



Rare malignant primary spinal intradural extramedullary mesenchymal chondrosarcoma: a case report and literature review

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Background: Mesenchymal chondrosarcoma (MCS) is a rare malignant chondrosarcoma with a high propensity for recurrence and distant metastasis. MCS usually arises from bone tissue, and rarely occurs outside the bone. MCS in the subdural and extramedullary regions of the spinal cord is especially rare. In this article, we report a case of spinal intradural extramedullary MCS with herpes virus infection, which is the first such case reported in East China.

Case Description: A 13-year-old male complained of intermittent low-grade fever, sweating, progressive constipation with weakness of both lower extremities and bilateral hypoesthesia after a 5-month history of herpes virus infection. Spinal magnetic resonance imaging (MRI) revealed a subdural-extramedullary solid nodular mass with isointensity on T1-weighted imaging and hyperintensity on T2-weighted imaging that was located behind the superior margin of the T5 vertebral body. The patient was initially diagnosed with thoracic meningioma and underwent spinal cord tumour resection followed by adjuvant chemotherapy. Histopathological examination revealed that the tumour was mainly composed of round or oval cells and mesenchymal chondroid matrix, and gene analysis showed the fusion of HEY1 exon 4 to NCOA2 exon 13. Both test results were consistent with the diagnosis of primary intraspinal MCS. At the 1-year follow-up, the patient received adjuvant chemotherapy, and the reexamination images revealed no evidence of tumour *in situ* tumour recurrence or distant metastasis.

Conclusions: As more research has been done on MCS, it has been found that the disease is more likely to occur in adolescents, but is often overlooked due to its lack of imaging characterization. Therefore, the misdiagnosis rate can be reduced only by closely considering clinical manifestations with pathology and imaging findings. Although MCS is a highly malignant tumour, early primary spinal intradural extramedullary MCS can cause neurological symptoms, early detection and treatment can achieve basic total surgical resection. Postoperative adjuvant chemoradiotherapy can further reduce recurrence.

Keywords: Mesenchymal chondrosarcoma (MCS); rare; spinal malignant tumour; adolescents; case report

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Introduction

Mesenchymal chondrosarcoma (MCS) is a rare, aggressive, high-grade malignant tumour that arises from cartilaginous bone or soft tissue. MCS was first described in 1959 by Lichtenstein and Bernstein (1) and accounts for approximately 1–10% of all chondrosarcomas (2). Although this primary malignant tumour usually originates from soft tissue and bone, up to one-third of MCSs are found in extraskeletal soft tissue, such as the central nervous system (CNS). Among MCSs, primary spinal intradural extramedullary MCS is exceedingly rare, and only 19 cases have been reported thus far. Although primary intraspinal MCS affects patients of all ages, MCS most frequently occurs during the second decade of life (3). In a recent study, some scholars further confirmed that a new product of gene fusion, HEY1-NCOA2, is a novel biomarker that increases the diagnostic accuracy of MCS (4). The therapeutic recommendation for primary intraspinal MCS is surgical resection, and there is no consensus on the protocol for adjuvant therapy. Herein, we report a case of spinal intradural MCS in a relatively young patient. The patient successfully underwent total surgical resection of the tumour followed by postoperative chemotherapy. Thoracic magnetic resonance imaging (MRI) showed no signs of *in situ* recurrence or distant metastasis at the 1-year follow-up. We present the following article in accordance with the CARE reporting checklist (available at <https://tc.amegroups.com/article/view/10.21037/tcr-21-2703/rc>).

Case presentation

The patient, a 13-year-old boy, was admitted to our hospital mainly due to back pain and fever. The patient had been infected with herpes virus 5 months prior to presentation and suffered recurrent low-grade fever and throat, intercostal and back pain for more than 3 months. During this period, he was diagnosed with a viral infection and given antiviral drug treatment. Ten days prior to presentation, the patient's symptoms gradually progressed to weakness and numbness of both lower limbs, with hypoesthesia, constipation, and difficulty squatting. Neurological examination revealed sanity, normal intelligence, grade 4/5 bilateral lower limb strength and hypesthesia below the xiphoid level; Babinski sign (+), Romberg sign (+) and Hoffman sign (–) results were recorded. The patient denied any previous surgical history and had no family history of cancer, genetic disease, or a similar illness.

Upon admission, the patient had an elevated temperature and no abnormal results on routine blood testing, but the patient was positive for herpes-simplex virus IgM. Considering the history of herpes virus infection, the patient was treated with antiviral drugs and human immunoglobulin, and his body temperature gradually returned to normal.

MRI of the thoracic spine was performed during hospitalization and revealed an intradural mass with dimensions of 1.2 cm × 0.8 cm on the right dorsal side of the spinal canal at the T5 level; this mass caused spinal canal stenosis and compression of the adjacent spinal cord (*Figure 1A-1D*). The lesion was small and circular and characterized by an intermediate signal intensity on T1-weighted image (T1WI) and a slightly hyperintense signal on T2-weighted image (T2WI). Homogeneously enhanced neoplasms with clear boundaries and the dural tail sign were observed on gadolinium enhanced T1WI. A relevant radiological examination revealed no evidence of brain or bone involvement. Based on the imaging diagnosis alone, we initially considered the mass to be a thoracic meningioma.

The patient underwent surgery with a median posterior approach. During the operation, after opening the dura mater, a solid, red mass was observed in the extramedullary region; the mass was located on the right side of the dural sac, and it had displaced the spinal cord anteriorly to the left. A stiff, well-demarcated tumour that weakly adhered to the dura on the right side was exposed when the arachnoid mater was peeled from the surface. Finally, *en bloc* tumour resection was performed, including removal of the attached dura mater, and the lesion was collected for histologic examination.

Histopathological examination showed that the tumour was composed of round cells and a cartilage matrix (*Figure 2A-2D*). Immunohistochemistry showed that the cells were positive for CD99 (*Figure 2D*) and CD10 (focal) expression but were negative for EMA, vimentin, PR, SSTR, GFAP, CD34, NSE, Syn, ERG, inhibin- α , SMA and CD56 expression. The Ki-67 labelling index was 40%. In addition, the genetic test report indicated that the patient harboured SMARCA4 mutations and an NCOA2 rearrangement. The specific manifestations were a V1281I gene point variation, NCOA2/UBXN2B rearrangement, and HEY1 exon 4–NCOA2 exon 13 fusion. The final diagnosis was MCS from the thoracic spinal intradural extramedullary region.

Within 1 week after surgery, the patient's back pain was significantly relieved, and the muscle strength of both lower limbs gradually improved. The postoperative

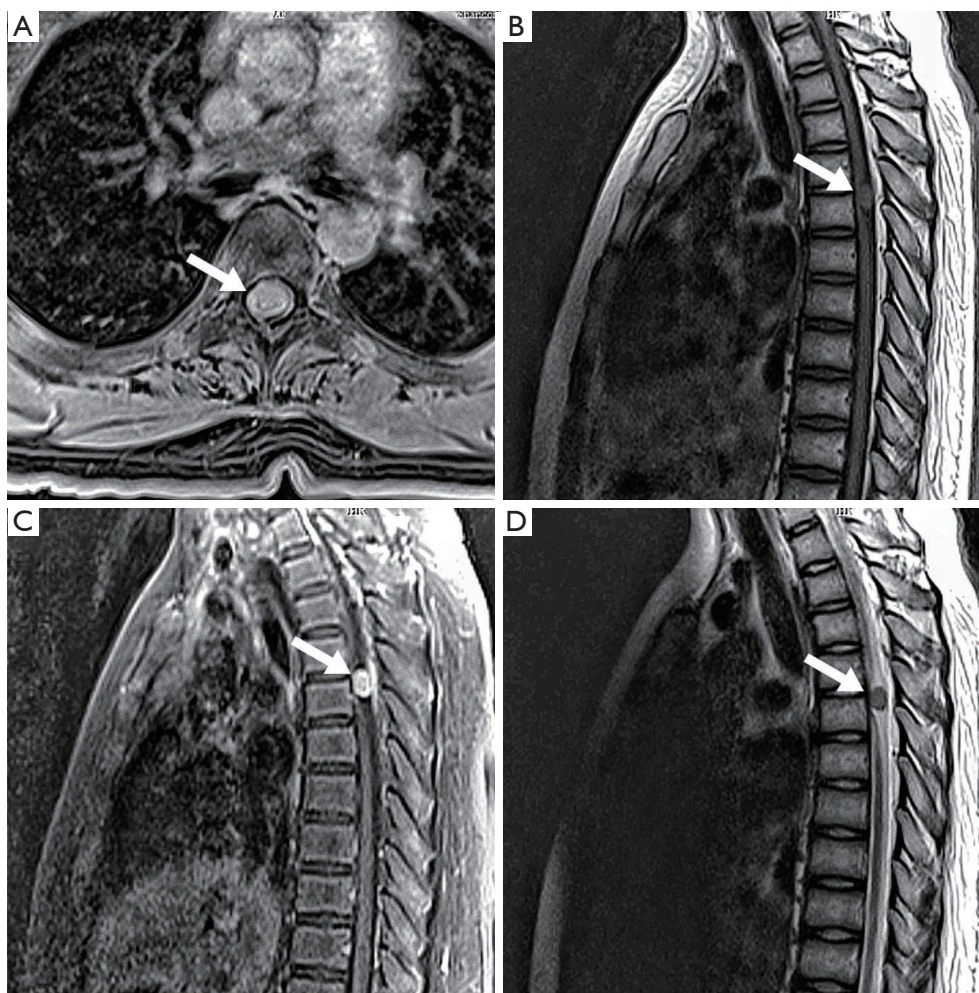


Figure 1 Preoperative MRI scans of spinal tumor. (A) Axial T1WI with gadolinium enhancement. (B) Sagittal T1WI. (C) Sagittal T1WI with gadolinium enhancement. (D) Sagittal T2WI. This epidural mass at the T5 level (white arrows) was characterized by an intermediate signal intensity on T1WI and slightly hyperintense signal on T2WI, with significant enhancement after gadolinium injection. Severe spinal cord compression by the tumour was observed (A). MRI, magnetic resonance imaging; T1WI, T1-weighted image; T2WI, T2-weighted image.

course was uneventful, and during the 6-month follow-up period, the neurological condition of the patient almost completely recovered. After the patient was discharged, he received adjuvant chemotherapy [first chemotherapeutic regimen: pirarubicin, (-)- β -elemene, cyclophosphamide, recombinant human endostatin, vindesine sulfate, and dexrazoxane; second chemotherapeutic regimen: etoposide, ifosfamide, recombinant human endostatin, and amifostine; administered twice as a group]. The patient showed a good tolerance to chemotherapy. Follow-up MRI showed no recurrence or distant metastasis 1 year after surgery (Figure 3A-3D).

All procedures performed in the study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient's legal guardian. A copy of the written consent is available for review by the editorial office of this journal.

Discussion

Spinal intradural extramedullary MCS is an extremely rare malignant tumour that has been described in only a few

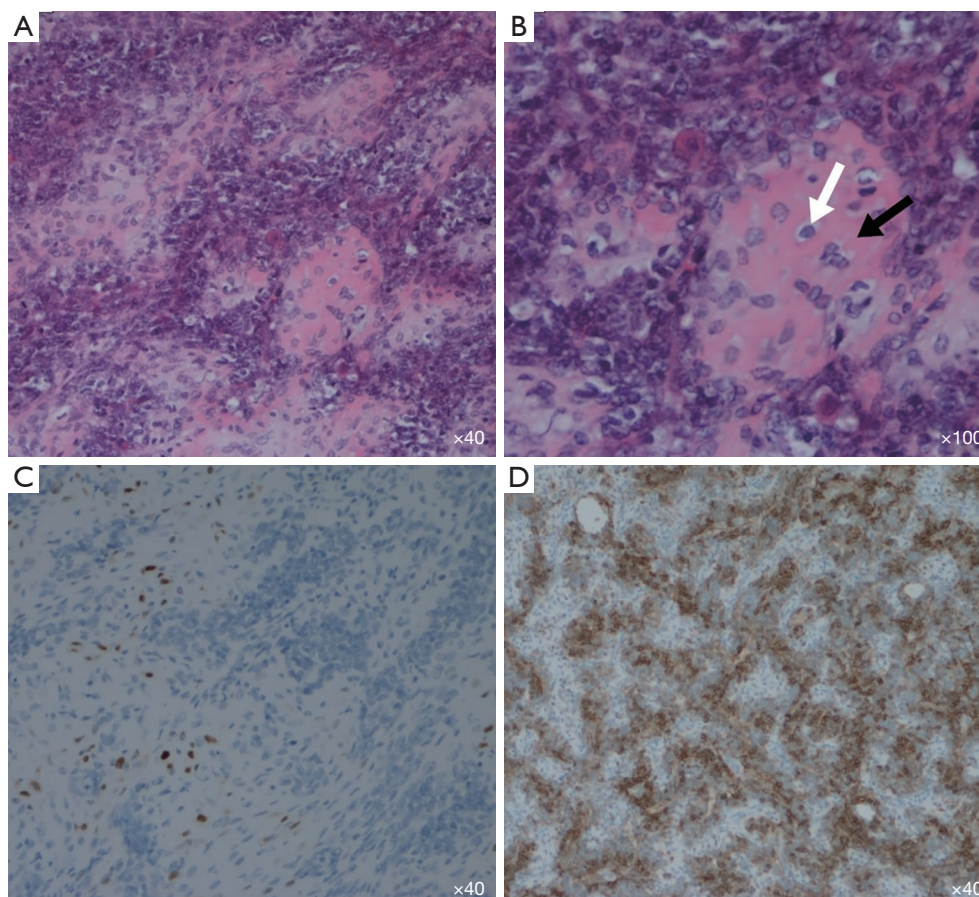


Figure 2 Pathological and immunohistochemical findings of the tumor. (A) At $\times 40$ magnification, the tumour was highly cellular, consisting of a large number of round and oval cells, surrounded by scattered eosinophilic chondroid matrix components. (B) At $\times 100$ magnification of conventional staining, well-differentiated cartilage islands (black arrow) and small round mesenchymal cells (white arrow) were clearly demarcated. Single diffuse and dense mesenchymal cells were observed, and there was a rich supply of small vessels. (C) S100 immunostaining showed many strongly stained chondroid components. (D) Positive staining for CD99 [haematoxylin and eosin, $\times 40$ (A), $\times 100$ (B); immunohistochemical staining with S100, $\times 40$ (C); immunohistochemical staining for CD99, $\times 40$ (D)].

case reports. Including our case, the clinical information of 20 cases of primary intradural MCS in the literature is summarized in (Table 1) (2-18). Although primary intraspinal MCS can occur at any age and in any organ or tissue in the body, the disease tends to occur in younger people, with a mean age of 11 years (18), and most commonly affects the upper lumbar and lower thoracic spine. These tumours are usually solitary and tend to be located on the right side of the spine. Moreover, the tumours are described as “hard” and “firm”, which may be related to local calcification.

Histologically, the main components of MCS are cartilage and undifferentiated round cells, which exhibit focal calcification or chondrogenic changes. Immunocytochemical staining for the S-100 protein can help to indicate the

chondroid component of the tumour (18). Positive staining for SOX9 in nuclei can confirm the diagnosis of MCS when the transitional area between the chondroid and mesenchymal parts or the chondroid part are unclear (19). HEY1-NCOA2 gene fusion is a powerful molecular diagnostic tool for MCS and has high specificity and sensitivity since it has only been detected in MCS (4). As MCS becomes better known, it should also be included in the preoperative differential diagnosis of spinal tumours in adolescents.

In our case, preoperative spinal imaging revealed that the lesion was small, circular, and characterized by an intermediate signal intensity on T1WI and a slightly hyperintense signal on T2WI, and the dural tail sign was observed on gadolinium enhanced T1WI; these findings

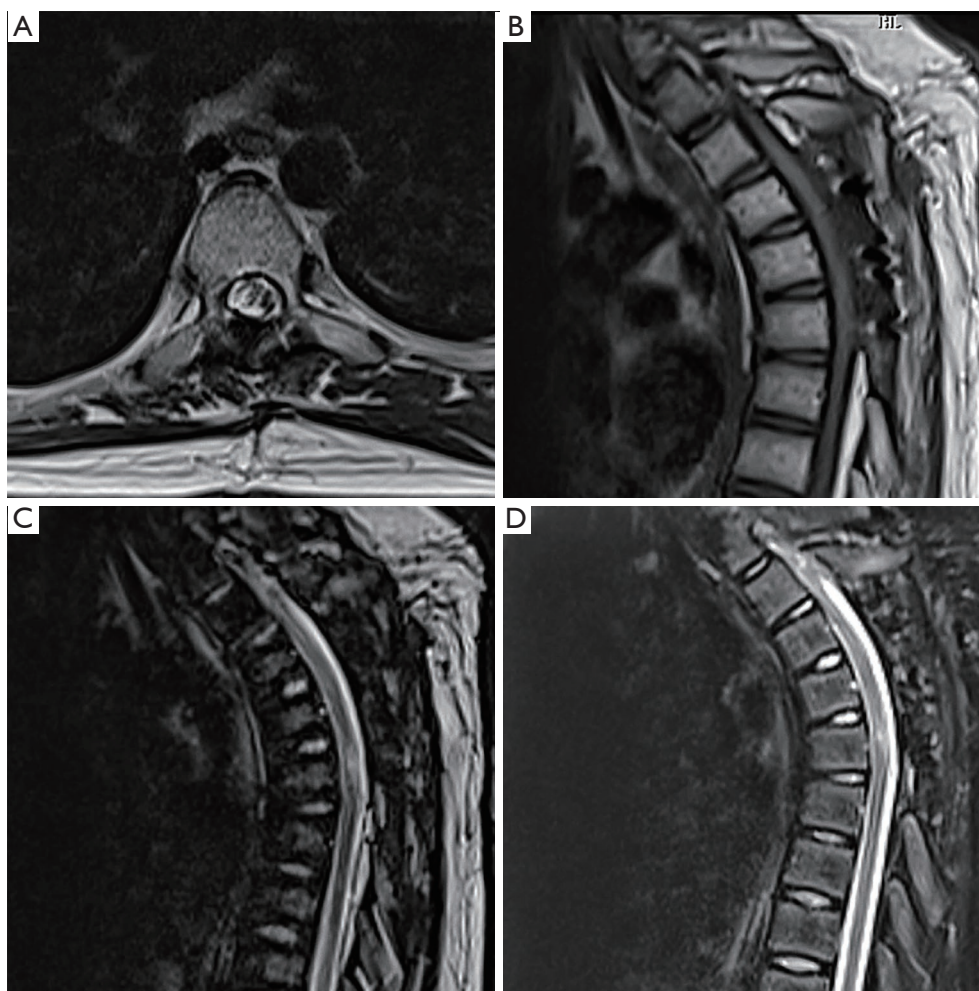


Figure 3 One-year postoperative MRI scans of spinal. (A) Axial T2WI. (B) Sagittal T1WI. (C) Sagittal T2WI. (D) Sagittal T2WI-SPIR. MRI of the thoracic vertebrae 1 year after surgery. After intraspinal tumour resection, some of the thoracic vertebral bones were absent, and the internal fixation instrumentation could be seen. No obvious foci of abnormal enhancement were observed in the thoracic pulp on enhanced imaging. The curvature of the thoracic vertebrae was fair, the vertebral body sequence was normal, no other obvious abnormal signal foci were observed, and there was no evidence of recurrence *in situ*. MRI, magnetic resonance imaging; T2WI, T2-weighted image; T1WI, T1-weighted image; SPIR, spectral presaturation with inversion recovery.

are similar to the imaging features of meningiomas and schwannomas. Thus, we propose the following suggestions for the differentiation of spinal MCS from other tumours on imaging. First, MCS, a malignant tumour, has an average disease duration of 3–4 months and may progress more rapidly than other benign tumours in terms of the time course of onset. Second, by combining the patient's age, it helps determine the diagnosis. Because patients with this disease are generally young. Third, tumour calcification can be observed using plain computed tomography (CT) scans of the spinal cord, which is also important information for

diagnosing MCS (3,18).

Since this disease mainly occurs in the thoracic spine, therefore the main manifestations and the initial clinical symptoms are back pain and nerve root pain, followed by muscle weakness and sensory loss, including Brown-Séquard syndrome and dysuria. It is well-known that the spinal canal diameter ranges from 13 to 19 mm, and most MCS tumours are greater than 10 mm (*Table 1*). Therefore, the pain is probably due to early spinal cord compression by the tumour due to the limited space. Although the severity and duration of symptoms vary and

Table 1 Reported cases of primary spinal intradural extramedullary MCS

Author	Age/sex	Symptoms (duration)	² Tumour location	Dural tail sign	³ Tumour description	Calcification	Treatment (recurrence)	Outcome
Di Giannatale <i>et al.</i> (2)	14/M	BP, RP, SD (2 w)	T11-T12	+	S, 2.2 (cm)	+	GTR (no)	Alive 2 y
Chen <i>et al.</i> (3)	64/M	BP, SD, MW, UD, BSS (1 m)	T3	-	S, red, hard 2×1.5 (cm)	N/A	GTR/RT (no)	Alive 5 y
Andersson <i>et al.</i> (4)	10/F	BP (9 m)	T4	-	S, solid, 1.5 (cm)	N/A	GTR/RT (no)	Alive 2 y
Scheithauer <i>et al.</i> (5)	5/M	N/A	L2-L4	N/A	N/A	N/A	R (no)	Alive 2 y
	7/M	N/A	T10	N/A	S, 1 (cm)	N/A	R (no)	Alive 3 y
	15/F	N/A	T9-T10	N/A	N/A	N/A	R (no)	Alive 2 y
Lee <i>et al.</i> (6)	18/F	BP, RP, SD, MW, BSS (8 m)	T5-T6 (right)	N/A	S, red, hard	N/A	GTR/RT (no)	Alive 3 y
Huckabee <i>et al.</i> (7)	7/F	BP, RP (8 m)	L3	-	S, hard, 3×2 (cm)	N/A	GTR (N/A)	N/A
Ranjan <i>et al.</i> (8)	52/F	RP, SD, MW, UD (1 y)	C3-C6 (right)	-	S, hard	N/A	GTR (no)	Alive 6 m
Rushing <i>et al.</i> (9)	19/M	N/A	T5-T10	-	N/A	N/A	GTR/RT (no)	Alive 14 y
Li <i>et al.</i> (10)	3/F	RP, SD, MW (10 m)	T11-L1 (right)	-	S, purplish, hard, 3×2×2 (cm)	+	GTR/RT (no)	Alive 2 m
Belhachmi <i>et al.</i> (11)	13/F	BP, RP, SD, MW (2 m)	T7-T8 (posterior)	-	S	N/A	GTR (no)	Alive 2 y
Sharma <i>et al.</i> (12)	46/M	SD, MW, UD (15 d)	N/A	-	Soft	N/A	R/RT (N/A)	Died at 5 d
Turel <i>et al.</i> (13)	6/M	BP, MW (4 m)	T9 (left)	-	S, 2 (cm)	N/A	GTR (N/A)	N/A
Lee <i>et al.</i> (14)	17/M	BP, RP (N/A)	N/A	-	N/A	N/A	STR/RT/CT (N/A)	N/A
Yang <i>et al.</i> (15)	33/F	BP, RP, SD (5 m)	L2-L3 (right)	-	S	N/A	⁵ GTR (no)	Alive 3 y
Derenda <i>et al.</i> (16)	22/F	SD, RP, UD (2 m)	T12-L1 (left)	-	S, 1, blue, soft; 2, yellowish-white, hard; 2×1.9×1.2 (cm)	N/A	GTR/RT/CT (⁶ yes)	Alive 14 y
Presutto <i>et al.</i> (17)	21/M	NP, RP, SD, MW (3 m)	C2-C3 (anterior)	-	S, 1.4×1.7×1.2 (cm)	N/A	STR/RT/CT (no)	Alive 2 y
Saito <i>et al.</i> (18)	42/F	BP, MW, UD, SD, BSS (2 m)	T8 (right)	-	S	N/A	GTR (no)	Alive 2 y
Current case	13/M	BP, MV, SD (3 m)	T5 (right)	+	S, red, hard, 1.2×0.8 (cm)	N/A	RT/CT (no)	Alive 1 y

², tumour location: location of the tumour relative to the spinal cord; ³, tumour description: including S, tumour texture, colour, size; ⁵, GTR: patient refused postoperative RT due to financial concerns; ⁶, yes: re-op 4, 6, 10 years for recurrence after the initial resection, respectively. MCS, mesenchymal chondrosarcoma; BP, back pain; RP, radicular pain; SD, sensory deficit; w, weeks; S, single tumour; y, years; GTR, gross tumour resection; MW, muscle weakness; UD, urinary difficulty; BSS, Brown-Séquard syndrome; m, months; N/A, limited information; RT, radiotherapy; d, days; R, resection; STR, subtotal resection; CT, chemotherapy; NP, neck pain.

can range from a few weeks to several months, early pain causes concern for patients and leads to timely treatment. Early therapeutic intervention tends to reduce spinal cord injury from spinal cord compression, so recovery in spinal MCS patients is usually ideal. Our patient had a shorter duration of symptoms from the onset of fever symptoms to hospitalization for surgery. We believe that the herpes virus may have lowered his immunity, causing his symptoms to rapidly worsen in a short period of time (20).

As MCS is a highly malignant tumour, complete surgical resection is currently the preferred treatment. Due to the particularity of the tumour location, pain will be the first

symptom prompting patients to seek medical treatment. Despite the bone tissue MCS has a poor prognosis, it is possible to achieve complete recovery of spinal cord MCS through early detection and complete resection of the lesion. The use of postoperative chemotherapy and radiotherapy remains controversial is still recommended. Subsequently, we carefully reviewed the cases of 12 patients with primary intraspinal MCS who had undergone surgery and had a documented survival of 2 years; we found that 10 of these patients had received adjuvant chemoradiotherapy. Among these patients, one received adjuvant radiotherapy with 44 Grays in 22 fractions and showed no signs of

metastasis within 5 years after surgery (3). Of course, due to the low value-added index of this pathology, a few patients have died of systemic metastasis within a relatively short time; thus, long-term follow-up monitoring is crucial (16).

In our case, during the 1-year follow-up period, the patient's neurological dysfunction gradually recovered, the muscle strength of both lower limbs reached level 5, and the other sensory and physical symptoms resolved. The reason for this recovery may be that the early persistent back pain prompted our patient to seek early treatment, leading to mild spinal cord compression and good postoperative recovery. Additionally, the patient received adjuvant chemotherapy and had no other discomfort. MRI of the thoracic vertebrae was performed twice, and no *in situ* recurrence or metastasis was observed. The patient continues to recover well.

Conclusions

Primary spinal intradural extramedullary MCS is an extremely rare malignant tumour that occurs more frequently in adolescents. MCS should primarily be treated with surgery and adjuvant chemoradiotherapy, and the recovery of neurological function is usually excellent. Finally, long-term monitoring and follow-up of patients with primary spinal intradural extramedullary MCS is essential.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at <https://tcr.amegroups.com/article/view/10.21037/tcr-21-2703/coif>). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are

appropriately investigated and resolved. All procedures performed in the study were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient's legal guardian for publication of this manuscript and any accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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