Primary spinal epidural Ewing sarcoma: a case report and review of the literature

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Primary extraosseous Ewing sarcoma is a rare entity, especially in the spinal epidural site. Less than 20 cases have been reported in the literature. Here, we present a previously healthy 12-year-old boy who complained of low back pain, progressive gait disturbance and weakness of right lower extremity for nearly one month before admission. Magnetic resonance imaging showed one solitary posterior extradural mass, measuring 4 x 2.2 x 2.1 cm, with severe cord compression at the level from T7 to T9. The mass appeared hypo-intense on both T1-weighted and T2-weighted images and homogeneous contrast enhancement after injection of gadolinium. He underwent laminectomies of T8 and T9 and complete resection of the tumor. The pathology confirmed a diagnosis of Ewing sarcoma after immunohistochemical staining. His profound neurological deficits recovered well and no recurrence was discovered after adjuvant chemotherapy and radiotherapy. The relevant literature is reviewed and the limited cases are also analyzed.

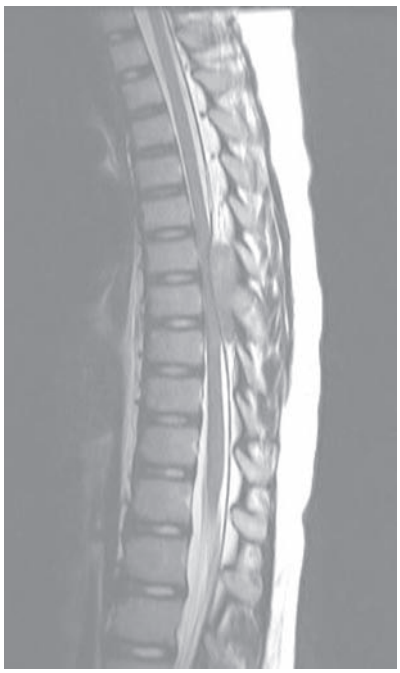
Key words: Ewing sarcoma, spinal neoplasms, extradural, magnetic resonance image.

Ewing sarcoma is defined as small round cell sarcoma with various degrees of neuroectodermal differentiation[1]. It is a relatively common bone and soft tissue sarcoma to occur in young adults and adolescents[2]. The first case of extraskeletal Ewing sarcoma was described by Angervall and Enzinger in 1975[3], and a few cases were reported in various sites thereafter. Primary epidural Ewing sarcoma (PEES) is a very rare entity, with less than 20 cases reported in the literature. We report herein a case of PEES and also review the relevant literature. Due to the aggressive behavior of the Ewing sarcoma, we emphasize the importance of the differential diagnosis, therapeutic modality and prognosis.

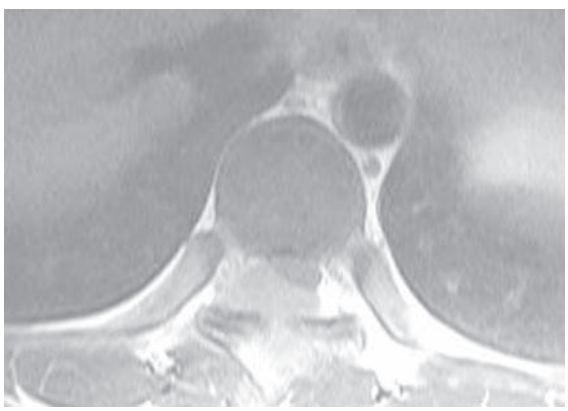
Case Report

A previously healthy 12-year-old boy complained of low back pain, progressive gait disturbance and weakness of right lower extremity for nearly one month before admission. On physical examination, decreased muscle power (strength score: 3/5) and numbness of right lower extremity were clearly identified. Neurological examination revealed an increased level of deep tendon reflex and the presence of Babinski's sign over right lower extremity. Laboratory examinations revealed no remarkable contribution. Radiographs of spine revealed no abnormal bony destruction. Magnetic resonance (MR) imaging showed one solitary posterior extradural mass, measuring 4 x 2.2 x 2.1 cm, with severe cord compression at the level from T7 to T9 (Fig. 1A and 1B). The mass appeared hypo-intense on both T1-weighted and T2-weighted images and homogeneous contrast enhancement after injection of gadolinium. Meningioma or neurogenic tumor such as neurofibroma or neurilemoma was highly suspected. The patient underwent laminectomies of T8 and T9 and complete resection of the tumor.

Grossly, the resected tumor mass was 3.6 x 2.5 x 1.0 cm with focal hemorrhage and necrosis. On light microscopy, diffuse homogeneous small, round tumor cells with uniform nuclei,



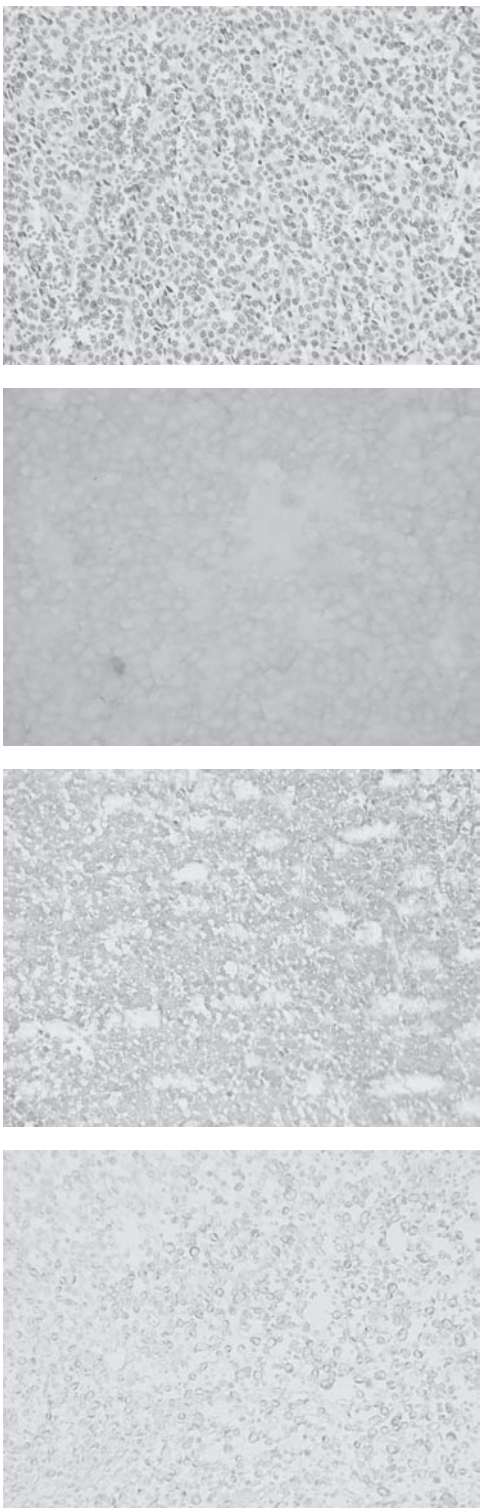
(a)



(b)

Fig. 1. (A) Sagittal view of T2-weighted MR images revealed an epidural solitary mass located at the level from T7 to T9, with compression of the spinal cord. (B) Axial view of T2-weighted MR images at T8 level revealed an epidural solitary mass located at the right, posterior aspect of the spinal canal, compressing the spinal cord.

fine chromatin, inconspicuous nucleoli, scanty cytoplasm and occasional mitosis were seen (Fig. 2A). Delicate vascular septae were also identified in the tumor substance. The immunobiochemical stainings were diffusely positive for CD99 (Fig. 2B), PAS (Fig. 2C), and vimentin (Fig. 2D), dot-like reactive for CD56 and chromogranin A but negative for CK, CD45,



(a)

(b)

(c)

(d)

Fig. 2. (A) High power view shows diffusely undifferentiated small, round tumor cells with delicate vascular septum (hematoxylin and eosin-H&E X400). The tumor cells were diffusely immunoreactive to CD99 (MIC2) (X400) (B); to PAS (X400) (C); and to vimentin (X400) (D).

actin and myo-D. In addition, the electron microscopy showed tumor cells with round to mildly irregular nuclei, high nucleus/cytoplasm ratio and scanty cytoplasmic organelles, but no electron-dense secretory granule was present. Based on these findings, the diagnosis of Ewing sarcoma was determined.

The patient recovered well from his neurological deficits. Adjuvant chemotherapy consisted of vincristine 2 mg per m^2 (on day 1), doxorubicin 60 mg per m^2 (on day 1), cyclophosphamide 1200 mg per m^2 (on day 1), etoposide 100 mg per m^2 (on day 1 to day 5), and ifosfamide 1800 mg per m^2 (on day 1 to day 5). The courses of chemotherapy were performed every three weeks for a total of 17 courses. Radiation therapy with a total of 45Gy was also delivered in the surgical site in fractionated doses (25 treatments of 180 cGy). No evidence of recurrence or metastasis was identified for nearly 20-months of follow-up.

Discussion

Ewing sarcoma is a primitive neuroectodermal tumor originating from the medullary cavity of the long bones often arising in the diaphysis or medullary-diaphyseal portion and occurring in the group of 10-30-year-old males[1,4]. PEES is a rare entity and only a few cases have been reported in the literature[5]. In 1991, Kaspers et al.[5] firstly reviewed 15 cases of PEES and presented the clinical features. However, there were still no reports about the treatment and prognosis of the epidural Ewing sarcoma. We reviewed 19 reported cases with our one additional patient[2,4,5,7-18].

Since combined radiotherapy and chemotherapy are effective for Ewing's sarcoma, extensive laminectomy could cause scoliosis or spinal deformities in children. Tru-cut biopsy for the diagnosis is recommended. In our case, marked spinal cord compression with symptoms of progressive neurological deficits was noted, so we performed laminectomies of T8, T9 and complete resection of the tumor for immediate decompression. Postoperatively, the patient demonstrated rapid recovery of his neurological deficits.

Table I summarizes the characteristic features, treatment and prognosis of the 20 reported cases of PEES. The mean age was 20.4 years with male predominance. The gender radio

Table I. Characteristic Features, Treatment and Prognosis of the 19 Reported Cases of Primary Epidural Ewing Sarcoma and our Case (n=20)

	Number		
Mean age, years (range)	20.8 (4-47)	Percentage	Survival in the follow-up
Gender			
Male	14	70	
Female	6	30	
Symptoms and signs			
Pain	20	100	
Weakness of limbs	14	70	
Numbness	10	50	
Urine retention	3	15	
Fecal incontinence	1	5	
Site			
Cervical	2	10	100% (2/2)
Thoracic	6	30	66.7% (4/6)
Lumbar	10	50	30% (3/10)
Sacrum	1	5	0 (0/1)
Unknown*	1	5	
Treatment			
Complete resection	7	35	71% (5/7)
Partial resection	8	40	25% (2/8)
Undetermined surgery**	5	25	60% (3/5)

*: no mentioned level reported by Kinsella TJ et al.[10].
**: surgical intervention without detailed content.[8,10,13,17]

of female: male was 1: 2.3. Lumbar spine (50%) followed by thoracic spine (30%) and cervical spine (10%) were the most common sites in patients with PEES. Symptoms and signs depended on the tumor location and the severity of spinal cord compression. Painful sensation (100%) followed by weakness of limbs (70%) and numbness of extremities (50%) were the most common clinical presentations. Regarding location of pain, 11 of 20 patients (55%) complained of backache. The time interval between initial clinical presentations to surgical intervention varied from one to 18 months, with a mean of five months. According to the surgical intervention, seven patients (35%) underwent total removal of tumor, eight patients (40%) underwent partial tumor resection, and the nearly 25% others had undetermined surgery. With respect to outcome, 10 patients died during a mean follow-up time of 16 months (1-48 months) and most patients (80%) had lumbosacral PEES. Comparing survival, 71% of patients who underwent complete resection of the tumor with adjuvant therapy were free of disease. In contrast, only 25% of cases who had partial tumor resection were disease-free. Complete tumor resection with adjuvant radiotherapy and chemotherapy seemed to be more beneficial for improving prognosis.

Tumor location may be one of the prognostic factors of the Ewing sarcoma, but the issue is still controversial[1]. In our review, cases with PEES occurring in the lumbosacral spine had a lower survival rate and highly metastatic tendency compared to cases with cervicothoracic localization. It seemed that the prognosis of PEES is much poorer over the lower spinal region, but it was still hard to draw any conclusion because of the limited number of cases. A possible explanation for the difference in prognosis may be that the larger epidural space in the lower-third of the spine delays the presentation of symptoms and the diagnosis of the cancer.

In the evaluation of an epidural spinal tumor, it is important to distinguish PEES from meningioma, neurofibroma, dermoid cyst, abscess, embryonal rhabdomyosarcoma, chondrosarcoma, schwannoma, synovial sarcoma, osteogenic sarcoma, hemangioma, nerve sheath tumor, lymphoma, and leukemia[2,5]. MR imaging, superior to myelography and computed tomography, is considered to be the best diagnostic method to delineate the spinal disorders. On MR images, PEES is generally of low-to-isointense signal compared with muscle on T1-weighted images, of high signal intensity on T2-weighted images, and exhibits heterogeneous enhancement[2]. However, it is difficult to differentiate between PEES and neoplasms based on clinical, radiological and laboratory examination. Immunohistochemical staining such as immunoreactivity to glycoprotein p30/32 (CD99), and ultrastructural and molecular biological technique could be helpful in establishing the diagnosis[1].

In conclusion, PEES is a rare and aggressive neoplasm. Early decompressive surgery is strictly indicated to secure the vital neurological functions. Complete tumor resection with adequate radiotherapy and chemotherapy is considered as the optimal therapeutic policy. However, due to the limited number of reported cases, an accumulation of such cases is needed for further evaluation and research to prove its histogenesis.

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