoma. Ito et al.[7] reported spontaneous regression after intramural hemorrhaging, and Kunnel Jomon et al.[8] observed multiple myeloma diagnosed after the tumor's discovery that was treated with pomalidomide and then regressed (Table 1).

In patients affected by neurofibromatosis type 2 (NF2) with bilateral VS, the gene responsible for NF2 is localized on chromosome 22[14]. However, there is currently no known genetic correlation with spontaneous shrinkage. von Eckardstein et al.[13] described two patients with NF2 who underwent unilateral resection of VSs and demonstrated regression of the contralateral medium-sized VSs during follow-up periods of four and nine years, respectively. To our knowledge, no large series have described spontaneous

shrinkage of VSs in patients with NF2. A multicenter study of 56 NF2 patients with 84 VSs reported 16 tumors out of 84 that regressed with a range of shrinkage between 1 and 7 mm during an average follow-up length of 51.3 months. Although genetic testing was not performed for NF2 in the present case, the shrinkage may be even greater in NF2 patients.

The principle of spontaneous tumor shrinkage is unclear, although there are a few theoretical conjectures in the literature[13,14]. Factors such as common genetics, environmental factors, and lifestyle influences are expected to affect this behavior. A reduction in vascular supply is the most promising hypothesis to date, and it is presumed to cause ischemic necrosis and fibrosis, resulting in spontaneous shrinkage of these tumors. A vascular genesis theory has been proposed that involves ischemic necrosis of the tumor caused by intra-tumorous thrombosis and subsequent fibrosis. The blood supply in the regional microenvironment where schwannomas grow may also contribute to spontaneous tumor shrinkage, especially in elderly patients. Tumor cell apoptosis or programmed cell death may also play a role in spontaneous tumor shrinkage. A comprehensive investigation of naturally occurring regression will be required to identify prognostic factors of spontaneous tumor shrinkage.

Our reported case indicates that simple follow-up visits can be helpful in the treatment of some tumors. It could make a chance that the surgical removal of schwannomas may be avoided if natural shrinkage of the tumor occurs.

CONCLUSION

The first choice of treatment for cervical schwannoma has typically been surgical resection. However, in this case, a tumor presumed to be a schwannoma naturally decreased in size. Clinicians should consider the potential for a spontaneous size reduction of cervical dumbell-shaped schwannomas.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Abernathey CD, Onofrio BM, Scheithauer B, Pairolero PC, Shives TC: Surgical management of giant sacral schwannomas. J Neurosurg 65:286–295, 1986
2. Albert TJ, Vacarro A: Postlaminectomy kyphosis. Spine (Phila Pa 1976) 23:2738–2745, 1998
3. Ando K, Imagama S, Ito Z, Kobayashi K, Yagi H, Hida T, et al.: How do spinal schwannomas progress? The natural progression of spinal schwannomas on MRI. J Neurosurg Spine 24:155–159, 2016
4. Arnautovic K, Arnautovic A: Extramedullary intradural spinal tumors: a review of modern diagnostic and treatment options and a report of a series. Bosn J Basic Med Sci 9 Suppl 1:S40–S45, 2009
5. Deutsch H, Haid RW, Rodts GE, Mummaneni PV: Postlaminectomy cervical deformity. Neurosurg Focus 15:E5, 2003
6. Garcia DM: Primary spinal cord tumors treated with surgery and postoperative irradiation. Int J Radiat Oncol Biol Phys 11:1933–1939, 1985
7. Ito K, Ando K, Kobayashi K, Tsushima M, Machino M, Ota K, et al.: Natural reduction in acute intratumoral hemorrhage of spinal schwannoma in the cauda equina. Nagoya J Med Sci 81:701–705, 2019
8. Kunnel Jomon M, Pepper J, O'Connor N, Price R: Regression of a spinal schwannoma after Pomalidomide. Br J Neurosurg:1-2, 2020.
9. Nakatomi H, Jacob JT, Carlson ML, Tanaka S, Tanaka M, Saito N, et al.: Long-term risk of recurrence and regrowth after gross-total and subtotal resection of sporadic vestibular schwannom. J Neurosurg:1-7, 2017.
10. Ozawa H, Kokubun S, Aizawa T, Hoshikawa T, Kawahara C: Spinal dumbbell tumors: an analysis of a series of 118 cases. J Neurosurg Spine 7:587–593, 2007
11. Romani R, Pollock J: Spontaneous shrinkage of vestibular schwannoma. Surg Neurol Int 7:59, 2016
12. Tish S, Habboub G, Lang M, Ostrom QT, Kruchko C, Barnholtz-Sloan JS, et al.: The epidemiology of spinal schwannoma in the United States between 2006 and 2014. J Neurosurg Spine:1-6, 2019.
13. von Eckardstein KL, Beatty CW, Driscoll CL, Link MJ: Spontaneous regression of vestibular schwannomas after resection of contralateral tumor in neurofibromatosis Type 2. J Neurosurg 112:158–162, 2010
14. Wolff RK, Frazer KA, Jackler RK, Lanser MJ, Pitts LH, Cox DR:

Analysis of chromosome 22 deletions in neurofibromatosis type 2-related tumors. Am J Hum Genet 51:478–485, 1992
15. Yasuda M, Bresson D, Cornelius JF, George B: Anterolateral approach without fixation for resection of an intradural schwannoma of the cervical spinal canal: technical note. Neurosurgery 65:1178–1181, 2009
16. Zong S, Zeng G, Xiong C, Wei B: Treatment results in the differential surgery of intradural extramedullary schwannoma of 110 cases. PLoS One 8:e63867, 2013

The Nerve

Case Report

The Nerve 2023;9(1):56-59
https://doi.org/10.21129/nerve.2022.00255
eISSN 2465-891X

Lumbar Calcifying Pseudoneoplasm as a Rare Cause of Cauda Equina Syndrome: A Case Report

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OPEN ACCESS

Received: December 18, 2022
Revised: February 3, 2023
Accepted: February 13, 2023

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A calcifying pseudo-tumor of the spine, also called calcifying pseudoneoplasm of the neuraxis (CAPNON), is a rare non-neoplastic lesion that can occur anywhere in the central nervous system. Although CAPNON shows tumor-like behavior, it is believed to be benign and of inflammatory-reactive origin. It may cause many neurologic symptoms by compressing adjacent structures. We report the case of a 45-year-old man who presented with cauda equina syndrome. Magnetic resonance imaging revealed a partially calcified mass compressing the spinal cord. Gross total resection was carried out and the patient's symptoms improved. Histopathology proved that the mass was CAPNON. Although spinal localization of CAPNON is rare, we should know and recognize this entity based on appropriate imaging findings because radical excision has an excellent prognosis.

Keywords: Calcinosis; Cauda equina syndrome; Lumbar vertebrae; Magnetic resonance imaging

INTRODUCTION

Calcifying fibrous pseudoneoplasm, also known as calcifying pseudoneoplasm of the neuraxis (CAPNON) when found in the central nervous system, are rare pathological entities that are benign non- neoplastic fibrous lesions[1,9,10,19]. It's usually found in patients who are above 50 years and, in some cases, is associated with neurofibromatosis type 2[4,5,14]. The disease may be found in the peritoneum, neck, mediastinum, breast, extremities, central nervous system, and spinal cord[11,12]. When the spine is involved, its most frequently located in cervical region followed by thoracic and lumber areas. CAPNON may be both intra- and extra-dural[16]. Pathogenesis of CAPNON is still unclear, however, it is thought of as reactive lesions with abundant hyalinized collagenous fibrous tissue with psammomatous or dystrophic calcification and focal lymphoplasmacytic infiltrate[3,7,13].

Patients who are diagnosed with CAPNON can have a variety of symptoms from no symptoms at all to myelopathies, depending on the location and compression of the surrounding neural structure[9,15]. Therefore, the management of CAPNON is largely dependent on the symptoms, and when patients show severe neurologic deficits, complete surgical removal is the treatment of choice[18]. Since CAPNON has excellent treatment outcomes when successfully removed, a thorough diagnostic screening needs to be carried out. Magnetic resonance imaging (MRI) is the modality of choice of investigation which shows hypo intense T1- and

T2-weighted images with limited edema and contrast enhancement[13,16,17].

We present a rare case of CAPNON in the lumbosacral region showing cauda equine syndrome, mimicking hourglass neurinoma or ependymoma.

CASE REPORT

A 45-year-old man came to the hospital emergency room (ER) with severe low back pain and motor weakness in both low extremities for 5 days (motor grade 3). Neurologic examination revealed altered sensations in his buttocks, inner thighs, backs of legs and feet, typically demonstrating saddle-like paresthesia in L5-S1 dermatome. He had also altered bowel and bladder habits prior to the visit to the ER. His overall symptoms suggested the possibility of cauda equina syndrome which could lead to a possible emergency operation and thus, was admitted to our neurosurgery department for further diagnostic evaluations.

MRI showed an intradural mass extending into the neural foramen where signals revealed partial calcification at the L5-S1 disc level (Fig. 1A, B). Surgical removal was carried out via laminectomy of L5 lamina to achieve clear access to intradural calcified lesions. The dura was incised vertically just above the mass. The incision was then extended just above and below the lesion to get a clear view of the tumor. The tumor was resting on the posterior dura, adhered with the fibers of S1 within the neural foramen.

During surgery, the nerve roots of the dural sac adjacent to the tumor were moved by gentle spatulation with a small dissector. The lesion had a fibrous consistency due to the presence of calcifications. There were no hemorrhagic focus and infiltration into the surrounding tissues. The mass was successfully removed without giving any injury to surrounding neurologic anatomy.

A biopsy was carried out with the mass acquired during surgery. It confirmed the diagnosis of CAPNON. The histopathological slide was stained for hematoxylin and eosin which showed positivity for the expression of factor XIIIa and vimentin and negativity for the expression of CD31, CD34, anaplastic lymphoma kinase (ALK)-1, smooth muscle actin (SMA), protein S100 and VIII factor (Fig. 2A, B).

On the first day after surgery the patient showed complete resolution of cauda syndrome. After three months, we performed a follow-up lumbosacral MRI with contrast which showed no recurrence (Fig. 3A, B). After 15 months, patients came for follow-up with no signs and symptoms of any re-

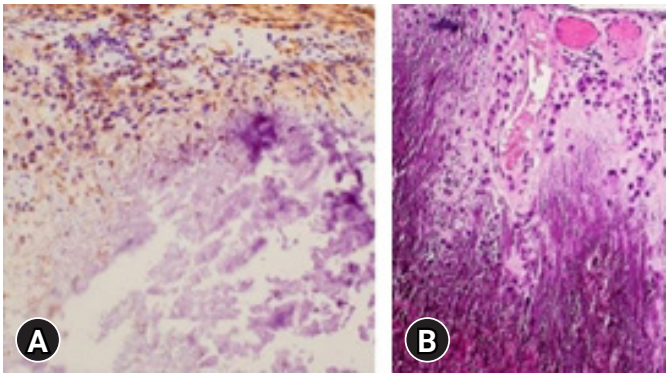

Fig. 2. (A) Histological findings include central calcification with surrounding chondroid matrix organized in a nodular pattern. There are palisade spindle cells around the nodules (hematoxylin and eosin stain [H&E], ×100 magnification). (B) Histological findings showing inflammatory cells in the fibrovascular stroma between chondromyxoid cells.

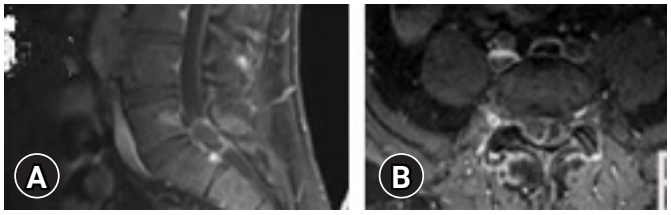

Fig. 1. (A) Preoperative sagittal T1-weighted magnetic resonance imaging (MRI) with gadolinium enhancement displaying the L5-S1 intradural neoplasm. (B) Preoperative axial T1-weighted MRI with gadolinium enhancement displaying the L5-S1 intradural neoplasm.

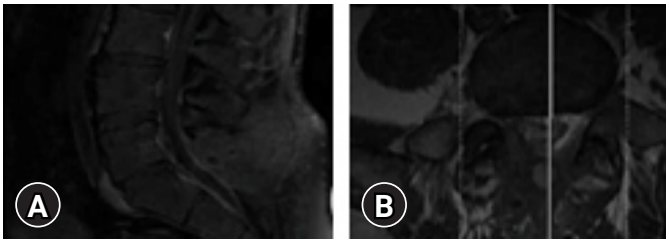

Fig. 3. (A) Postoperative sagittal T1-weighted MRI with gadolinium enhancement displaying no remnant tumor or recurrence. (B) Postoperative axial T1-weighted MRI with gadolinium enhancement displaying no remnant tumor or any recurrence.

current disease.

DISCUSSION

Calcifying fibrous pseudoneoplams occurring in the neuraxis is very rare. Nevertheless, it is rather more common for it to occur in the spine than in the brain[6,7]. To the author's knowledge, there are only 29 similar cases of CAPNON occurring in the spine so far (Table 1). According to previous studies, the tumor has a male preference occurring mostly in patients aging more than fifty and can be present in all levels of the spine[3]. The characteristics of the tumor also varied greatly from case to case, where it was interosseous, intradural, extradural and even intradural extramedullary[8,16].

CAPNON can only be diagnosed after a full histopathologic and immunohistochemical analysis[4,14,19]. It is difficult to suspect and diagnose the disease with only conventional imaging workup such as MRI, computed tomography (CT) scans and X-rays. The tumor usually displays partial calcifications on CT scans and on the MRI it usually shows a well-defined hypointense lesion in T1 and T2 weighted images along with limited hyperintensity after contrast enhancement T1 weighted imaging[13,15,20]. Due to these non-specific characteristics of the tumor, it is crucial for physicians to rule out other more common possible disease entities. Chondromas, chordomas, meningiomas and schwannomas were considered in the differential diagnosis for extra-axial localizations, while oligodendrogliomas and ganglioglioma for intra-axial localizations[3,12].

The typical histopathological characteristics of CAPNON are predominantly lymphoplasmacytic infiltrate with abundant hyalinized collagen, dystrophic calcifications, fibrous stroma with chondromixoid matrix, epithelioid cells arranged in palisades and similar inflammatory reaction with giant cells[3,7,16].

There have been some controversies regarding CAPNON being inflammatory or neoplastic. Pathologists had hypothesized that calcifying fibrous pseudotumor, as a slow-growing benign tumor, derived from inflammatory myofibroblastic tumor than from a typically inflammatory lesion[3]. The anatomopathologists in recent years have hypothesized that calcifying fibrous pseudotumor was true benign tumor entities without having an inflammatory origin because they did not present the characteristic immunohistochemical markers of inflammatory myofibroblastic tumors[2,14].

In the case presented in this study it showed similar results where it showed hyalinized leiomyoma (positive for smooth muscle markers, SMA, desmin, negative for the expression of factor XIII); Inflammatory myofibroblastic tumor (negative for SMA expression and only sporadically positive for Keratin and desmin expression, while always positive for the expression of factor XIIIa and ALK).

Table 1. Reported cases of calcifying pseudoneoplasm of the neuraxis located in the spinal cord

References	Year	Location of tumor	Recurrence	Neurologic outcome after surgery
Bertoni et al.[2]	1990	Lumbar	None	Improved
Fetsch et al.[4]	1993	Lumbar	None	Improved
Mayr et al.[15]	2000	Cervical and thoracic	None	Improved
Liccardo et al.[12]	2003	Dorsal	None	Improved
Aiken et al.[1]	2009	Dorsal	None	Not described
Mahapatra et al.[16]	2010	Lumber	None	Improved
Naidu et al.[17]	2012	Lumbar	None	Improved
Nathoo et al.[18]	2012	Lumbar	None	Improved
Stienen et al.[19]	2013	Lumber	None	Improved
Kocovski et al.[11]	2015	Lumbar	Not described	Not described
Lopes et al.[13]	2016	Lumbar	None	Improved
García Duque et al.[5]	2016	Cervical, dorsal, and lumbar	None	Improved
Gauden et al.[6]	2019	Cervical	None	Improved
Ho et al.[8]	2020	Cervical, dorsal, and lumbar	None	Variable
Ravi et al.[20]	2022	Lumbar	None	Improved

The data is presented as number (%) or mean ± standard deviation.
OPLL: ossification of the posterior longitudinal ligament.

The overall treatment outcome is known to be excellent with complete surgical removal[7]. Recurrences appeared rare even after complete or incomplete resection of the disease[3,7]. Stienen et al.[19] found no recurrence of lesion in 92.3% of the cases.

CONCLUSION

CAPNON is a rare but benign tumor now considered an autonomous anatomopathological entity. Neurosurgeons should be aware of the disease and recognize this entity through conventional image workups and histopathologic outcomes because radical excision determines an excellent prognosis.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Aiken AH, Akgun H, Tihan T, Barbaro N, Glastonbury C: Calcifying pseudoneoplasms of the neuraxis: CT, MR imaging, and histologic features. AJNR Am J Neuroradiol 30:1256–1260, 2009
2. Bertoni F, Unni KK, Dahlin DC, Beabout JW, Onofrio BM: Calcifying pseudoneoplasms of the neural axis. J Neurosurg 72:42–48, 1990
3. Chorti A, Papavramidis TS, Michalopoulos A: Calcifying fibrous tumor: Review of 157 patients reported in international literature. Medicine (Baltimore) 95:e3690, 2016
4. Fetsch JF, Montgomery EA, Meis JM: Calcifying fibrous pseudotumor. Am J Surg Pathol 17:502–508, 1993
5. García Duque S, Medina Lopez D, Ortiz de Méndivil A, Diamantopoulos Fernández J: Calcifying pseudoneoplasms of the neuraxis: Report on four cases and review of the literature. Clin Neurol Neurosurg 143:116–120, 2016
6. Gauden AJ, Kavar B, Nair SG: Calcifying pseudoneoplasm of the neuraxis: A case report and review of the literature. J Clin Neurosci 70:257–259, 2019
7. Hill KA, Gonzalez-Crussi F, Chou PM: Calcifying fibrous pseudotumor versus inflammatory myofibroblastic tumor: a histological and immunohistochemical comparison. Mod Pathol 14:784–790, 2001
8. Ho ML, Eschbacher KL, Paolini MA, Raghunathan A: New insights into calcifying pseudoneoplasm of the neuraxis (CAPNON): a 20-year radiological-pathological study of 37 cases. Histopathology 76:1055–1069, 2020
9. Hodges TR, Karikari IO, Nimjee SM, Tibaleka J, Friedman AH, Cummings TJ, et al.: Calcifying pseudoneoplasm of the cerebellopontine angle: case report. Neurosurgery 69:onsE117–onsE120, 2011
10. Kerr EE, Borys E, Bobinski M, Shahlaie K: Posterior fossa calcifying pseudoneoplasm of the central nervous system. J Neurosurg 118:896–902, 2013
11. Kocovski L, Parasu N, Provias JP, Popovic S: Radiologic and histopathologic features of calcifying pseudoneoplasm of the neural axis. Can Assoc Radiol J 66:108–114, 2015
12. Liccardo G, Lunardi P, Menniti A, Floris R, Pastore FS, Fraioli B: Calcifying pseudo-tumor of the spine: description of a case and review of the literature. Eur Spine J 12:548–551, 2003
13. Lopes AJ, Brock RS, Martins TG, de Medeiro RS, Montezzo D, de Oliveira MF, et al.: Intradural calcifying pseudoneoplasm of the neuraxis presenting as a cauda equina syndrome. Surg Neurol Int 7:S1102–S1105, 2016
14. Maeda A, Kawabata K, Kusuzaki K: Rapid recurrence of calcifying fibrous pseudotumor (a case report). Anticancer Res 22:1795–1797, 2002
15. Mayr MT, Hunter S, Erwood SC, Haid RW: Calcifying pseudoneoplasms of the spine with myelopathy. Report of two cases. J Neurosurg 93:291–293, 2000
16. Mohapatra I, Manish R, Mahadevan A, Prasad C, Sampath S, Shankar SK: Calcifying pseudoneoplasm (fibro osseous lesion) of neuraxis (CAPNON) - a case report. Clin Neuropathol 29:223–226, 2010
17. Naidu PK, Patel SC: Calcifying pseudoneoplasm of the neural axis arising within the lumbar spine: Implications of unique cross-sectional imaging characteristics of a rare spinal column lesion. Neurographics 2:27–30, 2012
18. Nathoo N, Viloria A, Iwenofu OH, Mendel E: Calcifying fibrous tumor of the spine. World Neurosurg 77:592.e1-592.e4, 2012
19. Stienen MN, Abdulazim A, Gautschi OP, Schneiderhan TM, Hildebrandt G, Lücke S: Calcifying pseudoneoplasms of the neuraxis (CAPNON): clinical features and therapeutic options. Acta Neurochir (Wien) 155:9–17, 2013
20. Ravi V, Srinath P: A rare case of calcifying pseudoneoplasms of the neural axis in lumbar spine. Indian J Neurosurg 11:177–178, 2021

The Nerve

Case Report

The Nerve 2023;9(1):60-68
https://doi.org/10.21129/nerve.2023.00283
eISSN 2465-891X

Extensive Central Nervous System Lymphoma Detected at the Time of Diagnosis of Chronic Lymphocytic Leukemia – An Isolated Central Nervous System Richter's Syndrome: A Case Report

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Received: February 10, 2023
Revised: February 17, 2023
Accepted: February 24, 2023

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When a central nervous system (CNS) lesion is found in patients with chronic lymphocytic leukemia (CLL), the diagnostic possibilities include CNS involvement of CLL, transformation to a large B-cell lymphoma (Richter's syndrome [RS]), or the coincidental presence of another tumorous or non-tumorous disease. CNS RS commonly occurs in preexisting CLL with other nodal/extra-nodal involvement, but it is extremely rare to find isolated CNS RS concurrently with the initial diagnosis of CLL. A 73-year-old woman presented with a headache and findings from another hospital of an elevated white blood cell count and intraventricular masses. A peripheral blood smear and a bone marrow biopsy revealed CLL. Brain magnetic resonance imaging with gadolinium enhancement showed a suprasellar mass and a pineal mass within the third ventricle, as well as extensive leptomeningeal enhancement. Whole-body fluorodeoxyglucose proton emission tomography-computed tomography showed no hot uptake except for the brain lesions. Cerebrospinal fluid cytology showed small atypical lymphocytes suggestive of CLL involvement. However, an endoscopic biopsy of the third-ventricle mass demonstrated diffuse large B-cell lymphoma. After 3 months of systemic high-dose methotrexate, all preexisting lesions disappeared, but new hemorrhagic masses were found in the right lateral ventricle and the fourth ventricle. The patient received palliative cranial radiotherapy but died 6 months after the initial diagnosis. Accurate CNS tissue diagnosis and appropriate treatment are critical.

Keywords: B-cell; Central nervous system neoplasms; Leukemia; Lymphocytic; Lymphoma; Large B-cell

INTRODUCTION

When a central nervous system (CNS) lesion is found in patients with chronic lymphocytic leukemia (CLL), it is rarely diagnosed as CNS involvement of leukemic cells, which is known to occur mostly in cases of acute lymphoblastic

leukemia. Richter's syndrome (RS) refers to the transformation of CLL to diffuse large B-cell lymphoma (DLBCL), which occurs in 90% to 95% of cases or other aggressive lymphomas[15]. Otherwise, other CNS malignancies, non-tumorous diseases, and so on can be considered. RS is rare and it occurs in approximately 5% of CLL cases[10]. The CNS involvement of RS can also be considered if the CNS lesion is confirmed to be a DLBCL. CNS RS commonly occurs with latency in the preexisting CLL or with systematic RS[13]. We introduce an extremely rare case of an isolated CNS DLBCL without other systemic RS at the time of the initial diagnosis of CLL, which was at first confused as a CNS involvement of CLL.

CASE REPORT

A 73-year-old woman with a history of diabetes mellitus and hypertension visited our hospital because of elevated white blood cell count and intraventricular masses (Fig. 1A), which were detected during a medical examination conducted at another hospital with a headache. Also, she has been complaining of general weakness but without a

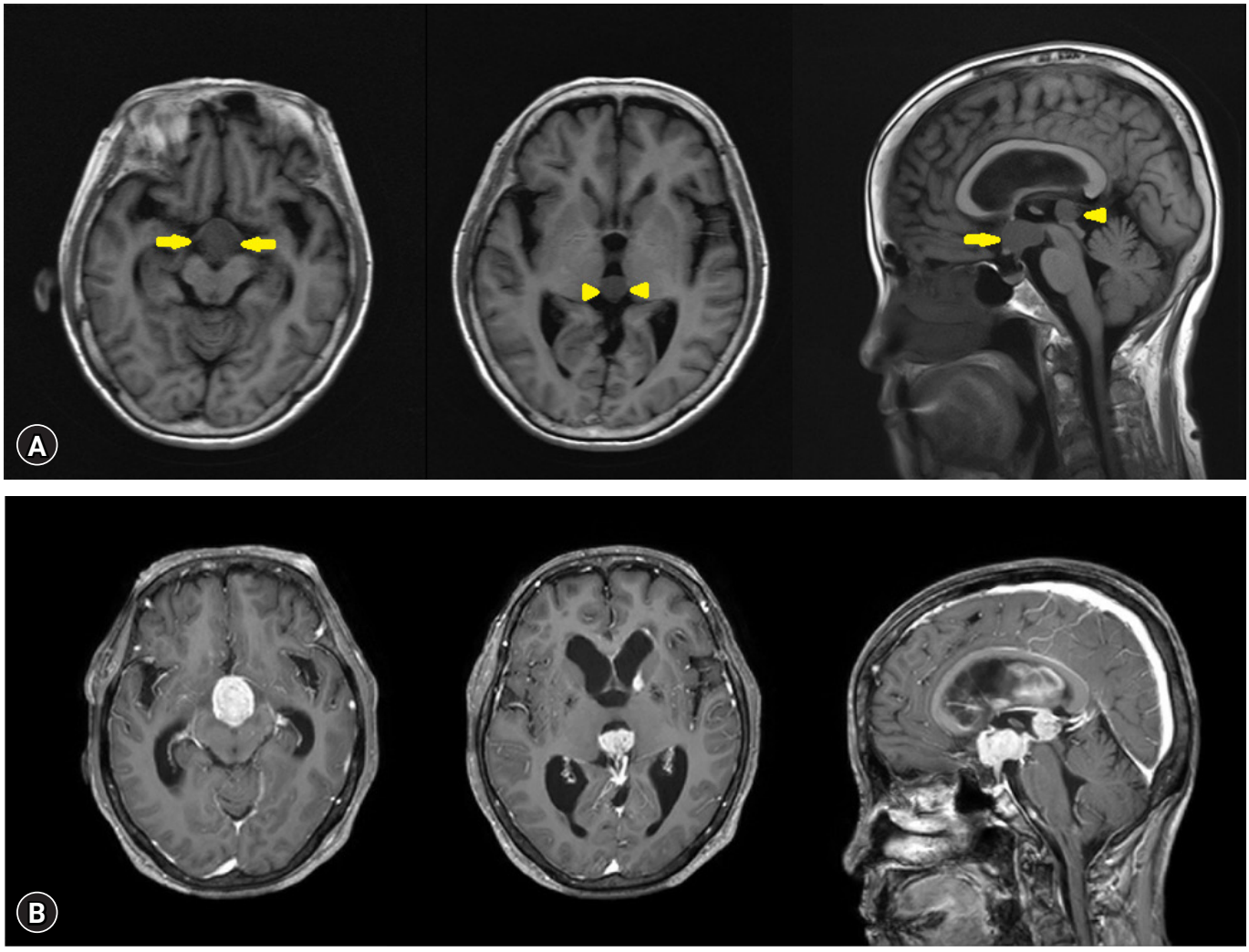

Fig. 1. Brain magnetic resonance imaging. (A) Initial T1-weighted image (WI) without enhancement performed at outside hospital showed a suprasellar mass (2.0 x 1.8 cm size; arrow) and a pineal mass (1.2 x 1.2 cm size; arrow head) in the 3rd ventricle. (B) Gadolinium enhanced T1-WI performed 8 days later showed that suprasellar mass (2.4 x 2.1 cm size) and pineal area mass (1.7 x 1.5 cm size) in the 3rd ventricle increased in size, and enhancements in the left caudate nucleus, left lateral ventricle wall, septum pellucidum, pituitary stalk, anterior surface of ponto-medulla.

specific neurological deficit. In our examination, her white blood cell count was 129,800/mm^3 with 90% lymphocytes, hemoglobin of 12.7 g/dL, hematocrit of 37.8%, platelet count of 157 × 10^9 /L, and lactate dehydrogenase of 226 IU/L (normal range, 120–250 IU/L). Her serum sodium level was very low at 119 mEg/L, and the basal hormonal study revealed panhypopituitarism. Her body temperature was 36.4°C. Brain magnetic resonance imaging (MRI) with gadolinium enhancement showed a suprasellar mass with a size of 2.4 × 2.1 cm, a pineal mass with a size of 1.7 × 1.5 cm within the 3rd ventricle, and enhancements in the left caudate nucleus, septum pellucidum, left lateral ventricle wall, pituitary stalk, clivus, inferior wall of the 4th ventricle, anterior surface of the ponto-medulla (Fig. 1B). Compared to the non-enhanced brain MRI performed at another hospital 8 days prior, the recent MRI showed that tumors in the 3rd ventricle increased in size and progression of hydrocephalus. The systemic evaluation was performed including whole-body fluorodeoxyglucose (FDG) positron emission tomography (PET)/ computed tomography (CT) and no hot uptake lesion was observed except the brain lesions (SUVmax 20.2) (Fig. 2). Lymph node (LN) enlargement or other extranodal lesions were not found.

Peripheral blood smear presented severe leukocytosis

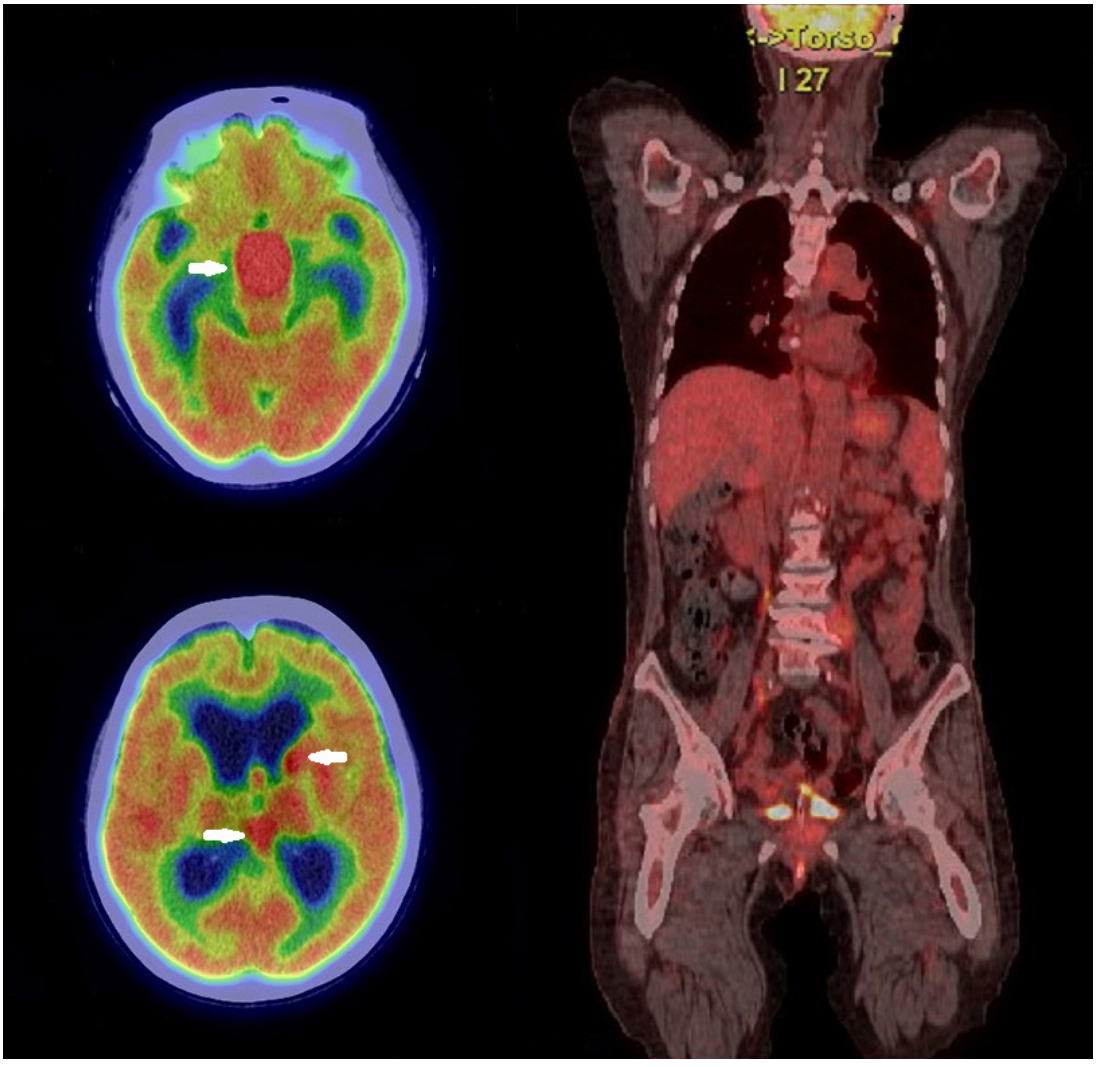

Fig. 2. Whole-body fluorodeoxyglucose positron emission tomography/computed tomography presented multiple variable sized masses with hypermetabolism (arrows) including suprasellar area, pineal gland and left caudate nucleus. Other hot uptake lesion was not observed in the body except the brain lesions.

made up of 90% of mature lymphocytes. Bone marrow (BM) biopsy revealed small mature lymphocytes with 80.6% being all marrow cells and concluded the development of CD5-positive small B-cell lineage CLL (Fig. 3A). Immunofluorescence exhibited CD3+(focal), CD5+, CD19+, CD20+, CD22+, CD45+, CD10-, CD23-, with ki-67 of 10% (Fig. 3B). A chromosomal study of BM lymphocytes showed an add 4p MAR, but without other CLL-related poor prognostic factors, such as deletion 17p, deletion 11q, or transformation.

For the CNS lesions, CNS involvement of CLL, germ cell tumor, CNS lymphoma, and so on were considered differential diagnoses. Cerebrospinal fluid (CSF) analysis via lumbar puncture showed the following results: red blood cell count of 100/μL, white blood cell count of 300/μL (poly, 1%; mono, 99%), protein level of 143.87 mg/dL, and glucose level of 12 mg/dL, and α-fetoprotein, human chorionic gonadotropin, and Epstein–Barr virus (EBV) DNA-polymerase chain reaction showed negative findings. CSF cytology showed small atypical lymphocytes, which is most likely indicative of leptomeningeal involvement in CLL. Since the patient did not have LN adenopathy, anemia, thrombocytopenia, and hepatosplenomegaly, CLL corresponds to Rai stage 0 and Binet stage A (Table 1)[1,18], both showing a low risk. With only aggressive involvement in CNS, it was necessary to ensure the CNS etiology. The patient underwent endoscopic biopsy for a suprasellar mass in the 3rd ventricle through the right Kocher's point and Ommaya reservoir implantation. On intraoperative finding, the mass in the 3rd ventricle appeared very hypervascular with a red surface (Fig. 4). Pathology result showed DLBCL (Fig. 5A). In situ hybridization for

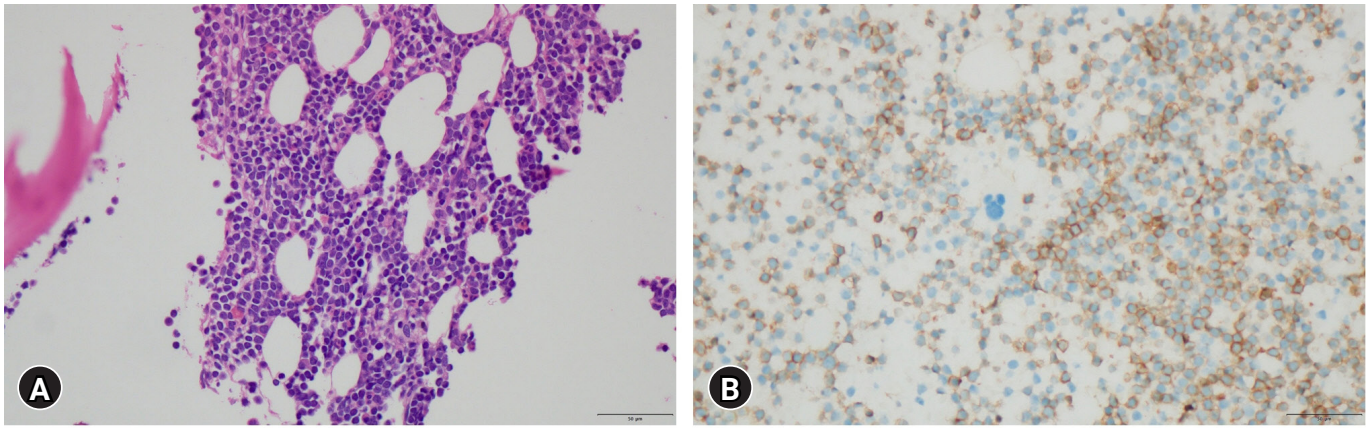

Fig. 3. Bone marrow aspiration findings. (A) Hematoxylin-eosin (H & E) staining (x400): small lymphocytes are counted up to 80.6% of all marrow cells. (B) Immunofluorescence by flow cytometry (x400): CD5 positive small B-cell lineage chronic lymphocytic leukemia.

Table 1. Clinical staging system of chronic lymphocytic leukemia

Staging system	Risk	Characteristics
Rai stage		
Stage 0	Low	Lymphocytosis alone (absolute lymphocytes ≥ 15,000/mm^3 in blood and ≥ 40% lymphocytes in marrow)
Stage I	Intermediate	Lymphocytosis + lymphadenopathy
Stage II	Intermediate	Lymphocytosis + spleen and/or liver enlargement
Stage III	High	Lymphocytosis + anemia (hemoglobin < 11 g/dL)
Stage IV	High	Lymphocytosis + thrombocytopenia (platelet count < 100 x 10^9 /L)
Binet stage		
Stage A	Low	<3 areas of lymphoid tissue enlarged, without anemia (hemoglobin < 10 g/dL) or thrombocytopenia (platelet count < 100 x 10^9 /L)
Stage B	Intermediate	≥3 areas of lymphoid tissue enlarged, without anemia or thrombocytopenia
Stage C	High	Anemia and/or thrombocytopenia present

EBV was negative. Disconcordantly with BM, immunohistochemical (IHC) staining of the 3rd ventricle mass showed CD10+, CD20+, CD3-, CD5-, CD23-, CD30-, SOX11- Bcl2-, and Bcl6- with ki-67 of 80% (Fig. 5B).

With administering 4 mg of dexamethasone every 6 hr for 9 days, suprasellar and pineal masses had already begun to decrease in size at postoperative serial brain CT/diffusion MRI, even before the chemotherapy was started. The patient underwent 3 cycles of systemic high-dose methotrexate. After 3 months of treatment, generalized tonic-clonic seizure occurred and a follow-up brain MRI showed that all the preexisting lesions have disappeared, but new hemorrhagic masses of approximately 1 cm were found in the posterior horn of the right lateral ventricle (Fig. 6A) and in the left superior wall of the 4th ventricle (Fig. 6B). In the CSF analysis, atypical lymphoid cells were detected at every examination during the treatment period. Due to the patient's poor general condition, additional chemotherapy was not performed and palliative intensity-modulated radiation therapy (33 Gy/15 fx) for the whole ventricle was performed. The patient has been in a bed-ridden state due to general weakness since the initial diagnosis of CLL and suffered from medical comorbidities. She died 6 months after the initial diagnosis.

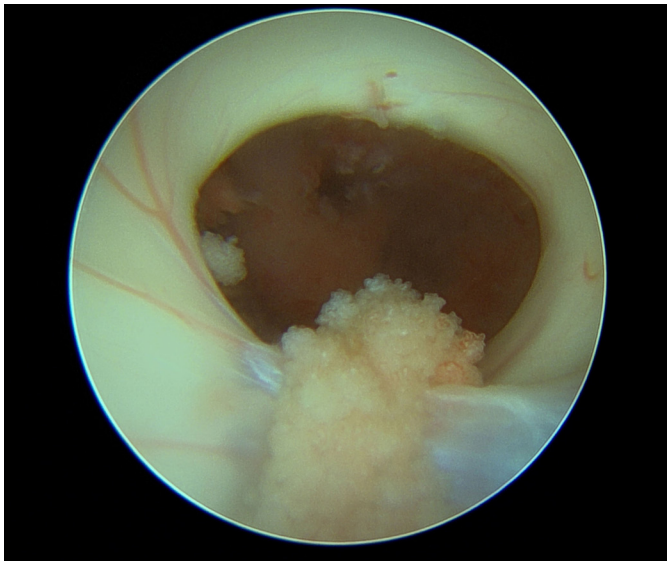

Fig. 4. Endoscopic finding of Foramen Monro (right lateral ventricle) and 3rd ventricle mass. The surface of the intraventricular mass is very hypervascular with red color.

DISCUSSION

The incidence of CNS involvement in CLL is 0.4% to 2% of cases diagnosed with clinical symptoms and 7% to 71% of cases found in autopsy as asymptomatic, which is highly subclinically present[20,23]. The incidence of overall RS in CLL is known to be approximately 5%[10]. LN or BM infiltration at the time of large cell transformation is typical with/without extranodal involvement. Particularly, it is extremely rare that the site localized to a single extranodal site is CNS[24,25]. According to previous data involving 4,147 CLL patients from the Mayo Clinic, there were 15 (0.3%) and 18 (0.4%) patients diagnosed with isolated CNS RS and CNS involvement in CLL, respectively[20]. Of the 204 CLL RS patients, 4 patients (2.0%) had isolated CNS RS out of 11 (5.4%) patients with

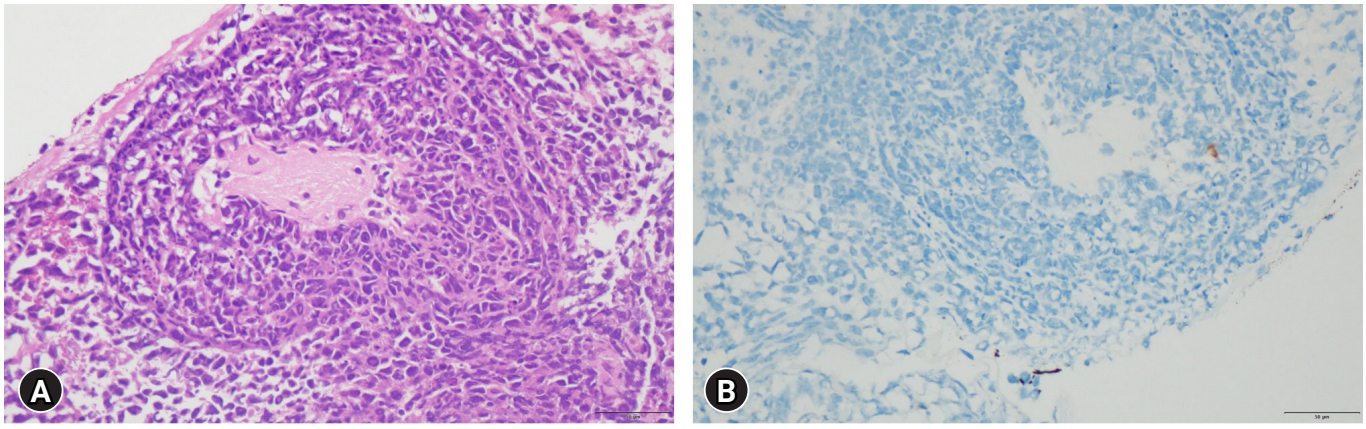

Fig. 5. Pathologic findings of 3rd ventricle mass. (A) Hematoxylin-eosin (H & E) staining (x400) revealed diffuse large B-cell lymphoma. (B) Immunohistochemical stain (x400) showed negative CD5 stain, disconcordant with bone marrow finding.

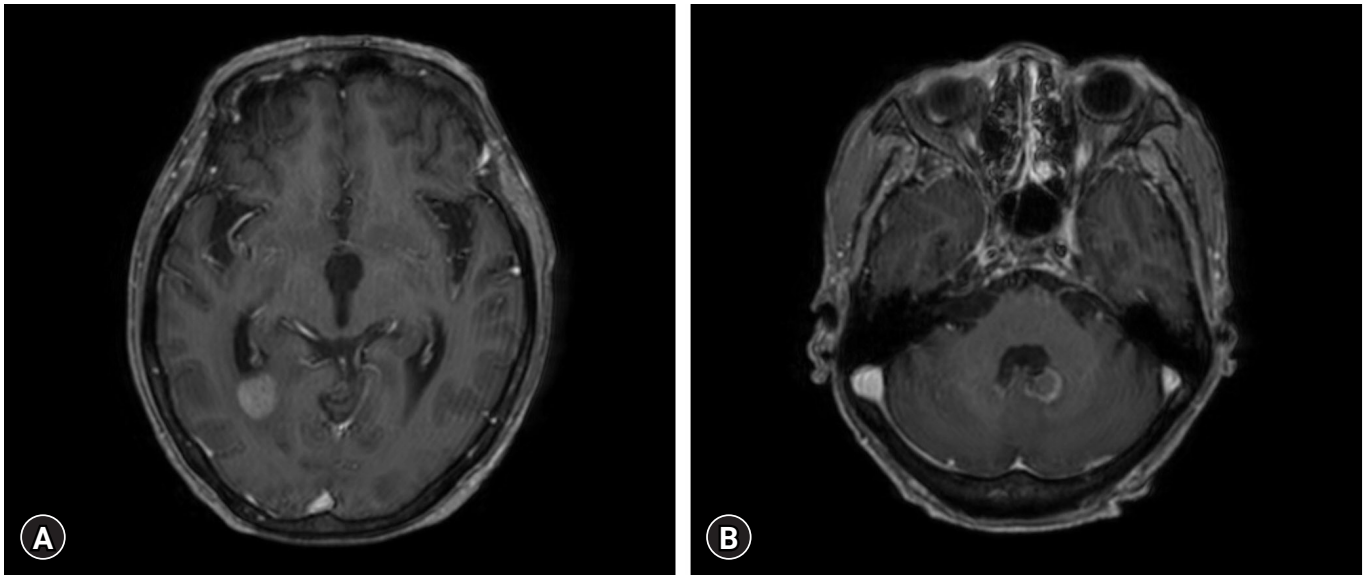

Fig. 6. After 3 months of treatment, brain magnetic resonance imaging with gadolinium enhancement presented all the preexisting lesions have disappeared, but new hemorrhagic masses of approximately 1 cm were found in the (A) posterior horn of the right lateral ventricle and (B) left superior wall of the 4th ventricle.

biopsy-proven CNS RS[5]. CNS involvement in both CLL and RS commonly occurs with latency in preexisting CLL[13]. It is extremely rare that isolated CNS RS is found simultaneously at the initial diagnosis of CLL, as our patient. Among the 19 isolated CNS RS cases reported by 2022, four were diagnosed simultaneously with the initial diagnosis of CLL[7,21,24,25].

CNS involvement in CLL/RS can present with visual changes(22%), encephalopathy (29%), and weakness with paresthesia (22%)[16]. Symptoms are based on the location of the lesion, both favor spreading via leptomeninges. If CNS symptoms occur in CLL patients, CSF analysis, and imaging studies such as brain MRI, are performed for differential diagnosis. Whole-body FDG-PET can help evaluate the existence of any systemic involvement. In our patient, CSF cytology and brain biopsy results showed a discrepancy. Patients diagnosed only by CSF analysis and/or brain MRI without biopsy confirmation may have been misdiagnosed. The true incidence of CNS CLL/RS may be different from the already reported incidence. Among the 31 symptomatic CLL patients with CSF analysis demonstrating the presence of CLL B-cells, 18 (58%) had an alternative diagnosis after tissue biopsy. This included CNS infections in 8 patients, autoimmune/inflammatory process in 5, metastatic cancer in 1, and non-CLL-related etiology in 4[20].

The IHC staining showed that the CLL cells in BM and DLBCL on brain biopsy showed slightly different surface markers, indicating different immunophenotypes. If different immunophenotypes are shown, there are both possibilities originating from the identical B-cell clonality, or activating from different clonality, and the definition of RS broadly includes both of these cases[22,24,25]. The type of clonal pattern has an impact on prognosis; clonally related RS has a dismal outcome, is resistant to chemotherapy, and has a median survival of approximately 12 months, whereas clonally unrelated RS has a median survival of 65 months[9,11]. Unfortunately, in our patient, immunoglobulin heavy chain rearrangement studies were not performed on the BM and brain specimen; thus, we cannot determine whether BM CLL and the CNS DLBCL had identical clonality.

In the case of CNS involvement in CLL/RS, most cases occur over a period of latency in preexisting CLL[13]. However, our patient presented isolated CNS RS simultaneously when CLL was initially diagnosed. Compared to the relatively stable systemic CLL, only CNS lesions progressed rapidly and extensively. Of the 19 reported isolated CNS RS cases, data were available for 10 patients, including 8 with Binet stage A, 2 with Binet stage B, and no patient with advanced Binet stage[7,21,25]. Our patient had Binet stage A, Rai stage 0 without LN adenopathy, splenomegaly, and thrombocytopenia, but she did not have other suspected clinical RS symptoms,

such as fever and elevation of serum LDH level. It may be difficult to suspect the first chance that isolated CNS RS occurred alone without other nodal/extranodal lesion[13]. Most studies suggest that there is no clear association between the Rai and Binet stages of CLL and CNS involvement in CLL/RS[6,14,23]. Although there is only a small number of cases, isolated CNS involvement, including our patient, seems to be independent of the CLL stage. However, if not limited to CNS, the advanced Rai/Binet stage is included as a risk factor for overall RS occurrence from CLL. Several studies have identified biological characteristics of CLL associated with an increased risk of RS: CD38, CD49d, and Zap-70 expression, unmutated IGHV, del11q, del17p, trisomy 12, complex karyotype, loss of cell cycle inhibitors CDKN1A/CDKN2A/CDKN1B, deletion of the p53/Rb/p27genes, mutations of the SAMHD1/XPO1/MED12/NOTCH1/MYC genes, overexpression of ZAP70/BCL2/LRP4 genes, decreased expression of MYBL1, and so on[5,9,25].

Negative Bcl-2 and positive Bcl-6 are related to better outcomes in cases with CNS lymphoma[2]. Furthermore, the existence of MYD88L265P and CD79b mutation, which are the major genetic abnormalities of primary CNS lymphoma, provided a therapeutic target and better outcomes[8,21].

It is known that long-term survival with a median survival of 111 months is possible among patients with normal karyotype CLL[4]. However, in the case of CNS involvement in CLL, a shortening of survival from 3 months to 3 years is observed[6]. A study showed a median survival of 12 (15 patients) and 11 (18 patients) months in the cohort with CLL and RS CNS involvement, respectively[20]. There was a trend toward better survival in those with CNS CLL as compared to those with CNS DLBCL[13]. In those with untransformed CLL presenting in the CNS, 14 of 23 (58%) patients were alive at the time of follow-up (median, 12 months), as compared to only 6 of 15 (33%) with RS and prior CLL alive at the time of follow-up (median, 3 months)[13].

Aside from CNS involvement, RS itself is a fatal complication of CLL, with an average survival of 8 to 12 months[3,12]. A previous study of 204 patients with RS from CLL as confirmed by biopsy showed overall survival (OS) of 9.4 months for 15 CNS RS patients[5]. The median OS of 16 isolated CNS RS cases was 6 months, which was shorter than that for other sites of RS (8 months)[19]. Since most cases are diagnosed with CNS RS after a latency period with preexisting CLL, it is difficult to derive an average survival rate using only the data obtained from an extremely small number of cases, which had a simultaneous diagnosis of isolated CNS RS when CLL was initially diagnosed.

Our patient survived for 6 months after the initial diagnosis of CNS RS, which is thought to correspond to the conventional survival of CNS RS. Five CNS RS patients who concurrently had CLL also showed a median OS of 5 months[13]. In addition to the survival rate itself, it is thought that neurological deficits due to CNS lesion reduced the patient's performance status, limiting the application of other treatments and affecting the patient's quality of life throughout his/her lifetime.

Both CLL and RS CNS involvement are rare entities, and no gold standard treatment or first-line regimen has been defined. The treatments include intrathecal/intravenous chemotherapy, radiation therapy, and stem cell transplantation. Established therapy for primary CNS lymphoma can be applied to treat CNS RS, which includes intravenous/intrathecal high-dose methotrexate combined with rituximab (chimeric anti-CD20 monoclonal antibody). Additionally, an intrathecal regimen, such as methotrexate, cytarabine, and corticosteroid, can be used, which is the treatment for leptomeningeal diseases in CLL[7,16]. Chemoimmunotherapy with the combination of fludarabine, cyclophosphamide, rituximab, ibrutinib (a selective inhibitor of Bruton tyrosine kinase), and/or Venetoclax (a selective inhibitor of BCl-2) may be considered[17]. One patient underwent 1 cycle of temozolomide and whole-brain radiation therapy without conventional chemotherapy due to old age. She survived for approximately 11 months from the initial diagnosis of CLL with concurrent CNS RS[7]. Treatment effects can be determined by image and CSF clearance. The results are generally disappointing because of the chemoresistance and poor performance status of patients to continue the therapy[25]. CNS RS, especially isolated CNS RS, is a rare entity and more case collection and analysis will help establish its future treatment strategy.

CONCLUSION

In CLL patients, both CLL and RS (DLBCL) CNS involvement are rare, and the presence of CNS RS with the initial diagnosis of CLL is extremely rare. Both diseases can be difficult to distinguish in terms of B-cell lymphocytes. Appropriate treatment should be selected through rapid and exact

CNS tissue diagnosis.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Binet JL, Vaugier G, Dighiero G, d'Athis P, Charron D: Investigation of a new parameter in chronic lymphocytic leukemia: the percentage of large peripheral lymphocytes determined by the Hemalog D. Prognostic significance. Am J Med 63:683–688, 1977
2. Chen L, Adar R, Yang X, Monsonego EO, Li C, Hauschka PV, et al.: Gly369Cys mutation in mouse FGFR3 causes achondroplasia by affecting both chondrogenesis and osteogenesis. J Clin Invest 104:1517–25, 1999
3. Eswarakumar VP, Monsonego-Ornan E, Pines M, Antonopoulou I, Morriss-Kay GM, Lonai P: The IIIc alternative of Fgfr2 is a positive regulator of bone formation. Development 129:3783–93, 2002
4. Hoshino Y, Takechi M, Moazen M, Steacy M, Koyabu D, Furutera T, et al.: Synchondrosis fusion contributes to the progression of postnatal craniofacial dysmorphology in syndromic craniosynostosis. J Anat 242:387–401, 2023
5. Kawakami M, Yamamura K: Cranial bone morphometric study among mouse strains. BMC Evol Biol 8:73, 2008
6. Kolpakova-Hart E, McBratney-Owen B, Hou B, Fukai N, Nicolae C, Zhou J, et al.: Growth of cranial synchondroses and sutures requires polycystin-1. Dev Biol 321:407–19, 2008
7. Kronenberg HM: Developmental regulation of the growth plate. Nature 423:332–6, 2003
8. Laurita J, Koyama E, Chin B, Taylor JA, Lakin GE, Hankenson KD, et al.: The Muenke syndrome mutation (FgfR3P244R) causes cranial base shortening associated with growth plate dysfunction and premature perichondrial ossification in murine basicranial synchondroses. Dev Dyn 240:2584–96, 2011
9. Lieberman DE, Hallgrímsson B, Liu W, Parsons TE, Jamniczky HA: Spatial packing, cranial base angulation, and craniofacial shape variation in the mammalian skull: testing a new model using mice. J Anat 212:720–35, 2008
10. Lieberman DE, Ross CF, Ravosa MJ: The primate cranial base: ontogeny, function, and integration. Am J Phys Anthropol Suppl 31:117–69, 2000
11. Liu J, Nam HK, Campbell C, Gasque KC, Millán JL, Hatch NE: Tissue-nonspecific alkaline phosphatase deficiency causes abnormal craniofacial bone development in the Alpl(-/-) mouse model of infantile hypophosphatasia. Bone 67:81–94, 2014
12. Macholán M, Mikula O, Vohralík V: Geographic phenetic variation of two eastern-Mediterranean non-commensal mouse species, Mus macedonicus and M. cypriacus (Rodentia: Muridae) based on traditional and geometric approaches to morphometrics. Zool Anz 247:67–80, 2008
13. Maga AM, Navarro N, Cunningham ML, Cox TC: Quantitative trait loci affecting the 3D skull shape and size in mouse and prioritization of candidate genes in-silico. Front Physiol 6:92, 2015
14. Nagata M, Nuckolls GH, Wang X, Shum L, Seki Y, Kawase T, et al.: The primary site of the acrocephalic feature in Apert Syndrome is a dwarf cranial base with accelerated chondrocytic differentiation due to aberrant activation of the FGFR2 signaling. Bone 48:847–56, 2011
15. Ochiai T, Nagayama M, Nakamura T, Morrison T, Pilchak D, Kondo N, et al.: Roles of the primary cilium component Polaris in synchondrosis development. J Dent Res 88:545–50, 2009
16. Panda SP, Guntur AR, Polusani SR, Fajardo RJ, Gakunga PT, Roman LJ, et al.: Conditional deletion of cytochrome p450 reductase in osteoprogenitor cells affects long bone and skull development in mice recapitulating antley-bixler syndrome: role of a redox enzyme in development. PLoS One 8:e75638. 2013
17. Perlyn CA, DeLeon VB, Babbs C, Govier D, Burell L, Darvann T, et al.: The craniofacial phenotype of the Crouzon mouse: analysis of a model for syndromic craniosynostosis using three-dimensional MicroCT. Cleft Palate Craniofac J 43:740–8, 2006
18. Rai KR, Sawitsky A, Cronkite EP, Chanana AD, Levy RN, Pasternack BS: Clinical staging of chronic lymphocytic leukemia. Blood 46:219–234, 1975
19. Singh N, Dutka T, Devenney BM, Kawasaki K, Reeves RH, Richtsmeier JT: Acute upregulation of hedgehog signaling in mice causes differential effects on cranial morphology. Dis Model Mech 8:271–9, 2015
20. Tsukamoto Y, Kajii TS, Oonishi Y, Sugawara-Kato Y, Hirabayashi Y, Iida J: Growth and development of the cranial base in mice that spontaneously develop anterior transverse crossbite. Am J Orthod Dentofacial Orthop 134:676–83, 2008
21. Vora SR: Mouse models for the study of cranial base growth and anomalies. Orthod Craniofac Res 20 Suppl 1:18–25, 2017
22. Vora SR, Camci ED, Cox TC: Postnatal ontogeny of the cranial base and craniofacial skeleton in male C57BL/6J mice: A reference standard for quantitative analysis. Front Physiol 6:417, 2015
23. Wei X, Hu M, Mishina Y, Liu F: Developmental regulation of the

growth plate and cranial synchondrosis. J Dent Res 95:1221–9, 2016
24. Wei X, Thomas N, Hatch NE, Hu M, Liu F: Postnatal craniofacial skeletal development of female C57BL/6NCrl mice. Front Physiol 8:697, 2017
25. Xu L, Song JC, Sun XH, Gao ZF, Lv L, Zhu J: Richter's syndrome of the central nervous system diagnosed concurrently with chronic lymphocytic leukaemia: A case report and literature review. Medicine (Baltimore) 97:e12701. 2018

The Nerve

Case Report

The Nerve 2023;9(1):69-74
https://doi.org/10.21129/nerve.2023.00262
eISSN 2465-891X

Ventriculitis Associated with Invasive *Klebsiella Pneumoniae* Syndrome: A Case Report

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OPEN ACCESS

Received: January 9, 2023
Revised: March 8, 2023
Accepted: March 10, 2023

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Invasive *Klebsiella pneumoniae* syndrome is defined as community-acquired liver abscess and metastatic infections in the lung, soft tissue, and central nervous system (CNS) caused by hypervirulent *Klebsiella pneumoniae*. Metastatic CNS infection in invasive *Klebsiella pneumoniae* syndrome shows rapid clinical deterioration and a high mortality rate. We present a case of ventriculitis caused by invasive *Klebsiella pneumoniae* syndrome successfully treated with a timely diagnosis, immediate surgical intervention, and administration of antibiotics.

Keywords: Drainage; Klebsiella pneumoniae; Magnetic resonance imaging; Ventriculitis

INTRODUCTION

Klebsiella pneumoniae is a gram-negative, anaerobic bacillus, a well-known nosocomial and community-acquired pathogen causing respiratory, urinary, and hepatobiliary infections[3,6,8]. Among them, hypervirulent strains have been reported to cause community-acquired liver abscesses and metastatic infections in lung, prostate, soft tissue, eye, and central nervous system (CNS) in non-immunocompromised individuals, defined as invasive *Klebsiella pneumoniae* syndrome (IKPS)[8]. The rate of metastatic infection ranges from 3.5% to 20%[6] with a mortality rate of 3% to 42%[8]. CNS infection shows a higher mortality rate 40% to 50%[7] than other metastatic infections[8]. It presents mostly as meningitis, encephalitis or cerebral abscess, and presenting primarily as ventriculitis or ventricular empyema is rare[7]. We present a case of IKPS with ventriculitis successfully treated with a timely injection of antibiotics and surgical intervention.

CASE REPORT

A 50-year-old male with no previous medical history came into the emergency room with acute mental status change with a Glasgow Coma Scale (GCS) score of 13. His mother

stated he presented with hemoptysis two weeks ago, subsequently a high fever of 39°C and right upper quadrant abdominal pain two days ago. He began to show disorientation and confusion a day ago. His pupils were isocoric and prompt with no other neurological deficits. There was no sign of neck stiffness or Brudzinski sign. Blood lab results showed an elevated white blood cell (WBC) count of 45,780/μL with 87% of neutrophil count, platelet count of 44,000/μL, elevated C-reactive protein level of 256.4 mg/L, along with elevated aspartate transaminase, alanine aminotransferase, and glucose. Urine analysis showed glucosuria, proteinuria, and hematuria. Enhanced abdomen computed tomography (CT) showed air-fluid lesion of 15 cm in left lobe of liver (Fig. 1A) and left renal abscess (Fig. 1B). Chest CT showed bilateral multiple scattered nodular and cavitary lesions suggestive of pneumonia with lung abscess (Fig. 1C). Non-contrast brain CT showed iso-dense fluid collection in depending portion of both lateral ventricles (Fig. 1D).

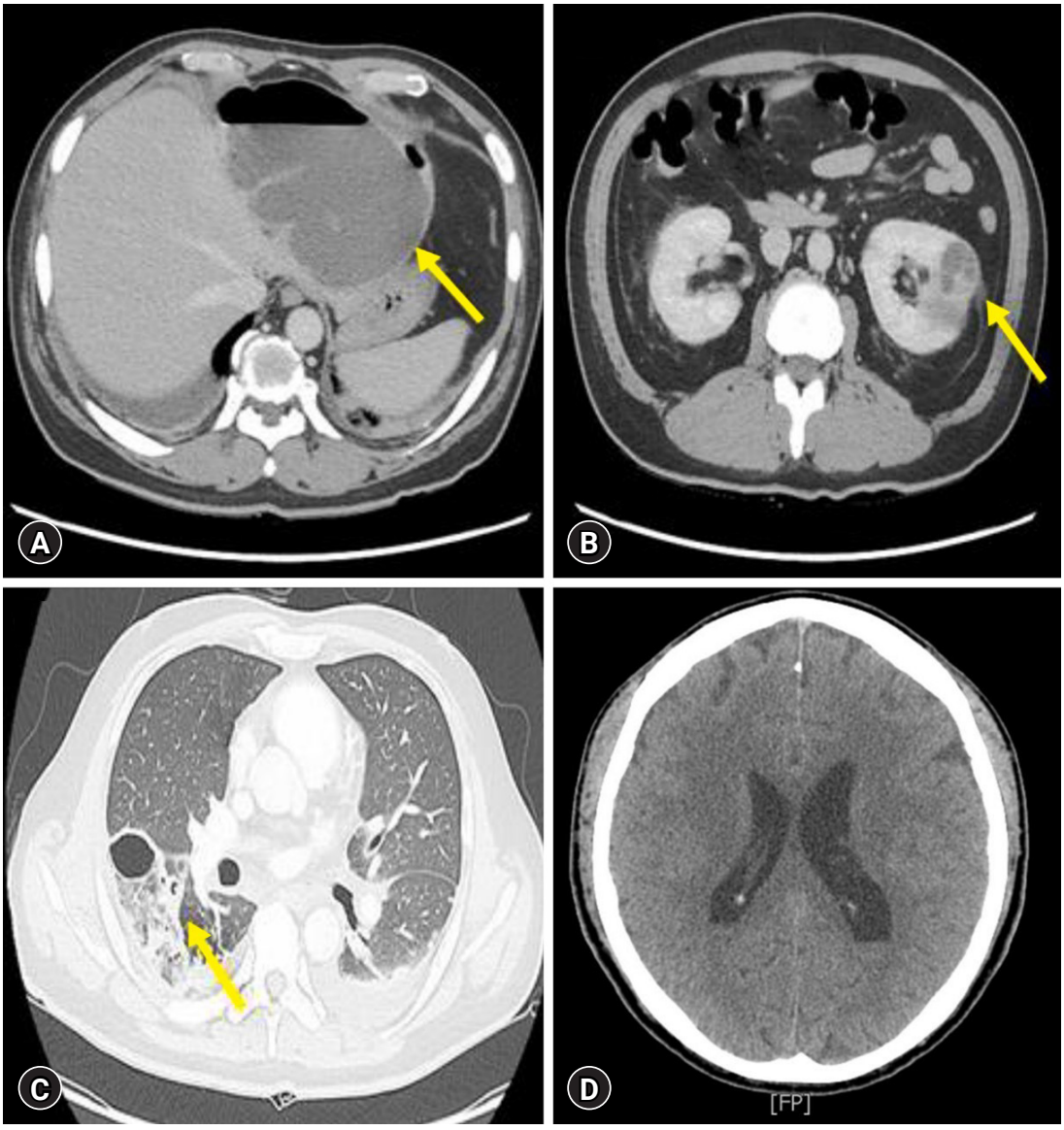

Fig. 1. Abdominal-pelvic computed tomography (CT) shows a 15-cm irregular cystic air-fluid lesion in the left lobe of the liver (A) and a well-defined low-density lesion in the left kidney (B), suggesting a liver abscess and renal abscess. Chest CT (C) shows multiple scattered nodular and cavitary lesions in both lungs, suggesting pneumonia with a lung abscess. Brain CT (D) shows isodense fluid collection in both lateral ventricles.

With CT showing multiple organ abscess, brain magnetic resonance image (MRI) was done in order to differentiate intraventricular pus and hemorrhage. Diffusion-weighted image showed hyperintensity in lateral and fourth ventricles with low apparent diffusion coefficient value (Fig. 2). Mild hydrocephalus was present and enhanced MRI showed no ependymal enhancement. With high suspicion of ventricular abscess accompanied by liver, renal, and lung abscess, a percutaneous drainage tube was inserted in liver abscess and 480 cc of pus was drained. Subsequently, immediate insertion of a bilateral extraventricular drain (EVD) was done. Draining cerebrospinal fluid (CSF) showed high opening pressure with a turbid, yellowish color. CSF analysis showed WBC count of 5,150/mm^3, low glucose level of 30 mg/dL, and an increased protein level of 446 mg/dL. During treatment, patient showed rapid progressive deterioration of the GCS score from 13 to 8. Patient was immediately started on meropenem and vancomycin IV. On fourth postoperative day, peripheral blood, liver and CSF culture showed growth of *Klebsiella pneumoniae* and antibiotic regimen was changed to ceftriaxone 2 g per 12 hr. Patient showed gradual improvement in GCS score, inflammation markers and body temperature. Both EVD were removed on eighth and tenth postoperative days and on twelfth postoperative day patient showed no fever or other systemic symptoms with a GCS score of 14. Patient was injected with ceftriaxone for four weeks and was discharged home without any neurological deficits followed by two weeks of oral cefixime.

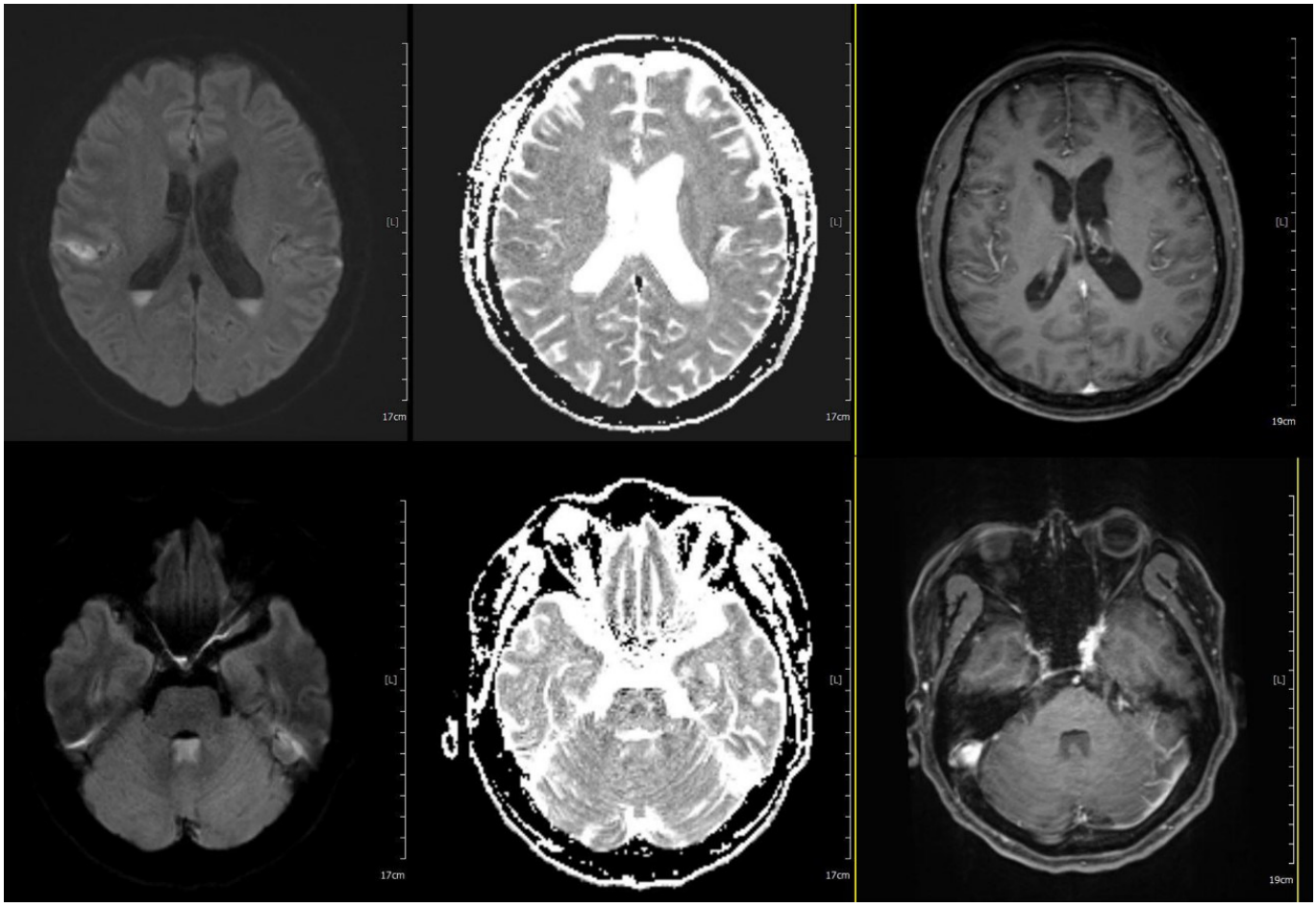

Fig. 2. The first column of brain magnetic resonance imaging (MRI) shows hyperintense lesions in the bilateral fourth ventricles and bilateral frontoparietal cortical sulcus in diffusion-weighted imaging (DWI). The second column shows low apparent diffusion coefficient values in the corresponding lesions in DWI. The third column of T1-enhanced MRI shows no meningeal or ependymal enhancement.

DISCUSSION

IKPS was first documented in 1980s in Taiwan and subsequently several cases were presented worldwide2). Its risk factors include diabetes mellitus and East-Asian descent[6,7]. Its etiology is yet poorly understood but is thought to be hematogenous through enterohepatic circulation8); and 75% of East-Asian are carriers of *Klebsiella pneumoniae* in contrast to 10%-19% in European[8].

Hypervirulent strains causing IKPS are known to have specific genes, rmpA (a regulator of the mucoid phenotype) and magA (mucoviscosity-associated gene A) which are exclusive for capsule serotype K1 and K2[4,6]. These genes are responsible for hypermucoviscosity of the capsule, making it resistant to phagocytosis[3]. Determination of hypermucoviscosity is based on a positive string test in which a bacterial colony on an agar plate can be stretched into viscous string of over 5mm in length with an inoculation needle[4].

Ventriculitis caused by IKPS is rare and documented in few case reports. However, these case reports tend to show similar clinical course; initially presenting with nonspecific symptoms, rapid deterioration of mental status, equivocal brain CT results, diagnosis through diffusion-weighted MRI, and the need for CSF diversion[1,3,7-10]. This is also shown in primary pyogenic ventriculitis caused by pathogens other than *Klebsiella pneumoniae*. According to Gronthoud et al.[2], 6 cases of primary pyogenic ventriculitis not associated with meningitis, abscess, surgical intervention or trauma were reported up to 2016. Most cases reported male patients with a median age of 63, initially presenting with nonspecific fever and headache with only one case showing meningism. Diagnosis of choice is MRI where ventricular infection shows high signal intensity in T1 and low signal intensity in T2. For early phase of infection, diffusion-weighted image tends to show higher sensitivity[2,7]. CT has limitations in differentiating intraventricular pus and hemorrhage, and are less sensitive in early phase of ventricular infection2). One report shows initial CT did not present an intraventricular lesion until clinical deterioration after two days, delaying diagnosis and treatment of the patient[5].

Presently, there is no concrete treatment guideline for ventriculitis caused by IKPS due to its small number of cases, but pyogenic ventriculitis caused by other bacterial agents was mostly treated with intravenous antibiotics for 6 to 7 weeks[2]. When reviewing reported cases of ventriculitis associated with IKPS (Table 1), those who were successfully treated were administered antibiotics for 6 weeks. Either 6 weeks of intravenous antibiotics or 4 weeks of intravenous and subsequent 2 weeks of oral antibiotics was sufficient for survived cases. Intraventricular antibiotics irrigation was not conducted in any of the reported cases, which may imply that intraventricular irrigation may not be mandatory for treating ventriculitis in IKPS. However, in one case[8], repetitive clogging of EVD was reported which required EVD exchange for six times. Further studies should be conducted to investigate whether intraventricular antibiotics irrigation might aid in facilitating patient's recovery and maintaining the patency of EVD.

Most cases that showed good outcomes have undergone EVD insertion, both in ventriculitis caused by IKPS and other bacterial species[2]. One case of ventriculitis associated with IKPS showed a good outcome without insertion of EVD or any form of CSF drainage. However, after 6 weeks of intravenous antibiotics, patient showed mental status decline due to progressing hydrocephalus. The patient fully recovered after insertion of ventriculo-peritoneal shunt. This may indicate that insertion of EVD or CSF drainage is not a definite prerequisite for successful treatment of ventriculitis but may reduce the burden of infection in early stage of disease and risk of developing delayed hydrocephalus.

Prognostic factors of ventriculitis associated with IKPS are not well-established due to their limited studies. Yet, previous studies regarding neonatal or adult bacterial meningitis show elevated protein levels in CSF might be associated with poor outcomes[10]. The intensity of inflammatory response in meningitis might be reflected by high protein level[10]. Reviewed cases (Table 1) also show patients with poor outcomes generally having higher CSF protein level than patients with good outcomes. However, some patients with good outcomes showed higher CSF WBC and lower CSF glucose level than patients with poor outcomes. High protein levels may reflect a high infection burden but may also suggest an active inflammatory response leading to the repair and regeneration stage of inflammation. Further investigation is needed to identify prognostic factors in CSF and blood lab results or previous medical history of IKPS patients presenting with ventriculitis.

Table 1. Summary of reported cases of ventriculitis associated with invasive Klebsiella pneumoniae syndrome

References	Sex	Age	GCS	Mental status change on hospital admission	Causative agent	String test	CSF lab tests			Blood lab tests		Antibiotic administration period	EVD	Intraventricular antibiotics	Liver abscess drain	Outcome
							WBC (/mm^3)	Glucose (mg/dL)	Protein (mg/dL)	WBC (/mm^3)	Platelet (/mm^3)					
Hyun et al.[3]	F	80	NA	HD 6	*Klebsiella pneumoniae*	Positive	7200	<10	359.3	13860	NA	28 days IV + 14 days PO	Yes	No	Yes (renal abscess)	Survived
Maheswaranathan et al.[8]	F	61	NA	HD -7	*Klebsiella pneumoniae*	Positive	5051	4	803	19900	170000	NA	Yes (repetitive clogging)	No	Yes	Died
Lee and Song[7]	F	84	NA	HD -1	*Klebsiella pneumoniae*	NA	NA	NA	NA	9330	70000	10 days	No	No	Yes	Died
Rasouli and Honeybul[9]	F	80	10	HD 14	*Klebsiella pneumoniae*	Positive	NA	NA	NA	NA	NA	NA	Yes	No	No	Survived
Sun et al.[10]	F	49	NA	HD 1	*Klebsiella pneumoniae*	NA	4263	10.8	882	24870	108000	NA	Yes	No	No	Died
Sun et al.[10]	M	62	5	HD 1	*Klebsiella pneumoniae*	NA	17148	<1.80	1282	12390	25000	NA	No	No	No	Died
Sun et al.[10]	M	39	5	HD 1	*Klebsiella pneumoniae*	NA	178640	183.8	3241	25730	NA	2 days	Yes	No	No	Died
Youn et al.[11]	M	60	9	HD 2	*Klebsiella pneumoniae*	NA	18500	6	344.7	12640	NA	42 days IV + PO	No (HD 42 VPS)	No	No	Survived
This case	M	50	13	HD 1	*Klebsiella pneumoniae*	NA	5150	30	446	45780	44000	28 days IV + 14 days PO	Yes	No	Yes	Survived

F: female; M: male; GCS: Glasgow Coma Scale; NA: not available; HD: hospital day; CSF: cerebrospinal fluid; WBC: white blood cell; IV: intravenous; PO: per os; EVD: external ventricular drainage; VPS: ventriculoperitoneal shunt.

CONCLUSION

As IKPS is also increasing in Western countries, due to its nonspecific presentation, rapid progression and high mortality rate, keen awareness of suspicion of CNS infection in multiple organ abscesses should be warranted. Although further studies are warranted, fast surgical intervention of CSF drainage combined with antibiotics is essential in improving patient's outcomes in ventriculitis associated with IKPS.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

ACKNOWLEDGEMENTS

This work has previously been presented as an oral presentation at the 108th Annual Meeting of Korean Taejon Chungcheong Regional Neurosurgical Society held in Cheongju on 2 December 2022.

REFERENCES

1. Correia Lopes J, Basílio AS, Amaro M: Pyogenic ventriculitis associated with urosepsis: A rare case report. Eur J Case Rep Intern Med 7:002178, 2020
2. Gronthoud F, Hassan I, Newton P: Primary pyogenic ventriculitis caused by Neisseria meningitidis: case report and review of the literature. JMM Case Rep 4:e005078, 2017
3. Hyun JI, Kim YJ, Jeon YH, Kim SI, Park YJ, Kang MW, et al.: A case of ventriculitis associated with renal abscess caused by serotype K1 Klebsiella pneumoniae. Infect Chemother 46:120–124, 2014
4. Kasuya K, Takayama K, Bito M, Shimokubo N, Kawashima R, Shibahara T: Septicemic invasive Klebsiella pneumoniae infection in a cynomolgus monkey (Macaca fascicularis) with severe diffused suppurative meningoencephalitis. J Vet Med Sci 79:1167–1171, 2017
5. Kobayashi H, Suzuki T, Tokuda Y: Pyogenic ventriculitis following urosepsis caused by Escherichia coli. BMJ Case Rep 2013:1–2, 2013
6. Lee SS, Chen YS, Tsai HC, Wann SR, Lin HH, Huang CK, et al.: Predictors of septic metastatic infection and mortality among patients with Klebsiella pneumoniae liver abscess. Clin Infect Dis 47:642–650, 2008
7. Lee Y, Song YM: Ventriculitis associated with liver abscess caused by Klebsiella pneumoniae. J Korean Neurol Assoc 38:210–213, 2020
8. Maheswaranathan M, Ngo T, Rockey DC: Identification and management of the hypervirulent invasive Klebsiella pneumoniae syndrome: A unique and distinct clinical entity. J Investig Med High Impact Case Rep 6:2324709618806552, 2018
9. Rasouli M, Honeybul S. Hydrocephalus as a delayed presentation of *Klebsiella pneumoniae* ventriculitis: A case report. Future Neurol [epub ahead of print, 2022. doi: 10.2217/fnl-2021-0011].
10. Sun R, Zhang H, Xu Y, Zhu H, Yu X, Xu J: Klebsiella pneumoniae-related invasive liver abscess syndrome complicated by purulent meningitis: a review of the literature and description of three cases. BMC Infect Dis 21:15, 2021
11. Youn M, Lee JJ, Kim BK, Kang K, Lee WW, Yoo I. A case of invasive *Klebsiella pneumoniae* syndrome with ventriculitis. Encephalitis [epub ahead of print, 2022. doi: 10.47936/encephalitis.2022.00010].

The Nerve

Case Report

The Nerve 2023;9(1):75-78
https://doi.org/10.21129/nerve.2023.00304
eISSN 2465-891X

Anterior Cage Migration during Transforaminal Lumbar Interbody Fusion: A Case Report and Review of the Literature

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OPEN ACCESS

Received: March 6, 2023
Revised: April 10, 2023
Accepted: April 13, 2023

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Transforaminal lumbar interbody fusion (TLIF) is a popular procedure for patients with lumbar instability with unilateral foraminal stenosis. Many complications can occur during the procedure. However, cage migration during the procedure is rarely reported. Anterior cage migrations can lead to catastrophic consequences due to the possibility of major vessel injuries. Here, we present a 76-year-old male patient whose cage extruded anteriorly during L5-S1 TLIF. Fortunately, he did not experience any life-threatening complications, and the migrated cage was visible just below the iliac vessels' bifurcation site on computed tomography angiography. As an alternative, an emergency anterior lumbar interbody fusion was successfully performed, and the TLIF cage was removed during this procedure.

Keywords: Longitudinal ligaments; Lumbar vertebrae; Spinal fusion

INTRODUCTION

Transforaminal lumbar interbody fusion (TLIF) is an effective operative procedure, showing satisfactory results with acceptable risk rates[16]. It has gained popularity due to its minimal invasiveness, lower blood loss compared to other surgical techniques, and shorter hospitalization period[8]. Ironically the increase in the popularity of TLIF has also resulted in increased complication rates, including dural tears, nerve root injuries, screw loosening, and cage mispositioning or migration. Here, we present a rare case of the intraoperative anterior extrusion of a fusion cage during TLIF.

CASE REPORT

A 76-year-old male patient had initially experienced a gradual aggravation of left lower extremity motor weakness and radiating pain in the L5 and S1 dermatome. His imaging workup carried out at a local spine center, showed severe left L4-5 and L5-S1 foraminal stenosis with central disc extrusion and spondylolisthesis at L5-S1 level (Fig. 1, 2). The patient underwent open lumbar microdiscectomy at the L4-5 level and TLIF at the L5-S1 level. Unfortunately, during the cage insertion procedure at the L5-S1 level, anterior migration occurred where the cage disappeared into the

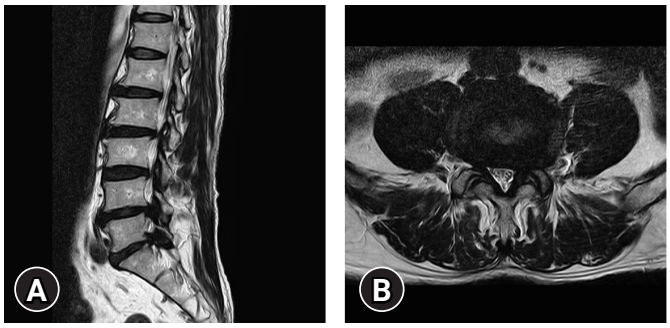

Fig. 1. (A) Sagittal T2-weighted magnetic resonance image (MRI) showing left foraminal stenosis at L4–5 level. (B) Axial T2-weighted MRI showing left foraminal stenosis at L4–5 level.

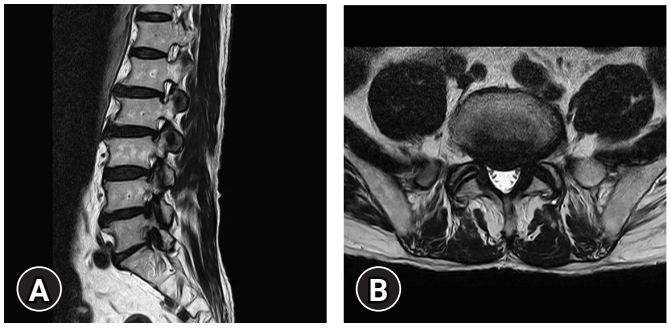

Fig. 2. (A) Sagittal T2-weighted magnetic resonance image (MRI) showing left severe foraminal stenosis at L5-S1 level. (B) Axial T2-weighted MRI showing central disc protrusion at L5-S1 level.

abdominal space. The patient was immediately transferred to our hospital for a thorough evaluation and possible emergency surgery. The patient was very stable when he arrived at our emergency room and his initial symptoms had subsided. Imaging workup X-rays and computed tomography angiography (CTA) (Fig. 3) revealed no major vessel injuries, and the lost cage was placed just below the iliac artery bifurcation area. The patient was hemodynamically stable and was sent to the intensive care unit.

With the help of the department of general surgery, anterior lumbar body fusion (ALIF) at L5-S1 was performed the next day to both remove the migrated cage and restore stability to the lumbar spine. In the surgical field, the cage was located in front of the L5-S1 disc space just below the iliac artery bifurcation, and no bleeding or vessel injury was observed (Fig. 4).

The cage was removed, and a large ALIF cage was inserted

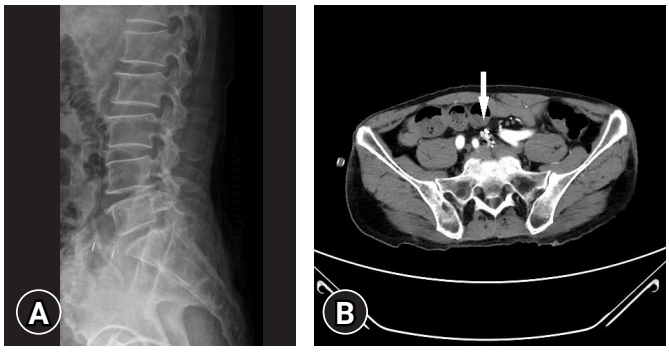

Fig. 3. (A) Lateral lumbar X-ray image showing anterior migration of fusion cage. (B) Axial image of abdominal computed tomography angiography showing fusion cage just below iliac artery bifurcation (white arrow).

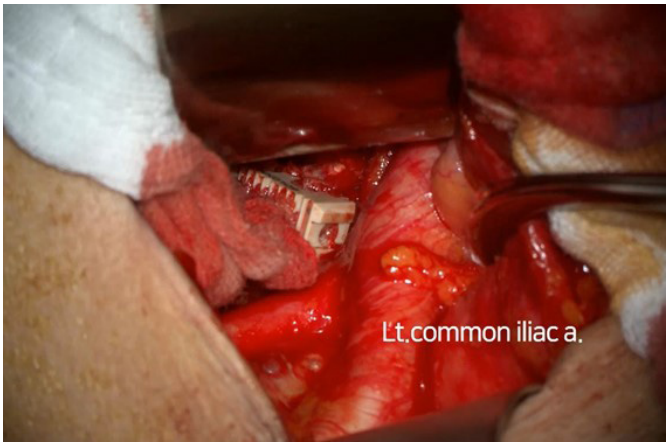

Fig. 4. Intraoperative field showing migrated cage above left iliac artery.

without any complications. Then, the patient was placed in the prone position, and pedicle screws were inserted percutaneously.

Surgery was completed successfully without complications (Fig. 5). The patient was discharged ten days after surgery with no neurological deficits.

DISCUSSION

TLIF surgery was first introduced in 1982 by Harms and Rolinger[6], and it is considered the preferred method of interbody fusion. There are several advantages of TLIF compared to previous conventional methods of spine interbody fusion. TLIF minimizes the possibility of dural and nerve

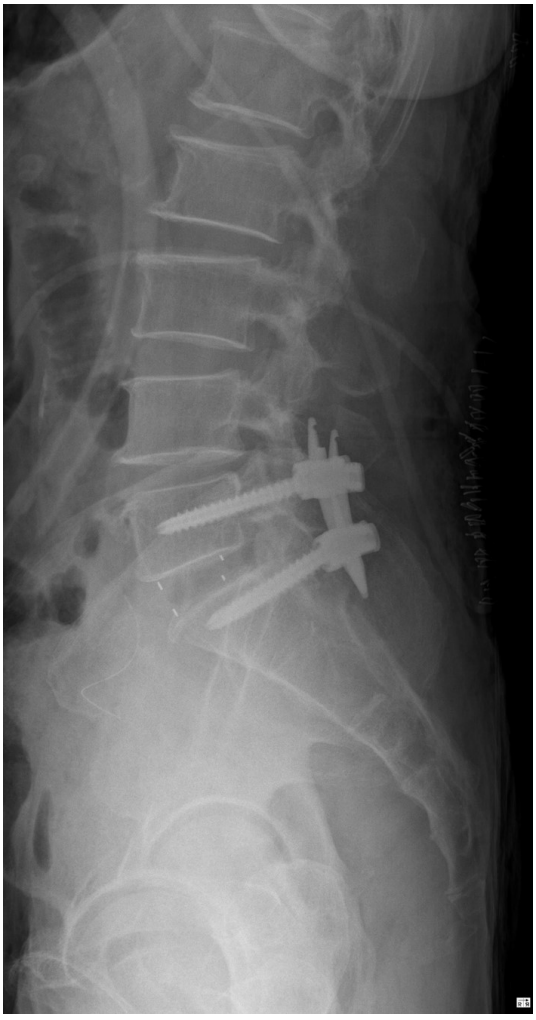

Fig. 5. Successful surgical removal of fusion cage and anterior lumbar interbody fusion.

injury since only minimal thecal sac traction is needed for cage entry after the removal of the ipsilateral facet. Also, through the removal of the facet, the problematic foraminal area can be exposed with little difficulty. Another benefit of TLIF is that additional posterolateral fusion is possible since the contralateral laminae and spinous processes are usually preserved[4].

However, even with these excellent features of TLIF, critical complications can occur during the procedure. Although rare, as the case presented in this study, one of the most infamous complications is anterior cage migration. Anterior migration during the procedure can occur when the operator is inserting the cage into the disc space. During this process, the surgeon's excessive curettage and strong impaction can result in an anterior longitudinal ligament (ALL) tear leading to instant anterior migration into the abdominal space. This could lead to major vessel injuries, resulting in catastrophic consequences3). Many studies have reported the risk factors of cage migration, such as old age, low bone quality, small or oversized cages, and rectangularly shaped cages[1,7-10,12,13,17,21]. However, these factors are usually related to postoperative migration during the follow-up periods after successful surgery[9,21]. The preservation of the ALL during disc preparation is especially crucial during TLIF. The ALL usually acts as a barrier during the cage insertion process and minimizes the possibility of the cage entering the abdominal space. It attaches firmly to the anterior surface of the vertebrae. It is not strong on the lateral side which makes it more vulnerable to unilateral and oblique disc procedures than other operations[11].

Table 1. Complications after the anterior migration of cage in transforaminal lumbar interbody fusion

References	Year	Complication
Proubasta et al.[15]	2002	Compressed major vessels
Yoshimoto et al.[20]	2007	Deep vein thrombosis
Cakmak et al.[2]	2010	Colon perforation
Pawar et al.[14]	2010	IVC injury
Garg et al.[5]	2017	Sigmoid colon perforation
Murase et al.[11]	2017	IVC injury
Xu and Zheng[19]	2017	Left femoral nerve injury following cage extraction
Kumar et al.[10]	2021	Potential risk of perforation of major vessels
Aleixo et al.[1]	2021	Iliac vein injury

IVC: Inferior vena cava.

There are no guidelines for reoperation due to anterior cage migration. Although it would be reasonable to consider removing a foreign body that has the possibility of becoming an infection source or a possible cause of delayed vessel injury, there are many arguments against the removal of a migrated cage, especially in hemodynamically stable patients[1,2,7,10,14,15,19,20] (Table 1).

CONCLUSION

TLIF is an increasingly popular procedure for lumbar interbody fusion, and it is mostly recommended for patients with unstable unilateral foraminal stenosis. Although TLIF is a common surgical procedure, it has possible severe compli-

cations and should not be taken lightly. Cage migration occurs in 1.8% of the patients and among them, anterior cage migration can cause lead to disastrous consequences[18]. Physicians should always take into account the possibility of anterior migration and try to preserve the ALL during disc preparation to reduce the chance of this critical complication.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Aleixo C, Pereira RS, Sousa H, Seabra P, Marinhas J, Santos FL: Iliac vein injury after anterior transforaminal lumbar interbody fusion cage migration. Int J Res Orthop 7:428–430, 2021
2. Cakmak A, Gyedu A, Kepenekçi I, Ozcan C, Unal AE: Colon perforation caused by migration of a bone graft following a posterior lumbosacral interbody fusion operation: case report. Spine (Phila Pa 1976) 35:E84–E85, 2010
3. Cavenaghi A, Hoffmann E, Labed P, Chiche L, Koskas F, Davaine JM: Anterior cage migration during spine surgery: An unusual and severe complication. J Vasc Surg Venous Lymphat Disord 9:497–498, 2021
4. Cole CD, McCall TD, Schmidt MH, Dailey AT: Comparison of low back fusion techniques: transforaminal lumbar interbody fusion (TLIF) or posterior lumbar interbody fusion (PLIF) approaches. Curr Rev Musculoskelet Med 2:118–126, 2009
5. Garg B, Singla A, Batra S, Kumar S: Early migration of bone graft causing sigmoid colon perforation after trans-foraminal lumbar interbody fusion. J Clin Orthop Trauma 8:165–167, 2017
6. Harms J, Rolinger H: A one-stager procedure in operative treatment of spondylolistheses: dorsal traction-reposition and anterior fusion (author's transl). Z Orthop Ihre Grenzgeb 120:343–347, 1982
7. Heary RF, Mummaneni PV: Editorial: Vascular injury during spinal procedures. J Neurosurg Spine 24:407–408, 2016
8. Hee HT, Castro FP, Majd ME, Holt RT, Myers L: Anterior/posterior lumbar fusion versus transforaminal lumbar interbody fusion: analysis of complications and predictive factors. J Spinal Disord 14:533–540, 2001
9. Jin L, Chen Z, Jiang C, Cao Y, Feng Z, Jiang X: Cage migration after unilateral instrumented transforaminal lumbar interbody fusion and associated risk factors: a modified measurement method. J Int Med Res 48:300060519867828, 2020
10. Kumar M, Kaucha D, Adsul N, Chahal RS, Kalra KL, Acharya S: Delayed asymptomatic retroperitoneal dislodgement into the pouch of Douglas of a TLIF cage: A case report and review of the literature. Surg Neurol Int 12:360, 2021
11. Murase S, Oshima Y, Takeshita Y, Miyoshi K, Soma K, Kawamura N, et al.: Anterior cage dislodgement in posterior lumbar interbody fusion: a review of 12 patients. J Neurosurg Spine 27:48–55, 2017
12. Oh HS, Lee SH, Hong SW: Anterior dislodgement of a fusion cage after transforaminal lumbar interbody fusion for the treatment of isthmic spondylolisthesis. J Korean Neurosurg Soc 54:128–131, 2013
13. Park MK, Kim KT, Bang WS, Cho DC, Sung JK, Lee YS, et al.: Risk factors for cage migration and cage retropulsion following transforaminal lumbar interbody fusion. Spine J 19:437–447, 2019
14. Pawar UM, Kundnani V, Nene A: Major vessel injury with cage migration: surgical complication in a case of spondylodiscitis. Spine (Phila Pa 1976) 35:E663–E666, 2010
15. Proubasta IR, Vallvé EQ, Aguilar LF, Villanueva CL, Iglesias JJ: Intraoperative antepulsion of a fusion cage in posterior lumbar interbody fusion: a case report and review of the literature. Spine (Phila Pa 1976) 27:E399–E402, 2002
16. Rosenberg WS, Mummaneni PV: Transforaminal lumbar interbody fusion: technique, complications, and early results. Neurosurgery 48:569–575, 2001
17. Smith AJ, Arginteanu M, Moore F, Steinberger A, Camins M: Increased incidence of cage migration and nonunion in instrumented transforaminal lumbar interbody fusion with bioabsorbable cages. J Neurosurg Spine 13:388–393, 2010
18. Tormenti MJ, Maserati MB, Bonfield CM, Gerszten PC, Moossy JJ, Kanter AS, et al.: Perioperative surgical complications of transforaminal lumbar interbody fusion: a single-center experience. J Neurosurg Spine 16:44–50, 2012
19. Xu Z, Zheng Y: Anterior dislocation of fusion cage after minimal invasive transforaminal lumbar interbody fusion (MI-TLIF): A case report. Biomed Res (Aligarh) 28:7834–7836, 2017
20. Yoshimoto H, Sato S, Nakagawa I, Hyakumachi T, Yanagibashi Y, Nitta F, et al.: Deep vein thrombosis due to migrated graft bone after posterior lumbosacral interbody fusion. Case report. J Neurosurg Spine 6:47–51, 2007
21. Zhao FD, Yang W, Shan Z, Wang J, Chen HX, Hong ZH, et al.: Cage migration after transforaminal lumbar interbody fusion and factors related to it. Orthop Surg 4:227–232, 2012

The Nerve

Case Report

The Nerve 2023;9(1):79-84
https://doi.org/10.21129/nerve.2023.00269
eISSN 2465-891X

Multiple Spinal Metastases of Anaplastic Meningioma: A Case Report

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OPEN ACCESS

Received: January 27, 2023
Revised: April 7, 2023
Accepted: April 20, 2023

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Meningiomas are primary benign tumors that occur in intracranial and intraspinal regions. Rarely, atypical and anaplastic meningiomas exhibit malignant tendencies and can metastasize. A 56-year-old female patient visited the hospital complaining of a dull headache, mild dysarthria, sudden onset of blurred vision, and mild weakness in the left upper limbs. A homogeneously augmented mass was revealed in the right temporal lobe following magnetic resonance imaging (MRI) and was determined to be an anaplastic meningioma after surgical resection. During follow-up, revision surgery was performed due to the recurrence of the primary tumor. After the revision surgery, the patient complained of new symptoms, which included paresthesia and muscle weakness in the right lower extremity. MRI revealed a mass in the cervical and lumbar vertebrae suspected to have been metastasized. Another revision surgery was conducted on the intracranial primary tumor. The tumor was resected from the cervical and lumbar vertebrae. Histopathology revealed that they were all anaplastic meningiomas. Although anaplastic meningioma is rare, it can cause extracranial metastases. This case shows that multiple spinal metastases of anaplastic meningioma require considerable attention in diagnosis and treatment.

Keywords: Meninges; Meningioma; Neoplasm metastasis; Neoplasms

INTRODUCTION

Meningiomas are primary benign tumors that occur in the intracranial and intraspinal regions. Although most meningiomas are benign, in rare cases, they could be malignant with aggressive metastases[12]. The types of meningiomas that can metastasize are the atypical (World Health Organization [WHO] grade II) and anaplastic (WHO grade III) types[2], which account for less than 5% of all meningiomas[9]. In particular, extracranial metastasis is rarer, with an estimated incidence of 1 to 5 cases per 1000, and spinal metastasis has been reported only in a few studies[1,3]. We present a unique case of a patient diagnosed with anaplastic meningioma in 2011 with spinal metastasis, confirmed during examination

for the second revision surgery due to the recurrence of the primary tumor.

CASE REPORT

A 56-year-old female patient at the time of diagnosis in January 2011 suffered from dull headaches, mild dysarthria, and sudden-onset blurred vision. On examination, she was lethargic with mild weakness (Medical Research Council [MRC] scale 4) in the left upper limbs. Contrast-enhanced computed tomography (CT) revealed a mass with peripheral vasogenic edema and a dense area in the right temporal lobe (Fig. 1A). Magnetic resonance imaging (MRI) showed a homogeneously enhanced mass (approximately 5.5 × 2.8 × 3.6-cm in size) (Fig. 1B). In June 2011, the patient underwent right craniotomy and gross total resection. After the first surgery, there was no improvement in left motor weakness, but consciousness and speech were restored. Histological examination revealed anaplastic meningioma (WHO grade III). Gamma knife radiosurgery was performed 4 times at post-operative 2-, 4-, and 6-years to remove the remnant tumors after the initial surgery. Subsequently, an increase in the size of the remnant tumor in the primary site was confirmed in a follow-up MRI 7 years post-operatively (Fig. 2). A revision surgery was conducted, and the patient received radiotherapy of 60 Gy over 6 weeks.

Spinal metastasis of the primary tumor was confirmed when the second revision surgery was to be performed. During the outpatient follow-up after the second revision surgery and radiotherapy, the patient complained of radiating back pain and weakness in the upper and lower extremities (MRC scale 3) which were absent before. A recurrence

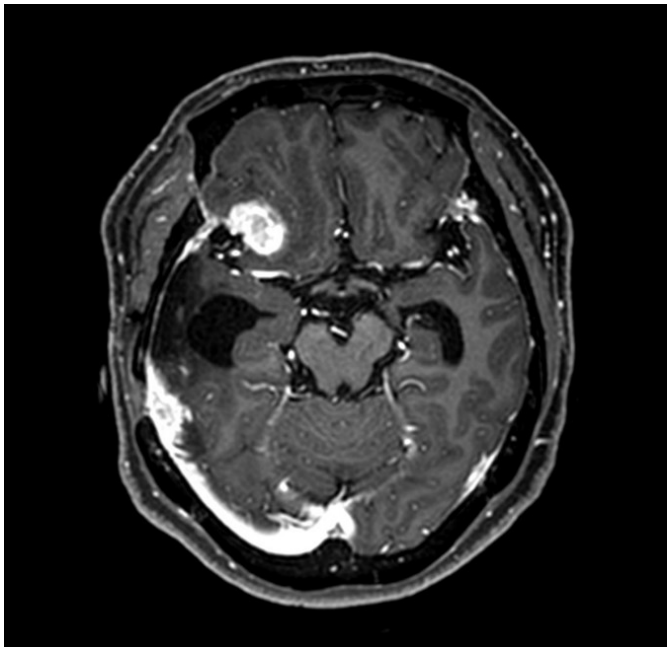

Fig. 2. Eight years after the initial surgery, brain magnetic resonance images revealed an increase in the size of the remnant tumor in frontal lobe.

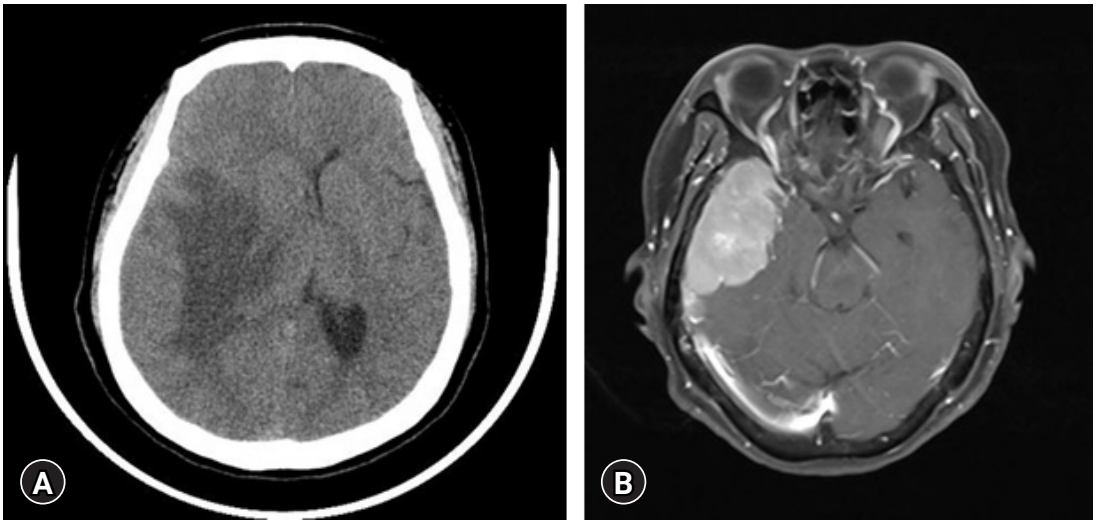

Fig. 1. Preoperative image. (A) Contrast-enhanced computed tomography shows a mass in the right temporal lobe with peripheral vasogenic edema. (B) Gadolinium-enhanced T1-weighted magnetic resonance images show a strong, homogenous large mass in the right temporal lobe.

of the lesion was suspected, and MRI was performed. A mass, mimicking an en-plaque meningioma with an irregular margin (3.3 × 2.0 × 1.2-cm), and perilesional edema were confirmed (Fig. 3). The peculiarity here is that, unlike before, the patient rarely complained of headaches. There was back pain, and the weakness in the upper and lower extremities worsened and was accompanied by leg numbness, predominantly on the right. After a physical examination of the patient, a contrast-enhanced spinal MRI was utilized to evaluate the presence of metastasis to the spine. Although with some degree of expectation, an MRI of the spine revealed a lesion that appeared to be a contrast-enhancing metastatic tumor. Two contrast-enhancing lesions were identified, two intradural extramedullary tumors at the C2–3 level approximately 2.0 cm in size (Fig. 4A, B), and at the L4–5 level approximately 3.6 cm in size (Fig. 4C, D). Including radiating back pain, and weakness in the right upper, lower limbs and left lower limbs that were not previously present had been assumed to be related to spinal metastasis. We performed three surgeries on the patient. First, we decided to operate on the recurring tumor in the brain. For the spinal tumors, we planned to operate on the lumbar region first, followed by the cervical region. Craniotomy was achieved using a previous incision. Gross total resection was performed, and this included the lateral walls of the superior sagittal sinus and falx, which were invaded by the tumor. In the lumbar region, subtotal laminectomy was conducted for the L3 lamina, and the tumor was removed by total laminectomy for the L4 lamina. Facetectomy was conducted to ensure complete tumor resection because it was difficult to remove the tumor while preserving the right facet. To prevent spinal instability, pedicle screw fixation and posterolateral fusion were performed on the L4 and L5 lamina. The tumor in the cervical area was removed by total laminectomy of the C2 lamina; however, the tumor in the left neural foramen area surrounded the vertebral artery and could not be completely removed. Biopsies and immunohistochemical staining were performed during each of the surgeries. Brain tumors showed the proliferation of atypical cells with positivity for epithelial membrane antigen, confirming the diagnosis of meningioma. The tumor was classified as an anaplastic meningioma (WHO grade III) because the tumor cells had nuclear atypia, indicating malignancy. The tumor also showed extensive necrosis, high mitotic activity (19 mitoses/10 high-power fields [HPFs]), and a high Ki-67 proliferation index (approximately 30%). Although tumors in the lumbar and cervical lesions had low mitotic activity (2 mitoses/10 HPFs versus 1 mitoses/10 HPFs), both tumors also showed the same nuclear atypia as tumors in the brain and were diagnosed as anaplastic meningioma. Necrosis and a high Ki-67 proliferation index were also identified in the cervical and lumbar tumors. Glial fibrillary acidic protein (GFAP) and S-100 proteins were absent in all three tumors (Fig. 5). The patient provided informed consent and this case report was approved by the Institutional Review Board (IRB) of Pusan National University Yang-san Hospital (IRB No. 2023-10-020).

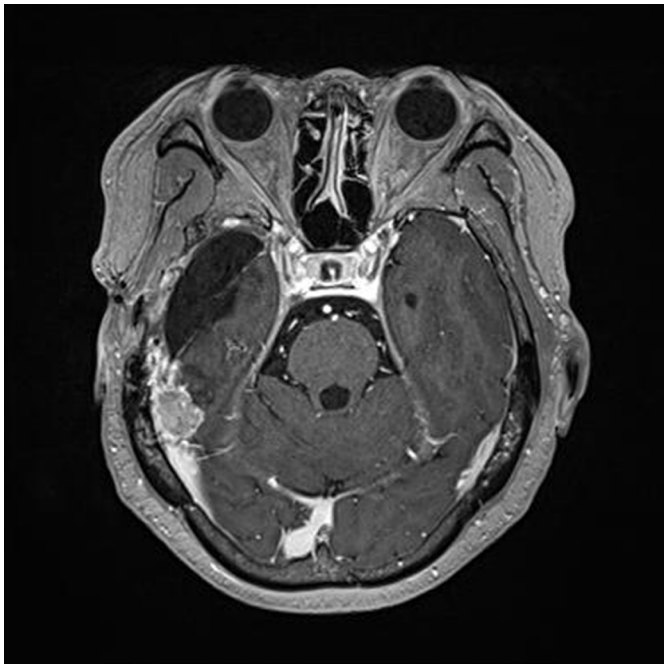

Fig. 3. Magnetic resonance images shows a new appearance of homogenous enhancing extra-axial and en-plaque type mass at the right parasagittal area.

DISCUSSION

Meningioma originates from the intracranial meninges, consists of meningeal epithelial cells, and is one of the most common tumors that affect the central nervous system[6]. Although meningiomas are often benign, their clinical characteristics are variable. In certain histologically distinct subsets, they may recur after complete resection[14]. Malignancy and extracranial metastasis are rare in meningioma[1,3].

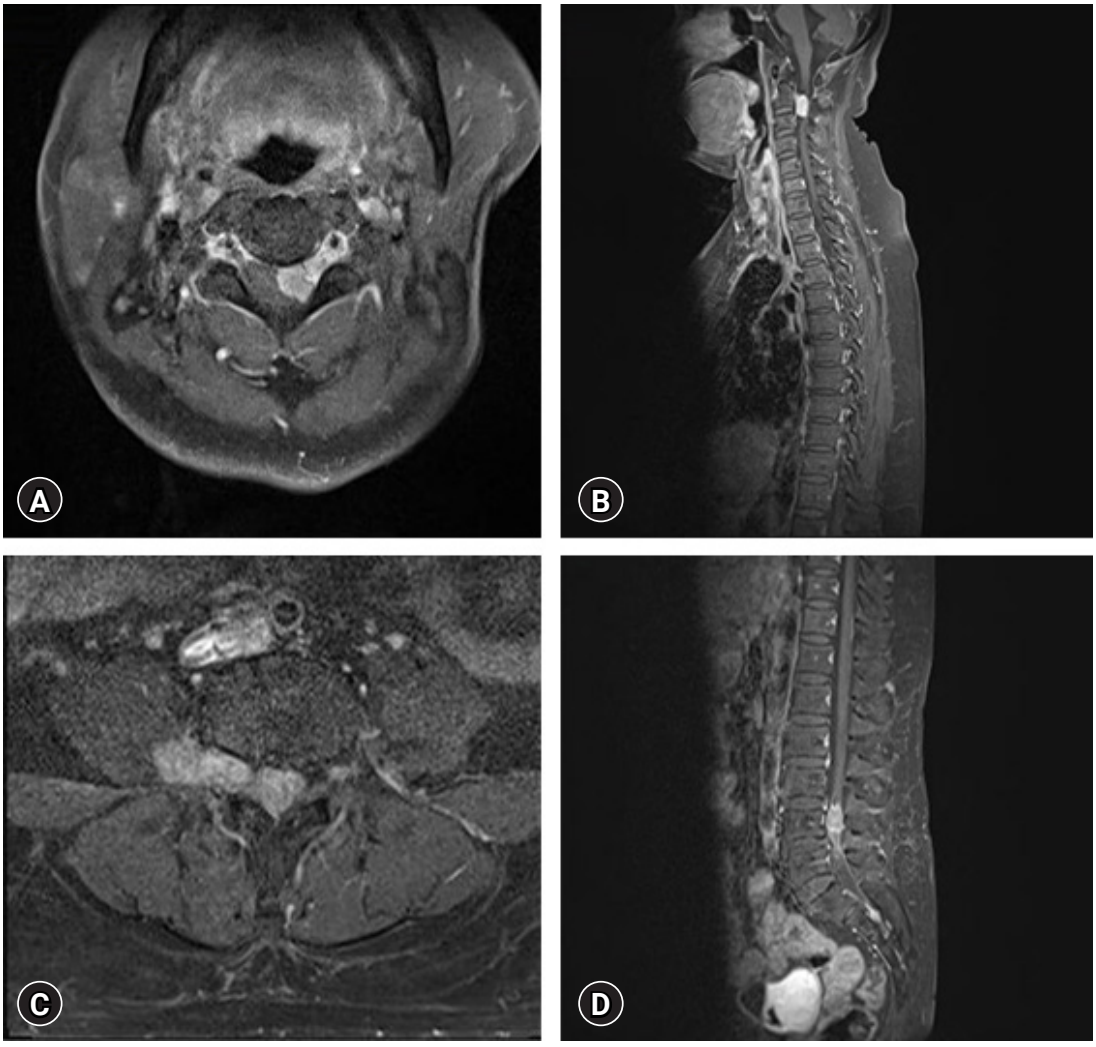

Fig. 4. Magnetic resonance images shows a homogeneously enhanced mass with suspected metastasis in the left extradural space at the C2-3 level and the right extradural space at the L3-4 level. T1-weighted axial and sagittal images with gadolinium enhancement. (A, B) Cervical lesion. (C, D) Lumbar lesion.

According to WHO criteria, meningiomas are histopathologically subdivided into three grades[8] (Table 1). A high probability of grade II and III extracranial metastasis has been reported in the literature[5,16]. The most frequent sites of metastasis for malignant meningioma are the lungs (60%), abdomen and liver (34%), cervical lymph nodes (18%), iliac, pelvic, and cranial cavity (11%), pleural (9%), central nervous system (7%), and mediastinum (5%), Only 7% occur in the vertebrae[7]. Cases of spinal metastases are rare. A few cases of spinal metastases have been published to date[13,17,18]. Immunohistochemical analysis of Ki-67 proliferation index or CDKN2A deletion, associated with 9p21 deletion, is also useful in assessing meningioma recurrence and/or metastasis[15].

Surgical resection may also increase the risk of iatrogenic metastasis of meningiomas with atypical histology, which is believed to be the case in this patient. The primary tumor was located around the Sylvian fissure, and it is presumed that the Sylvian fissure was exposed during the initial and revision surgeries. This iatrogenic cause created a passage between the tumor and the subarachnoid space, which eventually provided an opportunity for the tumor to spread freely along the pathway of cerebrospinal fluid[1,11]. In addition, the primary tumor was an anaplastic meningioma,

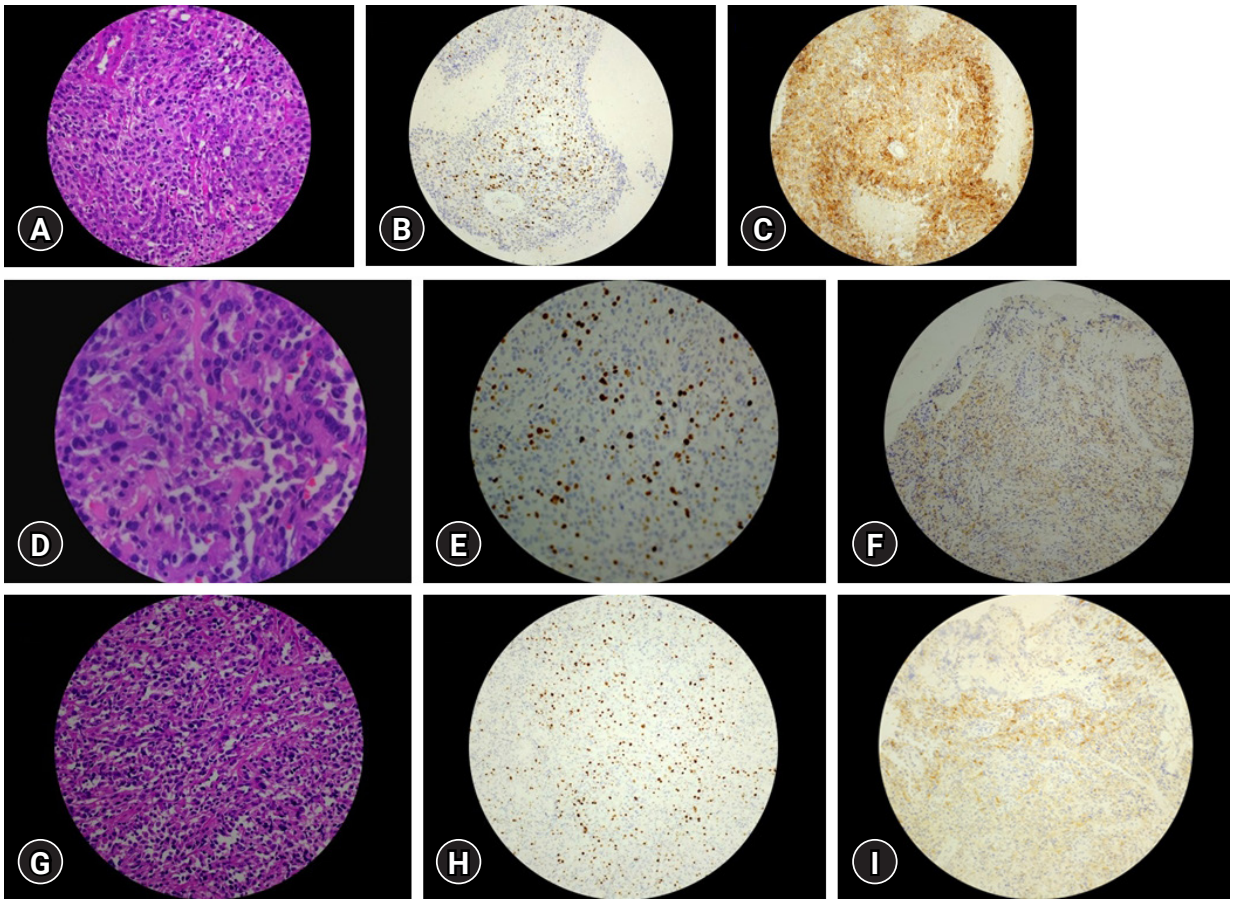

Fig. 5. Pathologic findings of the tumor. (A) Brain tumor has highly cellular, large cells exhibiting prominent and overlapping nucleoli. (hematoxylin and eosin [H&E], ×200 magnification). (B) Immunohistochemical stain showing focal positivity for epithelial membrane antigen (EMA) and (C) Ki-67 index about 30% in brain tumor (×100 magnification). (D) Tumor cells in the lumbar lesion show necrosis and moderate nuclear atypia (H&E, ×200 magnification). (E) Immunohistochemical stain showing focal positivity for EMA and (F) Ki-67 index about 30% in the lumbar lesion (×100 magnification). (G) Tumor cells in the cervical lesion show moderate nuclear atypia, although the area of necrosis was not definite (H&E, ×200 magnification). (H) Immunohistochemical stain showing focal positivity for EMA and (I) Ki-67 index about 30% in the lumbar lesion (×100 magnification).

Table 1. The World Health Organization classification of meningiomas

Grading	Definition
Grade I	- Mitotic count of less than 4 mitoses per 10 HPF
	- Absence of brain invasion
	- 9 histological subtypes: meningothelial, fibrous, transitional, psammomatous, microcystic, angiomatous, secretory, lymphoplasmacyte-rich, metaplastic
Grade II (atypical)	- Mitotic count of 4 to 19 mitoses per 10 HPF
	- Presence of brain invasion
	- 3 of 5 specific histological features: spontaneous necrosis, sheeting, prominent nucleoli, high cellularity and small cells
	- 3 histological subtypes: atypical, clear cells, chordoid
Grade III (anaplastic)	- Mitotic count of 20 or more mitoses per 10 HPF
	- Specific histologies: rhabdoid or papillary meningioma

HPF: high-power field.

and its multiple recurrences and short interval suggest that extracranial metastasis may have occurred[9,10]. Therefore, based on experience in our case, although the incidence of intracranial anaplastic meningioma is low, spinal metastases can occur even with small tumors.

Currently, there are no consensus guidelines for the treatment of metastatic meningioma[4]. The treatment methods for spinal metastases include medical therapy, surgery, and radiation therapy. Based on the extension of life expectancy of patients with tumors due to the development of modern medicine and experience in our case, it is thought that surgical intervention is necessary when pain control, nerve function recovery, and spinal stabilization are to be achieved.

CONCLUSION

Although uncommon, metastasis of primary malignant meningioma should always be included in the differential diagnosis once there is evidence of pathology and immunohistochemical analysis suggesting metastasis. In addition, if a patient is diagnosed with malignant meningioma, evaluation for spinal metastases is necessary.

FUNDING

This study was supported by a 2022 research grant from Pusan National University Yangsan Hospital.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Akimura T, Orita T, Hayashida O, Nishizaki T, Fudaba H: Malignant meningioma metastasizing through the cerebrospinal pathway. Acta Neurol Scand 85:368–371, 1992
2. Apra C, Peyre M, Kalamarides M: Current treatment options for meningioma. Expert Rev Neurother 18:241–249, 2018
3. Conrad MD, Schonauer C, Pelissou-Guyotat I, Morel C, Madarassy G, Deruty R: Recurrent lumbosacral metastases from intracranial meningioma. Report of a case and review of the literature. Acta Neurochir (Wien) 143:935–937, 2001
4. Durand A, Labrousse F, Jouvet A, Bauchet L, Kalamaridès M, Menei P, et al.: WHO grade II and III meningiomas: a study of prognostic factors. J Neurooncol 95:367–375, 2009
5. Estanislau ES, Carvalho GT, Reis BL, de Freitas Barbosa W, Brandão RA, Sousa AA, et al.: Malignant meningioma with extracranial metastases. Arq Neuropsiquiatr 67:730–732, 2009
6. Euskirchen P, Peyre M: Management of meningioma. Presse Med 47:e245–e252, 2018
7. Fabi A, Nuzzo C, Vidiri A, Ciccarese M, Felici A, Cattani F, et al.: Bone and lung metastases from intracranial meningioma. Anticancer Res 26:3835–3857, 2006
8. Harter PN, Braun Y, Plate KH: Classification of meningiomas-advances and controversies. Chin Clin Oncol 6:S2, 2017
9. Kessler RA, Garzon-Muvdi T, Yang W, Weingart J, Olivi A, Huang J, et al.: Metastatic Atypical and Anaplastic Meningioma: A Case Series and Review of the Literature. World Neurosurg 101:47–56, 2017
10. Lee GC, Choi SW, Kim SH, Kwon HJ: Multiple extracranial metastases of atypical meningiomas. J Korean Neurosurg Soc 45:107–111, 2009
11. Ludwin SK, Conley FK: Malignant meningioma metastasizing through the cerebrospinal pathways. J Neurol Neurosurg Psychiatry 38:136–142, 1975
12. Modha A, Gutin PH: Diagnosis and treatment of atypical and anaplastic meningiomas: a review. Neurosurgery 57:538–550, 2005
13. Palmer JD, Cook PL, Ellison DW: Extracranial osseous metastases from intracranial meningioma. Br J Neurosurg 8:215–218, 1994
14. Perry A, Stafford SL, Scheithauer BW, Suman VJ, Lohse CM: Meningioma grading: an analysis of histologic parameters. Am J Surg Pathol 21:1455–1465, 1997
15. Terzi A, Saglam EA, Barak A, Soylemezoglu F: The significance of immunohistochemical expression of Ki-67, p53, p21, and p16 in meningiomas tissue arrays. Pathol Res Pract 204:305–314, 2008
16. Thomas RZ, Dalal I: Extracranial metastases of anaplastic meningioma. BJR Case Rep 3:20150092, 2017
17. Tominaga T, Koshu K, Narita N, Yoshimoto T: Metastatic meningioma to the second cervical vertebral body: a case report. Neurosurgery 34:538–539, discussion 539-540. 1994
18. Tournat H, Huchet A, Ouhabrache N, Thomas IC, Roubaud G, Maire JP: [Bone metastatic evolution of a recurrent meningioma: case report]. Cancer Radiother 10:590–594, 2006

The Nerve

Case Report

The Nerve 2023;9(1):85-89
https://doi.org/10.21129/nerve.2023.00318
eISSN 2465-891X

Neurogenic Thoracic Outlet Syndrome Induced by Subclavius Muscle Hypertrophy: A Case Report

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OPEN ACCESS

Received: March 23, 2023
Revised: April 6, 2023
Accepted: April 20, 2023

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Neurogenic thoracic outlet syndrome (NTOS) is a complex disorder characterized by compression of the brachial plexus, resulting in pain, weakness, and sensory changes in the upper extremity. Traditional surgical treatments, such as first rib resection or anterior scalene muscle resection, can be invasive and associated with significant morbidity. We present a unique case of a patient diagnosed with NTOS who underwent a preoperative magnetic resonance imaging with the shoulder in an abduction position to identify the cause of NTOS. A minimally invasive subclavius muscle resection was subsequently performed, resulting in a dramatic reduction in pain and significant improvement in motor symptoms. This less invasive approach led to a quicker recovery time and reduced morbidity compared to traditional surgical methods. This case report suggests that before surgery, thoroughly investigating the causes of NTOS and selectively performing decompression only on the structures requiring intervention could also be considered a viable treatment option.

Keywords: Brachial plexus; Clavicle; Hypertrophy; Thoracic outlet syndrome

INTRODUCTION

Neurogenic thoracic outlet syndrome (NTOS) is a recognized condition resulting from insufficient space surrounding the brachial plexus. Multiple anatomical structures may compress the brachial plexus; recent findings indicate that subclavius muscle compression during shoulder abduction may also contribute. Specifically, subclavius muscle hypertrophy in overhead athletes may lead to neuronal structure compression. We present a case in which successful treatment of NTOS was achieved through addressing subclavius muscle hypertrophy.

CASE REPORT

A 41-year-old male visited the hospital with functional disorders, including pain, numbness, abnormal sensation, and right shoulder weakness. The pain and numbness were primarily located around the shoulder not along with any sensory dermatome, with the main symptom being a pain in shoulder abduction and flexion position. The patient mentioned that the symptoms listed above had been gradually worsening for the past three months. He experienced sudden right shoulder pain and tingling sensation, leading to multiple hospital visits. Persistent symptoms brought

him to our hospital. The patient had no relevant medical history and had been working as a heavy goods delivery worker for 10 years. Initial physical examination showed no right shoulder muscle atrophy or skin abnormalities, such as rashes or discoloration. Neurological examination revealed muscle strength was reduced to grade IV in right shoulder flexion and abduction, and there was end-range pain during passive range of motion, but a whole range was achievable. Furthermore, there was no motor weakness or sensory changes at the distal finger and wrist level, and the scapular area appeared normal, with no abnormal findings such as winged scapula observed., with severe pain (visual analogue scale [VAS] score 8) and radiating pain in the right upper extremity during shoulder flexion and abduction. A cervical spine magnetic resonance imaging (MRI) showed no abnormalities causing radiculopathy or myelopathy. X-ray and computed tomgoraphy imaging of the cervicothoracic spine and chest confirmed no clavicle or first rib deformities. Contrast-enhanced MRI was performed to explore the brachial plexus area, generating axial, coronal, and sagittal images and comparing anatomical neutral position and right shoulder abduction to verify potential brachial plexus compression.

MRI results revealed no contact between the brachial plexus and subclavius muscle in the anatomical neutral position (Fig. 1). However, a high-intensity signal was identified in the image taken at the right shoulder abduction position, indicating reduced fat tissue density around the nerve due to subclavius muscle compression. Additionally, reduced right subclavian artery diameter and collapsed right subclavian vein were observed (Fig. 2).

After symptom onset, conservative treatment was administered for six weeks, followed by an electrophysiological examination, revealing right brachial plexopathy at the medial cord or lower trunk level and partial axonal injury. Despite treatment, the patient continued experiencing shoulder weakness (grade IV), severe radiating pain, and numbness. Surgery was scheduled two months after symptom onset.

Under general anesthesia, the patient was placed in a supine position, and a paraclavicular approach was chosen with a 10 cm horizontal skin incision around the clavicle to decompress the brachial plexus in the subclavian area. A hypertrophic subclavius muscle was identified below the clavicle, along with structures like the artery, vein, and compressed brachial plexus. Fine dissection and careful coagulation were performed to expose both the origin and insertion site of the subclavius muscle using Metzenbaum scissors and a bipolar coagulator (Fig. 3). It was confirmed that there was no damage to the surrounding artery, vein, or nerve. The origin and insertion site of the subclavius muscle were clearly identified, and the final resection was done using a monopolar coagulator for cutting and coagulation. Upon examination with a microscope during surgery, it was confirmed that the compressed brachial plexus nerve was expanded and decompressed. The subclavius muscle was completely resected, and the subclavicular area became abundant. The space was large enough for finger exploration, and it was possible to confirm the expansion of the pre-

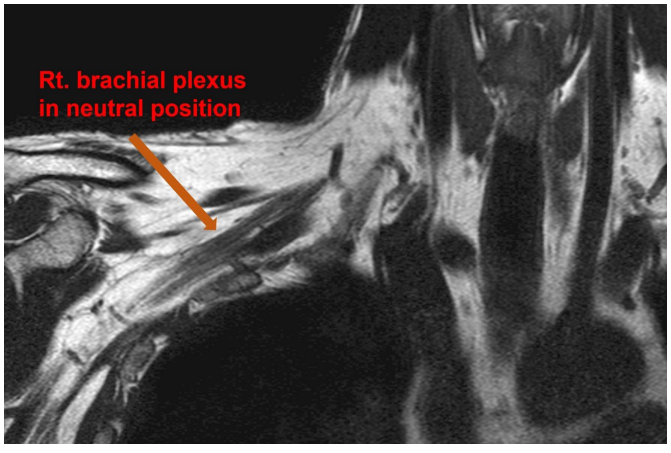

Fig. 1. Magnetic resonance imaging in neutral position. Rt.: right.

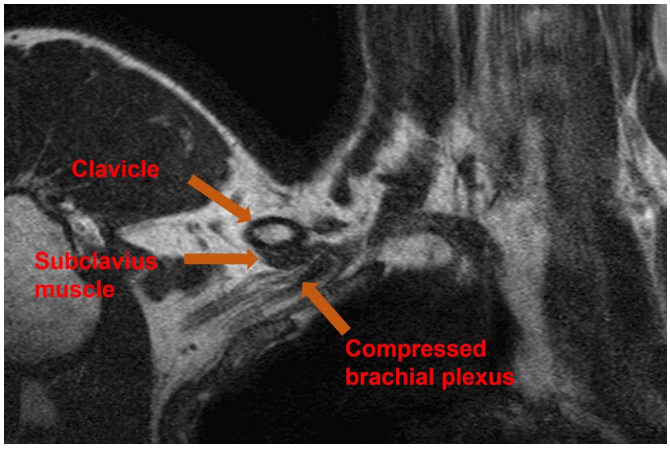

Fig. 2. Magnetic resonance imaging in shoulder abduction position.

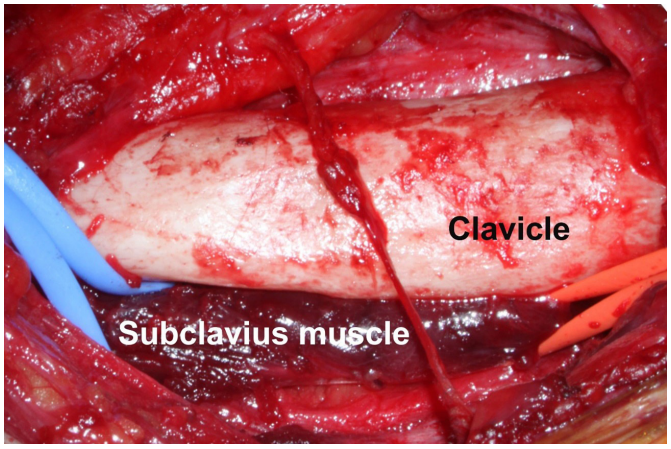

Fig. 3. Intraoperative photo.

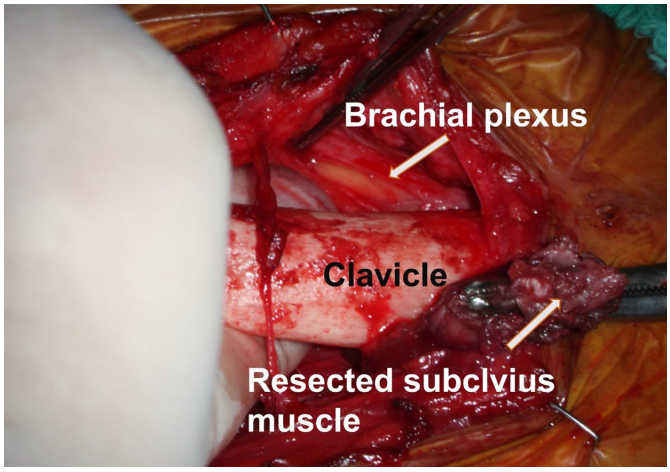

Fig. 4. Intraoperative photo. After resection of subclavius muscle. Upon resection of the subclavius muscle, the space beneath the clavicle became more spacious and was large enough to explore with a finger. We confirmed that the previously compressed brachial plexus was decompressed and had expanded.

viously compressed brachial plexus (Fig. 4). No abnormalities were found in other structures compressing the brachial plexus. First rib resection and anterior scalene muscle (ASM) release were not performed.

Post-surgery, the patient wore a shoulder brace, and a follow-up MRI was conducted one week later to confirm changes. Compared to preoperative MRI, perineural fat obliteration around the brachial plexus was recovered, and subclavian artery diameter reduction and subclavian vein collapse improved (Fig. 5). The patient was discharged two weeks after surgery, reporting significant numbness improvement. Three months after surgery, physical examination showed dramatic right shoulder muscle strength improvement (grade V) and no severe pain during shoulder abduction (VAS 1). Follow-up electrophysiological examination confirmed the disappearance of upper extremity muscle degeneration potential.

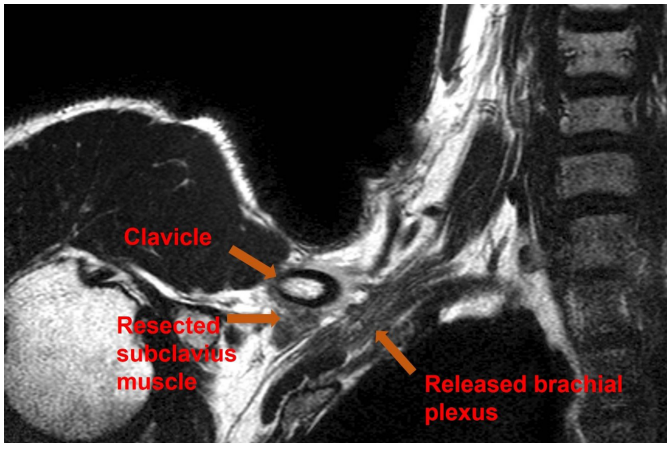

Fig. 5. Follow up magnetic resonance imaging in shoulder abduction position after 1 week from operation.

DISCUSSION

Thoracic outlet syndrome (TOS) was initially described in 1927 by Adson and Coffey[1], who coined the term 'scalenus anticus syndrome' and suggested that symptoms were caused by the compression of the subclavian artery by the ASM. TOS is currently defined as the compression of the brachial plexus, subclavian artery or vein, or the invasion of the brachial plexus in three distinct areas: the scalene triangle, costoclavicular space, and subcoracoid (pectoralis minor) space[13,19]. Additionally, a report has documented non-specific TOS types also[15].

Neurogenic TOS is differentiated from vascular TOS based on clinical presentations and symptoms[12]. Neurogenic TOS was characterized by pain, weakness, and paresthesia of the upper extremity, while vascular TOS was primarily characterized by symptoms of arterial or venous insufficiency such as coldness, cyanosis, and edema. In addition, vascular TOS patients tended to have a history of trauma, while neurogenic TOS patients were more likely to have repetitive strain injuries or other occupational factors.

Recently, standardized clinical diagnostic criteria for

neurogenic thoracic outlet syndrome have been published, leading to increased awareness of this condition[10]. Two large-scale studies demonstrated that over 90% of NTOS cases result from neural compression on the brachial plexus at the C5 to T1 levels[8,18]. First rib resection following standard surgical procedures has an approximate success rate of 90%[9,17].

The electrophysiological study results showed axonal injury of the lower trunk or medial cord, which may not fit well with the case patient's symptoms of decreased shoulder strength. However, the dynamic MRI results demonstrated brachial plexus compression due to subclavius muscle hypertrophy, causing symptoms limited to the right shoulder. We believe the decrease in shoulder motor strength is due to NTOS, as supported by the MRI findings. Additionally, it is believed that the finding that appeared preoperatively on the electrophysiological study and then disappeared was a secondary finding caused by the hypertrophied subclavius muscle mechanically irritating the nerve. We believe that the hypertrophy of the subclavius muscle exacerbates the compression and irritation of a portion of the brachial plexus in the narrow costoclavicular area during shoulder abduction or flexion. This is thought to have caused severe numbness and pain, which then led to a secondary reduction in muscle strength.

When selecting surgical procedures for NTOS, trans-axillary, superior clavicular, or supraclavicular approaches combined with infraclavicular approaches are typically considered. Before surgery, a thorough review of these three options is necessary. Distinguishing between NTOS and vascular TOS is also necessary too. A comprehensive assessment of the brachial plexus's surrounding structures and their compression degree should precede the surgical approach determination. In some instances, wide resection, including the first rib, may be required.

On the other hand, there have been several reports that the subclavius posticus muscle can contribute to thoracic outlet syndrome[2,3,6,7,14,16]. The connection between subclavius muscle hypertrophy and TOS has been investigated in multiple cadaveric studies[5,11]. The subclavius muscle's origin is the first rib and its costal cartilage, while its insertion is the subclavian groove. The muscle is known to cause clavicular depression and first rib elevation. One study reported that adding subclavius muscle resection to NTOS palliative treatment could improve results[13]. Another study suggested that botulinum toxin injections into the subclavius muscle could serve as a potential TOS treatment option[4].

Diagnostic technology advancements have enabled more detailed radiological evaluations of anatomical structures compressing the brachial plexus. In this case, preoperative MRI revealed brachial plexus compression due to subclavius muscle hypertrophy, causing symptoms limited to the right shoulder. Based on this finding, we planned right subclavius muscle decompression only, yielding a favorable outcome.

CONCLUSION

Through meticulous preoperative imaging studies and comprehensive evaluations of NTOS patients, functional recovery may be achieved with a minimal surgical approach in some cases.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Adson AW, Coffey JR: Cervical rib: a method of anterior approach for relief of symptoms by division of the scalenus anticus. Ann Surg 85:839–857, 1927
2. Akita K, Ibukuro K, Yamaguchi K, Heima S, Sato T: The subclavius posticus muscle: a factor in arterial, venous or brachial plexus compression? Surg Radiol Anat 22:111–115, 2000
3. Cavallieri F, Galletti S, Fioravanti V, Menozzi E, Contardi S, Valzania F: Botulinum toxin treatment for thoracic outlet syndrome induced by subclavius muscle hypertrophy. NeuroSci 2:135–140, 2021
4. Ciampi P, Agnoletto M, Scotti C, Ballis R, Gerevini S, Peretti GM, et al.: Thoracic Outlet Syndrome in the Overhead Athlete: A Report of 2 Cases of Subclavius Posticus Muscle. Clin J Sport Med 27:e29–e31, 2017
5. Forcada P, Rodríguez-Niedenführ M, Llusá M, Carrera A: Subclavius posticus muscle: supernumerary muscle as a potential cause for thoracic outlet syndrome. Clin Anat 14:55–57, 2001
6. Grigoriță L, Vaida MA, Jianu A: An Aberrant Subclavius Posticus Muscle: A Case Report. Med Princ Pract 27:579–581, 2018
7. Hempel GK, Shutze WP, Anderson JF, Bukhari HI: 770 consecutive supraclavicular first rib resections for thoracic outlet syn-

drome. Ann Vasc Surg 10:456–463, 1996
8. Illig KA, Donahue D, Duncan A, Freischlag J, Gelabert H, Johansen K, et al.: Reporting standards of the Society for Vascular Surgery for thoracic outlet syndrome. J Vasc Surg 64:e23–e35, 2016
9. Jones BM, Carey FJ: Hypertrophy of the subclavius muscle in conjunction with atrophy of the pectoralis muscles post mastectomy: a cadaveric case study. JOSPT Cases 0:1–24, 2023
10. Klaassen Z, Sorenson E, Tubbs RS, Arya R, Meloy P, Shah R, et al.: Thoracic outlet syndrome: a neurological and vascular disorder. Clin Anat 27:724–732, 2014
11. Liu Y, Zhang Z, Wang J, Wu G, Yu W, Cui S: Improved functional outcome in NTOS patients following resection of the subclavius muscle with radiological signs of nerve impingement: indication of participation of the subclavius in brachial plexus compression. J Neurosurg:1–11, 2018
12. Muellner J, Kaelin-Lang A, Pfeiffer O, El-Koussy MM: Neurogenic thoracic outlet syndrome due to subclavius posticus muscle with dynamic brachial plexus compression: a case report. BMC Res Notes 8:351, 2015
13. Ozçakar L, Güney MS, Ozdağ F, Alay S, Kiralp MZ, Görür R, et al.: A sledgehammer on the brachial plexus: thoracic outlet syndrome, subclavius posticus muscle, and traction in aggregate. Arch Phys Med Rehabil 91:656–658, 2010
14. Roos DB: The place for scalenectomy and first-rib resection in thoracic outlet syndrome. Surgery 92:1077–1085, 1982
15. Sanders RJ, Annest SJ. Anatomy of the thoracic outlet and related structures. In: Illig KA, Thompson RW, Freischlag JA, Donahue DM, Jordan SE, Lum YW eds. Thoracic outlet syndrome. Cham, CH: Springer Cham, 2021, pp37–44
16. Sanders RJ, Hammond SL, Rao NM: Thoracic outlet syndrome: a review. Neurologist 14:365–373, 2008
17. Smayra T, Nabhane L, Tabet G, Menassa-Moussa L, Hachem K, Haddad-Zebouni S: The subclavius posticus muscle: an unusual cause of thoracic outlet syndrome. Surg Radiol Anat 36:725–728, 2014
18. Urschel HC, Razzuk MA: Neurovascular compression in the thoracic outlet: changing management over 50 years. Ann Surg 228:609–617, 1998
19. Wilbourn AJ: The thoracic outlet syndrome is overdiagnosed. Arch Neurol 47:328–330, 1990

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