CASE REPORT

Giant Primary Epidural Extraskeletal Ewing Sarcoma in Cervical Spine of an Infant: Case Report and Review of the Literature

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ABSTRACT

Ewing sarcoma (ES) is a highly malignant tumor originating from bones, exceptionally long bones. ES arising from the epidural extramedullary space, primarily the cervical region, is highly unlikely. There have been only six cases of cervical epidural extraskeletal Ewing sarcoma (EEES) in children reported in the literature, all of whom were older than seven years old. Four of seven cases, including the one mentioned in this study, were male (57%). Herein, we report a 1.5-year-old girl who presented with quadriparesis without cognitive impairment and had initially undergone a metabolic disorder evaluation. The spine MRI revealed a mass in the C2-T6 region, and she underwent a biopsy of the tumor via laminectomy. Microscopic examination confirms a diagnosis of ES based on immunohistochemistry. This is the first literature that presents an infant with EEES.

Introduction

Ewing sarcoma (ES) is a primary malignant bone tumor characterized by small, round, and poorly differentiated cells commonly found in children and adolescents (1). This tumor typically arises from any site within the bone but commonly originates from the diaphysis of long bones (2). Primary extraskeletal presentation of ES has been reported in 15% of cases (3, 4). ES is frequently diagnosed in Caucasians and rarely in African American and Chinese people and has a slight predominance in men (61%), particularly as they get older (5, 6). However, reportedly, extraosseous ES presents equally in female and

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male subjects (7). ES is characterized by rapid growth and osseous destruction, which can result in bone pain and pathological fractures (8). The pain worsens during the night and can be accompanied by weakness and impaired gait (9). Although metastatic ES frequently invades the vertebral column, primary vertebral ES is notably rare. Previous studies reported that the most common region is the sacrum (55.2%), and the least frequent site is the cervical spine (3.2%) (10). Soft tissue compression in EEES may present with different neurological deficit patterns, such as rapidly progressing paraplegia, depending on the tumor location, but it is usually a delayed manifestation (11). Hence, a high index of suspicion is essential to diagnose the mentioned cases. Fever, weight loss, and other constitutional manifestations can be found in 20% of cases (12). This study reports a 1.5-year-old girl with EEES, previously managed as a neurodevelopmental delay.

Case presentation

The present study reported a 1.5-year-old girl with no parents' consanguinity from a Gravid 3, Para 3, Live 3, and Abort 0 mother with term gestational age and birth weight of 3200 g and normal APGAR score. The mother had a normal pregnancy with no complications. She weighed 7 kg at the visit.

Around six months ago, she was noted to have decreased movements of her lower and gradually upper extremities, and she was also in a state of agitation for a while. During her first admission, she had normal mental status, and only her gait and stance raised valuable concerns. In the examination, she had hyperreflexia and spasticity, but other neurological examinations were normal. She initially underwent a screening analysis with high-performance liquid chromatography (HPLC) and tandem mass spectrometry (MS/MS) to detect the metabolic disorder, but the results were normal. Furthermore, she had undergone brain magnetic resonance imaging (MRI) and other paraclinical assessments to find out the possible causes of her problem. Only a small cyst was found in the left internal capsule, which could not explain her manifestations (Figure 1). Other tests, such as an eye exam and eye movement study, were taken to discover Niemann-pick disease, and the results showed no abnormality. Meanwhile, she received Piracetam and Topiramate as medical treatments. However, they had no effects on her symptoms. The child was alert during the visit and had normal cranial nerve function and verbal ability. Since she was suffering from quadriparesis and hyperreflexia without any cognitive disorder, a spinal cord lesion was suspected, and she underwent a spinal MRI. The MRI showed a mass in the spinal canal involving 12 levels between the C2 and T6 vertebrae (figure 2), extending to paraspinal tissue, retropharyngeal space, and also both anterior and posterior bony tissue of involved vertebrae, leading to severe cord compression.

Considering the diagnosis of neuroblastoma, the patient was referred to the neurosurgery department and underwent a T1 laminectomy. An extradural biopsy was taken from the cervicothoracic region. Since 12 vertebrae were involved in a patient suspected of sarcoma, resection of the tumor was hard to accomplish. Pathological examination showed infiltration of small round cells into fibroconnective and bone tissue with rich vascularization and dense cellularity (Figure 3). The tumor cells were immunopositive for CD99 and vimentin and weakly positive for NSE. LCA, myogenin, Syn, and CG were negative. Therefore, the obtained results were

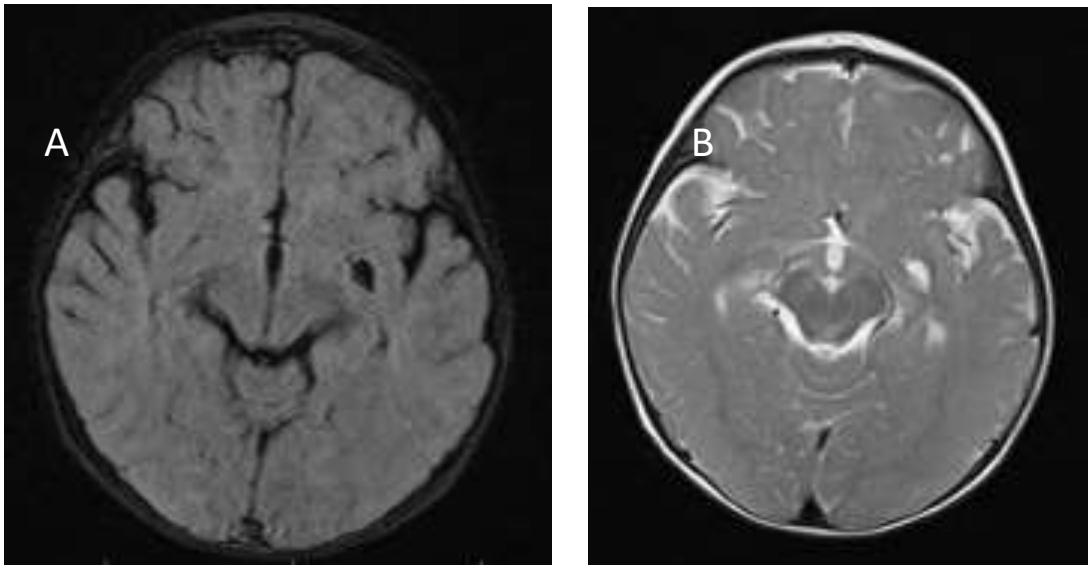

Figure 1. Brain MRI images. In an axial image of the brain, a small cyst in the left internal capsule is seen. (A) Fluid-attenuated inversion recovery image. (B) T2-weighted image

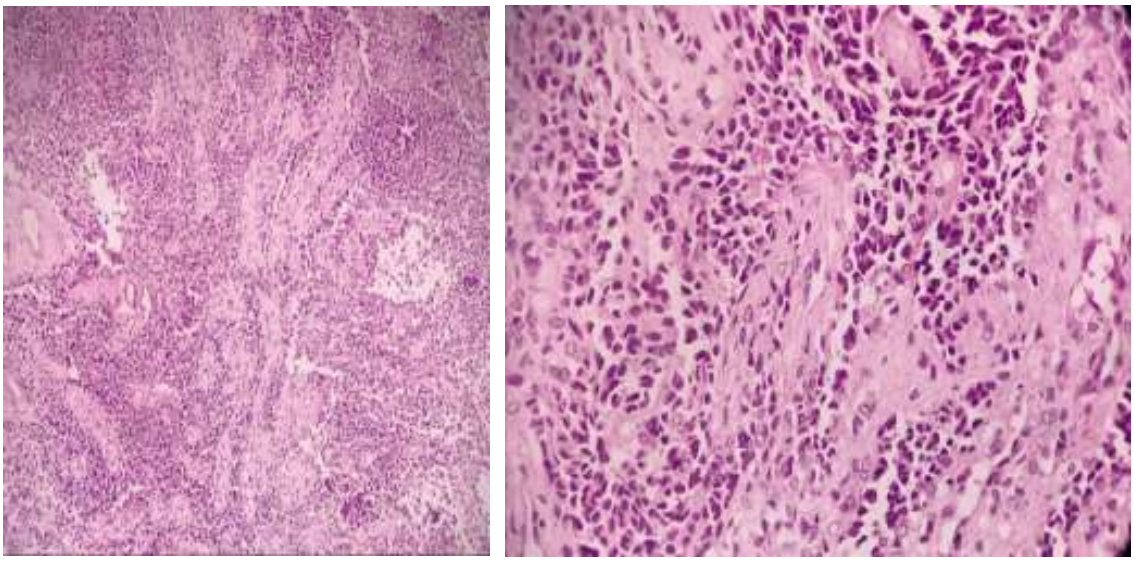

Figure 2. (A) Low power view shows malignant small round cell tumor including primitive monotonous cells (hematoxylin and eosin-H&E). (B) High power view of small round cell tumor with some perivascular rosettes

more compatible with ES. Due to the rarity of EEES, it was not considered until a pathological examination was conducted. After a biopsy from the T1 region and confirmation of the diagnosis, the child underwent neoadjuvant chemotherapy. She was submitted to thirteen chemotherapy sessions at 22-day intervals. At present, she has been showing improvement in limb movements. After completion of the chemotherapy, further evaluation will be performed.

Discussion

ES is a highly malignant osteogenic neoplasm first described by Tefft et al. (13) in 1969. The most common symptom of EEES is back pain with or without radicular pain, paralysis, sensory

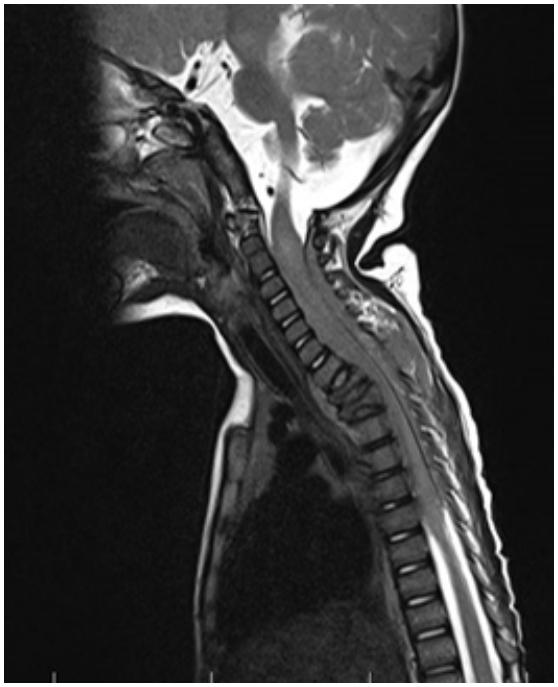

Figure 3. Sagittal view of T2-weighted MR images revealed an epidural mass located at the level from C2 to T6, with spinal cord compression

disturbance, and sphincter dysfunction. All these clinical manifestations are related to cord compression (14). A high possibility exists for a physician to fail to diagnose at an early stage because of nonspecific symptoms at presentation and also the rarity of this tumor. The mean delay to diagnosis is 5.7 months (range four days to 18 months) (15). Computerized tomography (CT) and MRI are the most valuable modalities for diagnosis (16). Differential diagnosis of spinal EEES based on radiological data includes a wide variety of disorders such as hematoma, hemangioma, nerve sheath tumors, primary or metastatic vertebral tumors, and various epidural metastases. Since differentiating EEES from these tumors based on clinical presentation and imaging alone is challenging, immunohistochemistry and cytogenetics are vital adjuncts in its diagnosis (17). Immunohistochemistry can help by recognizing a cell surface marker, CD99, on ES to distinguish these neoplasms (18). Neuroblastoma would be positive for CD56 (19). Metastasis has been detected in about a quarter of patients at diagnosis, the most common sites being lung (50%), bone (25%), and bone marrow (20%) (20, 21). Only 3.5-7% of cancer patients have evidence of metastases to the spinal column (22). The diagnostic gold standard for extraosseous ES relies on pathological assessment and molecular analysis of the translocation t (11;22) (q24;q12) (23).

The treatment includes surgical decompression, radiotherapy, and chemotherapy. To choose the best modality, the age, size, and location of the mass, neurological deficit, and long-term complication of therapy should be considered. In a patient with a stable neurological state, management of ES begins with neoadjuvant chemotherapy to shrink the primary mass. In the cases where chemotherapy and radiotherapy are not effective, surgical resection (within a safe margin) is indicated. Complete resection is the surgical approach to malignant spinal tumors. The way the ES mass is partially resected is of

utmost importance and critical value because it changes the prognosis and the risk of local recurrence. Thus, careful recognition and expertise of the neurosurgeon are crucial to having the mass removed with the most minor neurological deficit (22). Adjuvant chemotherapy can be used to eliminate the residual mass and also metastasis. The chemotherapy regimen often includes adriamycin, cyclophosphamide, and vincristine (24). The combination of radiotherapy with chemotherapy is the routine treatment to eliminate the microscopic tumor, which is more effective than using only one of these treatments (25). Since this aggressive tumor has a high incidence of metastasis and recurrence, routine follow-up is necessary to detect them both as soon as possible (26).

A detailed search on PubMed in English literature brings in only six cases younger than 18 years old with EEES located in the cervical spine (Table 1). The youngest patient in these reported cases was seven years old. The most common presenting feature of these patients was neck pain and paralysis. In this literature, a 1.5-year-old infant with cervical and thoracic involvement is reported. This girl was initially evaluated for metabolic disorders and Niemann-pick disease, but a careful, timely, and accurate examination of the patient led us to consider a spinal cord lesion.

In Conclusion

This study tends to emphasize that EEES can present with progressive neurological deficits, spinal pain, and sphincter disturbance. The physician should keep in mind that the only clinical presentation of EEES in children and infants can be tetraparesis or tetraplegia. Therefore, if the patients suffer from the mentioned symptoms while abnormal neurological examination and MRI findings suggest an extradural mass, EEES should be considered. Initially, this study considered the case to be neuroblastoma. However, it was ultimately diagnosed as EEES. Notably, EEES should be considered as another

Table 1. Case reports of primary EEES of the cervical region in children

Author (year)	Region	Sex/Age	Chief complaint	Treatment	Outcome
Mukhopadhyay (2001) (27)	C3-C5	M/13 y	Neck pain	STR/RT/CT	Disease-free at 11 m
Harimaya (2003) (28)	C6-T3	M/10 y	NR	STR/RT/CT	Dead after 22 m
Kogawa (2004) (29)	C2-C4	F/7 y	Tetraplegia	STR/RT/CT	Disease-free at 60 m
Ozturk (2007) (30)	C6-T1	M/18 y	Right shoulder pain progressing to complete paraplegia and urinary retention	TTR/CT	Disease-free at 13 m
Aydin (2013) (31)	C2	M/7 y	Neck pain	Biopsy/RT	NR
Kutty (2017) (32)	C2-C4	F/12 y	Neck pain and progressive weakness of four limbs	Biopsy/CT/RT	Disease-free at 16 m
Current case	C2-T6	F/1.5 y	Quadriparesis	Biopsy/CT	Ongoing

differential diagnosis for extradural mass lesions. Based on the previous studies carried out to date, neoadjuvant chemotherapy, surgical decompression, and adjuvant therapy, including chemotherapy and radiotherapy, are necessary in order to make sure that more patients undergo complete remission.

Ethics

The work described in this article has been carried out in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki) for human experiments.

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Authors' Contribution

Sousan Mousavi contributed to writing the draft, and data collection. Ehsan Keykhosravi. clinical examination, data interpretation, manuscript revision. Hamid Rezaee provided feedback on the draft and contributed to writing the draft. Paria Dehghanian. contributed to data collection. Farnoosh Ebrahimzadeh provided feedback on the draft and contributed to writing the draft. Amin Tavallayi provided feedback on the draft. Mehran Beiraghi Toosi. clinical examination, data interpretation, manuscript revision.

Conflict of Interest

The authors declare no conflict of interest.

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