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CASE REPORT

Low grade spinal malignant triton tumor with mature skeletal muscle differentiation

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Abstract

Malignant peripheral nerve sheath tumor (MPNST) is an uncommon sarcoma which arises from pluripotent stem cells of the neural crest and differentiates predominantly towards Schwann cells. Low grade spinal MPNST with skeletal muscle differentiation (malignant triton tumor) is vanishingly rare. In this study, we report a case of a 53-year-old female with a homogenously enhancing C2-C4 extradural lesion. The lesion demonstrated a biphasic histologic pattern with a diffusely infiltrating, atypical spindle cell component strongly positive for vimentin and focally positive for S-100. The second component consisted of diffusely scattered clusters of mature skeletal muscle cells which were positive for desmin, fast myosin and muscle specific actin but negative for Myogenin and MyoD-1. The Ki-67 labeling index was low (< 1%) and no necrosis was identified. The present case is remarkable because of its rare location, low grade histology and unusual immunophenotype of the skeletal muscle component, which were not previously described.

Key words: Malignant triton tumor; Cervical spine; Mature skeletal muscle differentiation; Prognosis

Core tip: Malignant peripheral nerve sheath tumor (MPNST) is an uncommon sarcoma with dismal prognosis. Low grade MPNST with skeletal muscle differentiation (malignant triton tumor) in cervical spine is vanishingly rare. The present case is remarkable because of its rare location, low grade histological features and unusual immunophenotype of the mature skeletal muscle component, which were not previously described. Thus, our study expands the morphological spectrum and the clinicopathological significance of this uncommon tumor. These novel findings should be interesting to the neuropathologists, neurologists and neurosurgeons.

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INTRODUCTION

Malignant peripheral nerve sheath tumor (MPNST) is an uncommon soft tissue sarcoma which arises from pluripotent stem cells of the neural crest and differentiates towards Schwann cells[1]. Spinal MPNSTs are rare and have dismal prognosis[2]. MPSNT with coexistence of rhabdomyosarcomatous elements are termed malignant triton tumor (MTT)[3] and have been rarely reported in the spinal cord[4]. Typically, they are high grade with

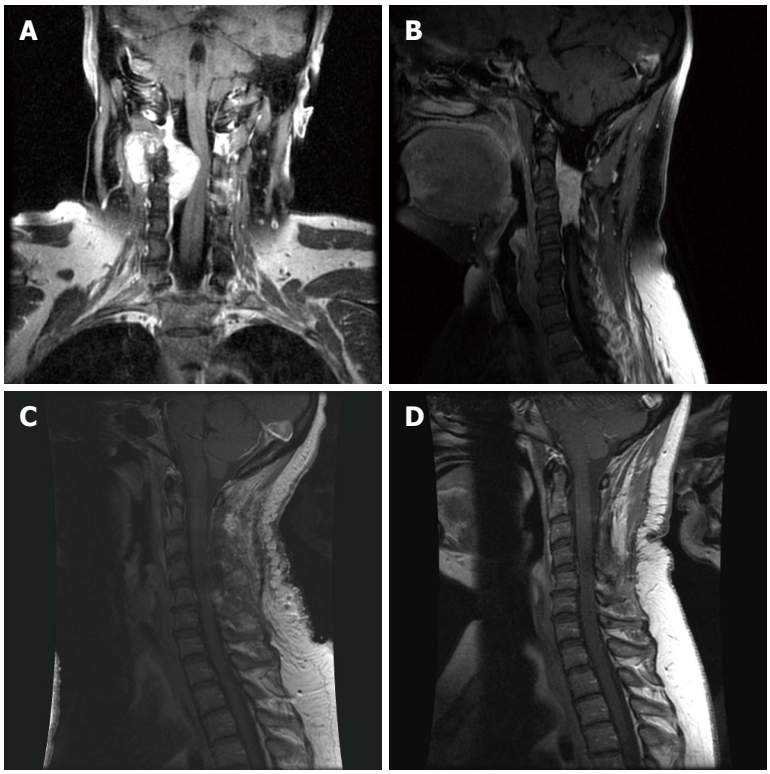

Figure 1 Pre-operative magnetic resonance imaging of the cervical spine. On coronal (A) and sagittal (B) view showed an extradural soft tissue mass at C2-C4 levels. After debulking of the mass (C) and at 10 mo post-operative follow up (D) showed markedly decreased mass effect on the cervical cord.

worse prognosis compared to conventional MPNST[5,6]. Low grade spinal MTT is vanishingly rare with a single case reported in literature[2]. A low grade spinal MTT with cytologically benign and immunophenotypically mature skeletal muscle component has not been previously described.

CASE REPORT

Clinical history

A 53-year-old female without family history or stigmata of neurofibromatosis presented with worsening neck pain and right sided neck stiffness. The pain is present in the left side (buzzing in left hip and left heel). The quality of the pain is described as aching and shooting (pulling, popping) and the severity of the pain is at 6/10. The symptoms are aggravated by position and twisting. The pain is worse during the night while the stiffness is present all day. Physical examination is unremarkable except for right facial nerve weakness nerve. MRI showed a homogenously enhancing C2-C4 intraspinal extradural lesion exiting out the foramen at C2-C3 in a dumbbell fashion (Figure 1A and B). A C2-C4 laminectomy was performed by using a combination of Leksell rongerus, Kerrisons and curettes. A tannish shear mass was identified in the epidural space from C2 to the top of C4. The mass was debulked from the inside using the combination of pituitary rongeurs as well as cavitron ultrasonic surgical aspirator debulking and bipolar electrocautery. The post-operative MRI showed markedly decreased mass effect on the cervical cord (Figure 1C). Bone stimulator and cervical collar were placed after surgery. The patient is treated with Percocet for analgesia and managed by physical therapy. No adjuvant treatment no radiation treatment were started. She is currently under regular follow up every six month (Figure 1D, 10 mo post-operative MRI), without evidence of recurrence (23 mo post surgery).

Pathological findings

The tumor was received as tan soft tissue aggregates measuring 5.0 cm × 3.4 cm × 0.8 cm. Microscopic examination demonstrated a distinctly biphasic neoplasm with an infiltrating, moderately atypical amitotic spindle cell component (Figure 2A). This component had hypercellular areas that alternate with paucicellular highly collagenized areas containing small-spindled nuclei with a wavy appearance, suggestive of a low grade malignant peripheral nerve sheath tumor[7]. The second component consisted of diffusely scattered clusters of mature appearing amitotic small skeletal muscle cells (Figure 2B). The immunohistochemical studies showed the spindle cell component to be strongly positive for vimentin (Figure 3A) and focally positive for S-100 (Figure 3B), CD57. Rare cells were positive for CD34 and CD117. The neoplastic cells were negative for smooth muscle actin, estrogen receptor, EMA, AE1/AE3 and p53. The small round cells with skeletal muscle morphology showed a mature skeletal muscle phenotype with expression of desmin, fast myosin and muscle specific actin (Figure 3C). However, they were negative for rhabdomyoblastic markers Myogenin and MyoD-1. Neurofilament protein immunostain did not show any entrapped axons in the lesion. The Ki-67 labeling index was low (< 1%) (Figure 3D) and no necrosis was identified. The immunomorphological features were interpreted to be consistent with unusual low grade variant of MPNST with mature

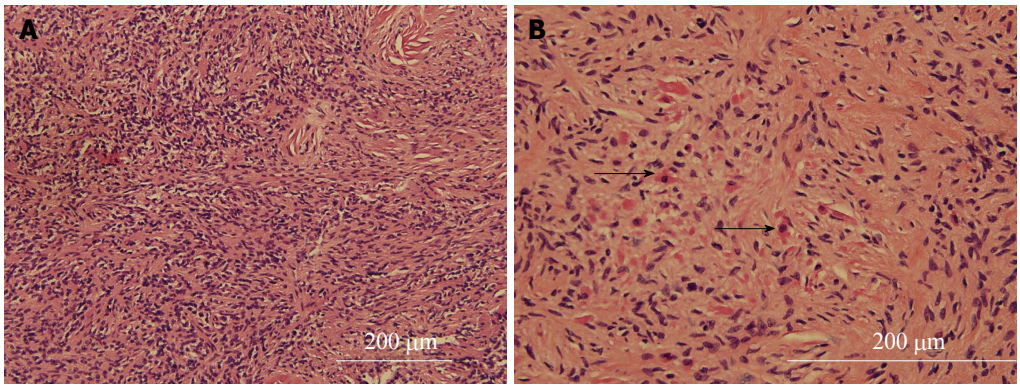

Figure 2 Histopathology of the tumor. A: High-power micrographs show a spindle cell lesion with focally increased cellularity and nuclear atypia; B: Scattered clusters of mature-appearing, small round cells with moderately abundant eosinophilic cytoplasm (arrow head) resembling a skeletal muscle differentiation.

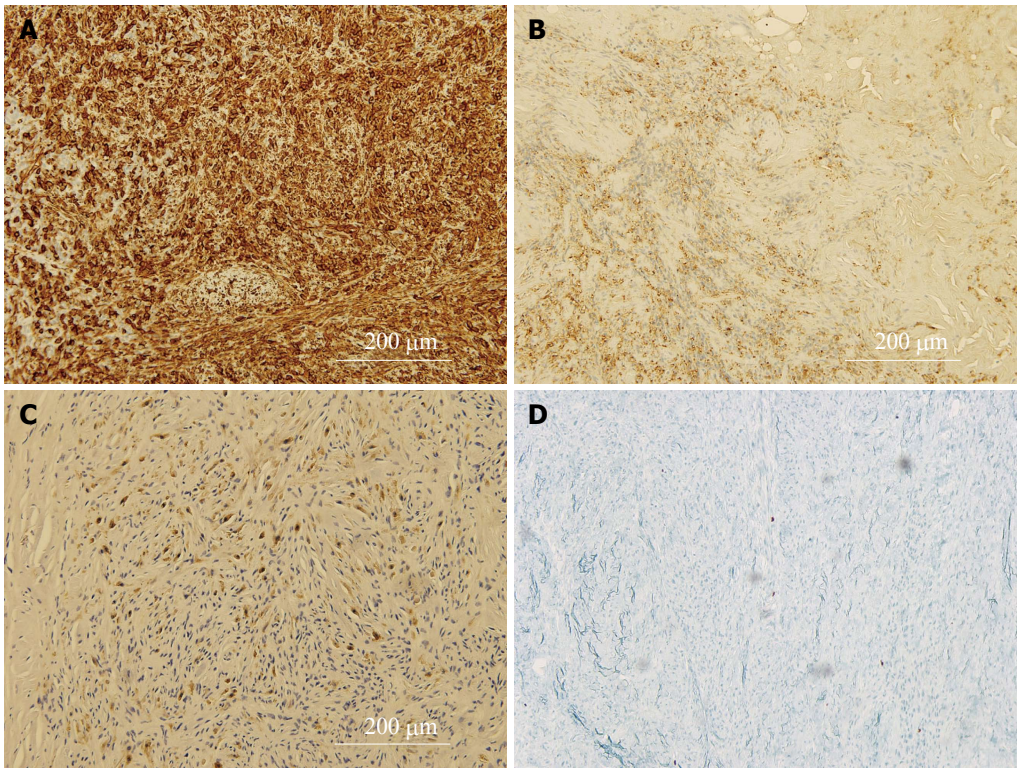

Figure 3 Immunohistochemistry. The spindle cells are diffusely and strongly positive staining for vimentin (A) and focally positive for S-100 protein (B); The small round cells with skeletal muscle morphology showed positivity of muscle specific actin (C); The Ki-67 immunostaining shows low labeling index (D).

skeletal muscle differentiation. Neurofibroma and cellular schwannoma were also considered in the differential diagnosis. But hypercellularity, nuclear enlargement (three times the size of neurofibroma nucleus), infiltrative growth pattern, lack of neurofilament immunostaining and focal S-100 positivity favored the diagnosis of low grade MPNST. Of note, cellular schwannoma is typically strongly and diffusely positive for S-100 and neurofibromas shows entrapped neurofilament positive axons.

DISCUSSION

The present case is remarkable because of its location, low grade histology and unique phenotype of the skeletal muscle component. A literature review of the spinal MPNSTs revealed a total of 59 reported cases with only one case showing exclusive extradural location in cervical spine[2,8]. Exclusively extradural cervical spinal location of our case is unusual. Spinal MPNSTs, reported in the literature typically show high grade histology (necrosis, high mitotic rate and Ki-67 labeling index) and have worse prognosis compared to conventional MPNST[5,8,9]. Only a small number of MPNSTs are low grade (15%) and they can have diverse histopathology, location and growth patterns[7,9]. Smooth muscle differentiation has been reported in a case of low grade MPNST[10]. However, mature skeletal muscle component in a low grade MPNST has not been previously reported.

The skeletal muscle component was diffuse and seemed an integral part of the tumor. The diffuse nature of the skeletal muscle component excluded the possibility that this was entrapped muscle at the edge of the tumor. Malignant triton tumors typically have a rhabdomyosarcomatous component[3]. Benign triton tumor usually refers to neuromuscular hamartomas, where mature skeletal muscle replaces nerve fascicles[11]. In contrast to conventional MTT which are positive for rhabdomyoblastic markers Myogenin and MyoD-1, both markers are negative in our case. MyoD-1 and myogenin are members of the Myogenic transcriptional regulatory protein, are the

most widely used markers to express the early in skeletal muscle differentiation. They are very sensitive and specific for the diagnosis of immature skeletal muscle in rhabdomyosarcoma. Mature skeletal muscle component in a diffusely infiltrating peripheral nerve sheath tumor with hypercellularity and nuclear atypia is very unusual. Low grade MTT has been reported in the oral cavity[12] and recently in lumber spine[2]. In both the cases, immunophenotypic maturity of the skeletal muscle component was not evaluated by MyoD-1 and Myogenin immunostain. In the only reported low grade spinal MTT, the patient is alive after 18 mo with no evidence of disease following total surgical removal and radiotherapy[2]. Although the clinical indication of such features is still undetermined, the mature skeletal muscle differentiation might indicate a better prognosis than the conventional MTT, evidenced by the prolonged disease free interval of our patient (23 month post surgery without chemotherapy and radiation therarpy).

In conclusion, here we have reported a case of low-grade MTT with unusual location and distinctive mature skeletal muscle differentiation, which expands the morphological spectrum of this rare tumor.

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