Unusual clinical presentation of cervical extradural meningioma detected with neuromuscular ultrasound: A case report

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Received May 12, 2023; Accepted February 12, 2024

DOI: 10.3892/etm.2024.12493

Abstract. Extradural meningiomas are rare in the cervical region. A total of 70-77% of reported cases have occurred in the thoracic region. Tumors that occur in the cervical region may invade the adjacent nerve root and brachial plexus. Typically, diagnoses of extradural meningioma are made after patients present with signs of myelopathy, such as progressive paresis and numbness. In the current study, a 64-year-old male patient presented with neck pain, numbness and mild weakness in the left hand over a 6-month period. The general neurological examination was unremarkable, except for mild grasping weakness on the left side. Needle electromyography revealed complex repetitive discharges in the left 5 and 6th cervical paraspinal muscles. Neuromuscular ultrasound revealed a lesion over the left 7th cervical root, which enabled the early detection of an extradural meningioma before notable focal neurological defects developed. The patient underwent a subtotal tumor excision, followed by radiotherapy for residual tumor. Histopathological examination confirmed atypical meningioma.

Introduction

Spinal meningiomas represent 1.2-12% of all meningiomas (1,2). Most spinal meningiomas originate in the intradural extramedullary region, and extradural spinal meningiomas are infrequent (2.5-3.5% of all spinal meningiomas) (3,4). The age-adjusted incidence of spinal meningioma ranges between 0.193 and 0.33 cases per 100,000 individuals (5,6) in the United States (7). Spinal meningiomas are primarily located in the thoracic region but, on rare occasions, may occur in the cervical (14-27%) or lumbar regions (2-14%) (1,2,8). Furthermore, these tumors are most commonly observed in individuals aged between 40 and 80 years (1), with a higher prevalence among female individuals (female to male ratio of 4:1) (2,9). Diagnosis is typically based on evident neurological decline, with symptoms usually manifesting as focal weakness, gait disturbances, pain, sensory deficits and neurogenic bowel or bladder dysfunction attributable to spinal cord compression (1,3). The current primary treatment option is complete surgical resection to prevent further neurological deterioration (10,11). The present study examined a unique case involving an extradural meningioma that infiltrated the brachial plexus, cervical root and spinal cord following a subtotal resection. The patient experienced distant metastasis to the liver within 1 year postoperatively.

Case report

A 64-year-old male patient with type 2 diabetes mellitus and left frozen shoulder (diagnosed in December 2021) was admitted to Chang Gung Memorial Hospital at Linkou Medical Center (Taoyuan, Taiwan) on July 2022. The patient reported progressive pain in the left shoulder, which had persisted for 6 months since December 2021. Before the patient came to Chang Gung Memorial Hospital, a shoulder X-ray, which revealed normal findings, had been performed at a local clinic (Taoyuan, Taiwan). The patient described that the level of pain over the left shoulder was more intense at night than during the day and was accompanied by numbness and tingling sensations, which negatively affected their quality of sleep. The patient complained of experiencing mild weakness in the left upper extremities over the last 3 months (starting approximately in April 2022). Although the patient attended physiotherapy and took general painkillers, the treatment outcome was poor, and the numbness and weakness persisted. No complaints of urinary or bowel disturbances were reported. On admission to Chang Gung Memorial Hospital, a neurological examination revealed full muscle strength in both the upper and lower

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Abbreviations: MRI, magnetic resonance imaging; H&E, hematoxylin and eosin

Key words: nerve tumor, neuromuscular ultrasound, shoulder pain, spinal meningiomas

limbs. The grip strength of the patient was 30 kilogram-weight (kgw) in the right hand and 20 kgw in the left hand. Pin-prick sensation tests revealed diminished sensation over the left C5-C6 dermatome. Deep tendon reflexes were normal for both upper and lower limbs. Regarding the left shoulder, the range of motion was limited, with 170˚ abduction and 70˚ external rotation; however, the patient had a full range of motion in terms of internal rotation and adduction. The patient exhibited a typical gait pattern during walking.

Considering the neurological findings, a diagnosis of cervical radiculopathy accompanied by a concurrent case of mild frozen shoulder was hypothesized. To thoroughly evaluate the condition, electrophysiological and ultrasound examinations of the neck and shoulder were performed.

Electrophysiological studies and neuroimaging. An assessment of nerve conduction in the upper extremities revealed a reduction in the amplitude of sensory nerve action potentials, particularly in the left median and ulnar nerves. Needle electromyography revealed complex repetitive discharges in the left 5 and 6th cervical paraspinal muscles. Subsequent examination using neuromuscular ultrasound revealed a lesion localized to the left 7th cervical root (Fig. 1). Magnetic resonance imaging (MRI) further revealed a hyperintensity fusiform mass measuring 5.5x6 cm on T2-weighted short inversion time inversion recovery sequences. The mass extended from the left 6/7th cervical to the 7th cervical/1st thoracic neural foramens and reached into the left brachial plexus. Additionally, T1-weighted images with contrast demonstrated an enhanced mass extending into the left brachial plexus accompanied by compression on the spinal cord (Fig. 2A and B).

Based on these findings, the presumptive diagnosis before surgery was schwannoma or malignant nerve sheath tumor.

Surgical intervention and histopathological findings. An incomplete tumor excision was performed due to the encasement of the tumor around the vertebral artery. This intervention involved a laminectomy of the 6 and 7th cervical vertebrae, an excision of the 7th cervical nerve root, a phrenic nerve transfer and neurolysis of the 8th cervical spinal nerve. Intraoperative observations and gross pathology revealed tumor-like masses (Fig. 2C and D).

The resected tissues were fixed with 10% neutral-buffered formalin [4% (v/v) formaldehyde solution diluted using phosphate buffer at pH 7.0] at room temperature for 8-24 h and then cut into 4- to 6-μm thick sections. Hematoxylin and eosin staining was performed at room temperature using Mayer's hematoxylin solution for 15 min and eosin solution for 40 sec. Sections were observed using a light microscope (Olympus BX51) with a digital slide scanner (Hamamatsu NanoZoomer S360). The proliferation of epithelioid to spindle tumor cells was observed. Furthermore, a sheet-like growth pattern, focal necrosis and increased mitotic activity were also observed (Fig. 3A and B).

Immunohistochemical (IHC) analysis was performed. Following tissue fixation (as aforementioned), the samples were embedded in paraffin and cut into 4-μm thick sections. The Bond-III Fully Automated IHC and ISH Staining System (Leica Biosystems) was used and sections were dewaxed using Bond Dewax Solution (cat. no. AR9222; Leica Biosystems),

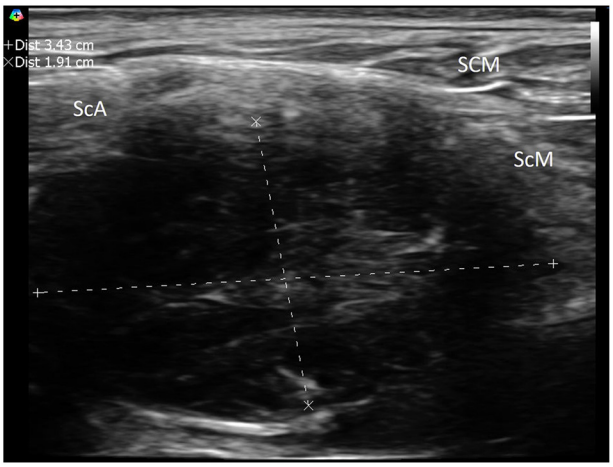

Figure 1. Neuromuscular ultrasound. A hypoechoic mass lesion (3.49x1.91 cm) was revealed over the left C7 cervical root, which extended to the interscalene brachial plexus. Dist, distance; ScA, anterior scalene; ScM, medial scalene muscle; SCM, sternocleidomastoid muscle.

rehydrated with 100% alcohol, and then washed using Bond Wash Solution (cat. no. AR9590; Leica Biosystems). Antigen retrieval was performed using Bond Epitope Retrieval Solution 2 (cat. no. AR9640; Leica Biosystems) in pH 9.0 for 30 min, or in acidic condition using Bond Epitope Retrieval Solution 1 (cat. no. AR9961; Leica Biosystems) pH 6.0 for 20 min at 100˚C. Subsequently, the peroxide block reagent in Bond Polymer Refine Detection kit (cat. no. DS9800; Leica Biosystems), which contained 3-4% (v/v) hydrogen peroxide, was applied at room temperature for 5 min. The following primary antibodies were incubated with the sample for 15 min at room temperature: Epithelial membrane antigen (EMA; 1:200; cat. no. EMA-L-CE; Leica Biosystems), somatostatin receptor 2A (SSTR2A; 1:100; cat. no. RBK046-05; Zytomed Systems GmbH), S100 (1:500; cat. no. S100-167-L-CE; Leica Biosystems), SOX10 (1:100; cat. no. Z2293ML; Zeta Corporation) and Ki-67 (1:300; cat. no. M7240; Dako; Agilent Technologies, Inc.). The Bond Polymer Refine Detection kit also contained a post primary linker (incubated with the sample for 8 min), DAB for visualization (incubated with the sample for 5 min) and hematoxylin counterstain (incubated with the sample for 5 min), which were all used at room temperature. Samples were then imaged using a light microscope. IHC analysis indicated positive reactions to EMA and SSTR2 and negative reactions to S100 and SOX10 (Fig. S1A-C). This distinct immunoprofile serves a role in differentiating this tumor from neurogenic mimics, such as cellular schwannoma or malignant peripheral nerve sheath tumor.

The Ki-67 labeling index was determined to be 15%. Based on these pathological characteristics, the tumor was classified as a World Health Organization Grade II atypical meningioma (12) (Fig. 3C and D).

Postoperative follow-up. Following the surgical intervention, radiotherapy was administered to target any remaining tumor tissue, with a total dose of 5,000 cGy provided in 25 fractions (five sessions per week, administered once daily, over a period of 5 weeks). The pathology findings confirmed the classification of grade II meningioma. However, during the 1-year

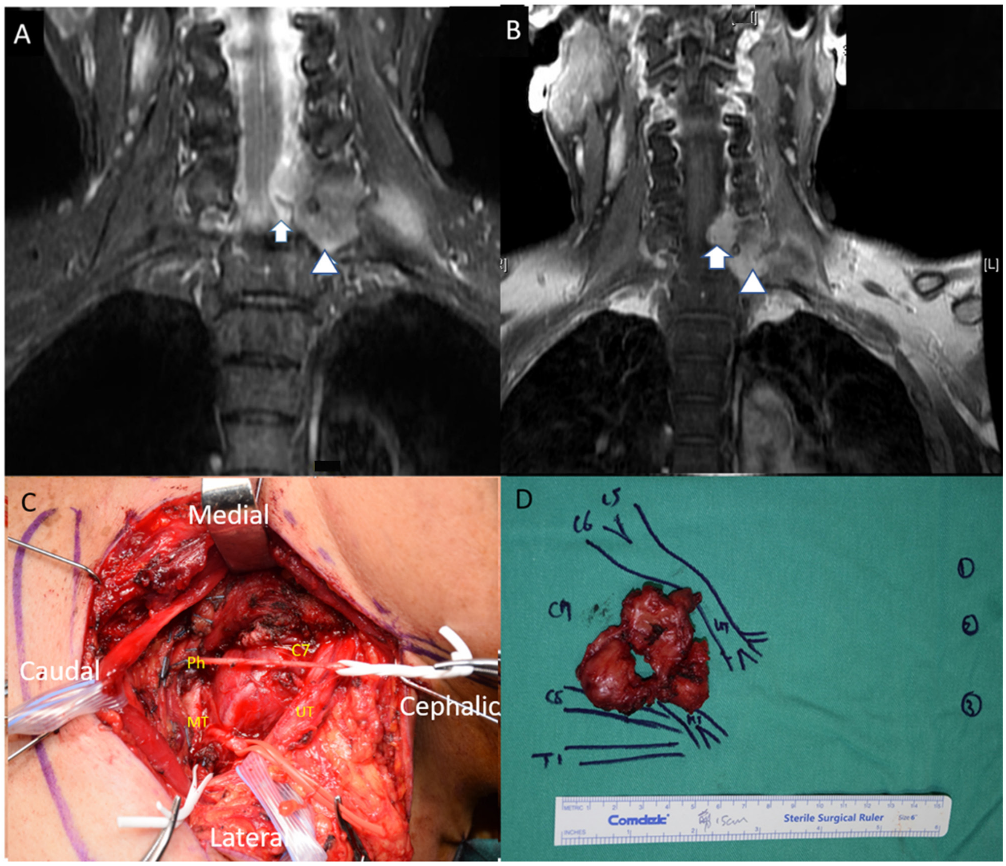

Figure 2. MRI of the cervical brachial plexus. A predominant hyperintense mass lesion originated from the left C7 root (arrow) and extended to the brachial plexus (arrow head) in (A) T2-weighted short inversion time inversion recovery sequence and (B) T1-weighted image with contrast medium. (C) Intraoperative image revealing an undefined mass, which affected the brachial plexus. (D) Macroscopic features that had well-circumscribed, lobular and firm lesions. C7, 7th cervical root; UT, upper trunk of brachial plexus; MT, middle trunk of brachial plexus; Ph, phrenic nerve.

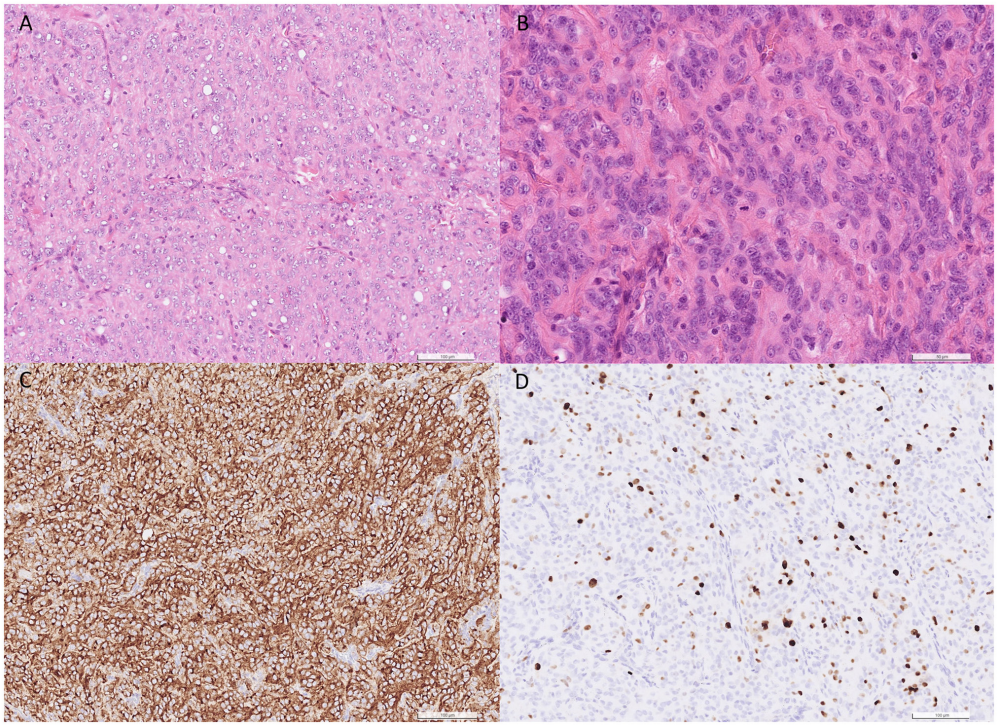

Figure 3. Histopathology of atypical meningiomas. (A) H&E staining demonstrated a sheet-like growth pattern and proliferation of spindle tumor cells (arrows; magnification, x200). (B) H&E staining demonstrated a high cellular density and an increased presence of mitotic cells (arrow head; magnification, x400). (C) Epithelial membrane antigen staining (magnification, x200). (D) Ki-67 staining demonstrated an elevated Ki-67 labeling index (magnification, x200). H&E, hematoxylin and eosin stain.

Table I. Extradural spinal meningiomas: A literature review.

First author, year	Age, years	Sex	Clinical features	Duration of symptoms	Location	Histopathology	Treatment	(Refs.)
Raesh and Shetty, 2021	18	M	Swelling on the left side of the neck for 1 year associated with neck pain radiating to the left upper limb	1 year	C4-C5	Fibroblastic meningioma	C4-C5 laminectomy; subtotal tumor excision	(19)
Sakamoto *et al*, 2018	57	F	Progressive sensorimotor disturbance in the left upper extremity	1 year	C6-T1	Fibrous meningioma	C5-C7 hemilaminectomy; subtotal excision	(20)
Zevgaridis and Thomé, 2002	75	F	Incidental finding by magnetic resonance imaging	Unknown	T11-T12	Psammomatous meningioma	laminectomy of T11 and T12; total tumor excision	(21)
Saade *et al*, 2014	59	M	Right neck stiffness	Several months	C1-C3	Pathognomonic spindled or polygonal cell	Complete resection	(22)

M, male; F, female; C, cervical root; T, thoracic.

follow-up of the patient in Chang Gung Memorial Hospital (Taoyuan, Taiwan) on October 2023, distant metastasis to the liver and lumbar spine was observed in the patient without local recurrence. The patient continues to receive follow-up care in the Department of Radiation Oncology at Chang Gung Memorial Hospital (Taoyuan, Taiwan).

Discussion

Spinal meningiomas are more common (approximately a 4:1 ratio) in women compared with in men (6,13,14), and the majority occur in the thoracic region (77%), followed by the cervical region (14-27%), and less frequently in the lumbar region (2-14%) (1,2,8). Extradural spinal meningiomas are rare (2.5-3.5% or lower of all spinal meningiomas) (3,4) and are associated with a more rapid progression and an aggressive phenotype compared with intradural spinal meningiomas (7,15). In previous studies, the nerve root tumor was usually found in patients that already had obvious neurology signs, such as paraplegia (9,16-18), and to the best of our knowledge, there have only been four previous reports of extradural spinal meningiomas diagnosed without signs of clinical myelopathy (19-22); these are presented in Table I.

The present case presented with left neck and shoulder pain, both subtle clinical signs commonly encountered in clinical practice. Compared with previous cases, the present case was atypical meningioma with brachial plexus involvement. The abnormality detected during electrophysiological examination and the neuromuscular ultrasound provided an indication that led to the to the investigation of a tumor on the left cervical root. Furthermore, the previous 4 cases (Table I) also exhibited no apparent signs of myelopathy, despite the prior observation of radiculopathy signs or the existence of a neck mass. Despite aggressive treatment, the patient in the present study demonstrated an occurrence of distant metastasis, an atypical finding in a meningioma case. According to Kobayashi *et al*, it took a mean time of 11.3 months for the tumor to be revealed in patients (1), and that more than half of the diagnoses were made after clinical signs of weakness and the development of gait disturbance (1). Due to this, these tumors typically usually have long delays between the onset of symptoms and diagnosis.

We hypothesize that cervical and thoracic spinal meningiomas may exhibit distinct clinical features. In cases of cervical spinal meningiomas, the tumor may be in close proximity to the brachial plexus. Unlike thoracic spinal meningiomas, which typically cause direct compression on the spinal cord, cervical tumors may extend through the neuroforamen into the brachial plexus. This anatomical association can pose a challenge for early detection, as the presence of the tumor might not immediately manifest as sensory deficits or signs of myelopathy (9,22,23). Instead, the extension into the brachial plexus may allow for further growth of the tumor before clinical symptoms become evident (9,22,23). Extradural meningiomas in the cervical region are more difficult to excise compared with those in the thoracic region, leading to variations in prognoses between cervical and thoracic extradural meningiomas. Cervical extradural meningiomas are difficult to excise because of their close proximity to the vertebral artery (9,24-26). However, extradural meningiomas located in

the thoracic region generally allow for a total excision of the tumor (9,24-26).

Since the clinical features of extradural and intradural meningiomas are not markedly different, in cases where patients exhibit an inadequate response to conservative treatment for shoulder pain, a comprehensive examination, including electrophysiological studies and neuromuscular ultrasound, may serve as valuable and cost-effective screening tools for detecting structural lesions affecting the nerve root (27,28). Neuromuscular ultrasound is a portable and real-time tool that is useful for disease diagnosis in an outpatient setting (27,29,30). However, MRI remains the gold standard for diagnosis and surgical planning (31). Risk factors for the recurrence of extradural meningioma are being of a younger age, being of the male sex, having dural tail signs on an MRI and a high Simpson grade (1,13). The majority of patients experience improvement after surgery, leading to improved functional outcomes (13). However, distance metastases in meningioma to the liver have been reported, even when the extradural meningioma was detected before notable neurological defects and standard aggressive treatment was used (32). This suggests a more aggressive course of the meningioma. Furthermore, the occurrence of distant metastasis in meningioma is rare, with an incidence rate of ~0.18% across all types of meningioma. A larger tumor size, being of male sex and having a high Simpson grade have been identified as independent factors contributing to the likelihood of distant metastasis (33,34). The spread of meningioma metastases is hypothesized to occur through the venous system, lymphatics or cerebrospinal fluid (32,35).

In the extradural space, arachnoid cells are typically absent. The development of extradural meningiomas is considered to occur through two possible mechanisms: i) Tumor cells arising from ectopic arachinoidal cap cells surrounding the periradicular root sleeves (24,36,37); and ii) embryonic cell remnants of the arachnoid mater in the thin periradicular dural producing extradural meningiomas near the root (24,38).

In the present case, regular clinical monitoring and close long-term follow-up are required for further management. In conclusion, detecting cervical extradural meningioma at an early stage is challenging when a patient presents with non-specific clinical symptoms or signs. Early detection is necessary for a timely and effective treatment. This case demonstrated that neuromuscular ultrasound is a valuable tool, aiding physicians in identifying lesions over the nerve root and brachial plexus, thereby enhancing the screening and diagnosis of meningiomas.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

The data generated in the present study are included in the figures and/or tables of this article.

Authors' contributions

PCH performed the ultrasound, followed the patient clinically and was responsible for the initial drafting of the manuscript. JCYL performed the operation. SCH performed the histological and pathological analyses. CHT was responsible for analyzing the MRI images. HCK was responsible for the interpretation of data. PCH and HCK confirm the authenticity of all the raw data. All authors contributed to revising the draft critically for important intellectual content. All authors read and approved the final version of the manuscript.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent was obtained for the publication of the details of the patient described in this report.

Competing interests

The authors declare that they have no competing interests.

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