Ewing sarcoma of the thoracic epidural space in a young child

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Abstract

Purpose To report on the clinical course and treatment of Ewing sarcoma of the thoracic epidural space in a 5-year-old girl.

Methods We present the case of a 5-year-old girl who experienced back pain (day 1); on day 10, the pain had exacerbated and involuntary movements in the lower limbs occurred, and an MRI performed in her local hospital revealed a tumor lesion at the upper thoracic level.

Results On day 13, emergency surgery was performed for partial resection of the tumor. Pathological examination of the resected tumor by immunostaining and gene testing revealed that it was MIC2 positive and an EWS-FLI 1 chimera, respectively, and Ewing sarcoma was diagnosed. The involuntary movements resolved immediately after the surgery. Three weeks after the operation, chemotherapy and radiation therapy were commenced. After 5 months, deep tendon reflexes recovered to normal. MRI showed that the tumor has not recurred at 29 months after surgery.

Conclusions The majority of epidural patients undergo emergency surgery only after symptom exacerbation, which includes the development of neurological deficits. Thus, preoperative diagnosis of Ewing sarcoma of the

epidural space is difficult and diagnosis is frequently made by a post-operative gene test. The resection area is limited to the intralesional margin area because a larger resection is difficult due to the characteristics of the affected region; thus, there is a higher possibility of recurrence and careful follow-up of the case is necessary.

Keywords Ewing sarcoma · Thoracic epidural space · Child

Introduction

Ewing sarcoma is a bone tumor that frequently appears in the long bones or pelvis of teenagers. It is reported to occur in approximately 6–10 % of all primary bone tumors of children; however, it seldom appears outside of the bone, and rarely in the epidural space. We would like to present a case of Ewing sarcoma of the thoracic epidural space in a 5-year-old girl. A surgical resection was performed with post-operative chemotherapy and radiotherapy. The clinical course and outcome are reported with a discussion comparing our case to other previously reported cases.

Case report

Informed consent was obtained from the parents of the patient. A 5-year-old girl experienced back pain (day 1). On day 10, the pain became severe and involuntary movements in the lower limbs occurred, and a magnetic resonance imaging (MRI) performed in her local hospital revealed a tumor at the upper thoracic level. She was transferred to our unit on day 11. Highly increased deep tendon reflexes of the patella and achilles were present with

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Fig. 1 Plain radiograph that does not show a compression fracture or osteolytic lesions

bilateral Babinski sign. The alkaline phosphatase (ALP) and lactate dehydrogenase (LDH) levels were increased (673 IU/l and 307 IU/l, respectively).

Plain radiographs did not reveal obvious osteolytic lesions or enlarged intervertebral foramen (Fig. 1). Although a plain computerized tomography (CT) scan did not show obvious osteolytic lesions or tumor in the spinal or posterior region, an enhanced CT scan showed a lesion on the left of the T1–2 level with a light ring-shaped enhancement (Fig. 2). MRI revealed a dumb-bell-type tumor lesion with intermediate signal to muscle tissue (on T1 images) and with high signal intensity (on T2 images). The spinal cord was compressed and shifted to the right. A contrast effect was not observed in the tumor (Fig. 3). On the basis of the MRI findings, the radiologist in our hospital suspected the development of neurinoma or neuroblastoma in the thoracic epidural space as the differential diagnosis. Evaluation of the condition of the bone by CT did not show osteolysis and irregular cortical margins and, thus,

neoplastic changes were absent. Emergency surgery was performed on Day 13.

A T1–T2 laminectomy was performed, and a red-brown tumor was found in the epidural space. A margin between the tumor and dura mater was seen on the right side of the tumor, and the tumor was retracted and removed piecemeal as much as possible (Fig. 4). Approximately 80 % of the visually observed tumor was removed, and the left T1 and T2 nerve roots were preserved. An intra-operative frozen section showed round nucleated cells with increased chromatin, and neuroblastoma and lymphoma were part of the differential diagnosis.

The involuntary limb movement disappeared 1 day after the surgery, and movement without limitation became possible 1 week after surgery. Pathological testing of the tumor with hematoxylin-eosin staining showed widely spread necrotic tissue around the tumor, and an increase in the amount of cells with a high nuclear-cytoplasmic ratio was also observed (Fig. 5). Higher magnification showed

Fig. 2 Evaluation of the condition of the bone by CT (*left*) did not show osteolysis and irregular cortical margins; thus, there was no evidence of neoplastic change. Enhanced CT (*middle, right*) revealed

ring enhancement that projected from the intra-canal space to the intervertebral foramen

Fig. 3 Plain MRI (*left*) revealed a dumb-bell-type tumor lesion on T1 and T2 (low and high signal, respectively) images, which projected to the left intervertebral foramen of T1/2. A contrast MRI (*right*) did not show an internal contrast effect

Fig. 4 Above a red-brown tumor (arrow) was observed. The tumor was adjacent to the dural sac, but infiltration of the dural sac as well as bone infiltration was not found. Below partial resection was performed and the compression on the dura mater was released

Fig. 5 Hematoxylin-eosin (HE) staining showing widely spread necrotic tissue around the tumor and an increase in the number of cells with a high nuclear-cytoplasmic ratio

small round cells with decreased cytoplasm and proliferation with a solid or partial alveolar structure (Fig. 6).

Immunostaining showed that the specimen was MIC2 positive (Fig. 7), and a gene test detected EWS-FLI 1 chimera (Fig. 8). With these test results, Ewing sarcoma was diagnosed.

Three weeks after surgery, chemotherapy with vincristine, doxorubicin, and cyclophosphamide (VDE), and ifosfamide and etoposide (IE) was given, and radiotherapy (total 45 Gy) was commenced. Five months after the operation, the deep tendon reflexes had recovered to normal. An MRI taken after 1 year and 2 months showed the disappearance of the intra-canal tumor; growth of the residual tumor and recurrence were not observed. One year and 5 months after surgery, peripheral blood stem cell transplantation (PBSCT) was performed after megatherapy using cyclophosphamide (CY, 1500 mg/m², 4 days) and L-phenylalanine mustard (L-PAM, 60 mg/m², 3 days), and no major complication was observed. Two years and 5 months after the operation, the patient's motor and sensory functions are normal. We evaluated the affected lesion by MRI: no recurrence was observed (Fig. 9), and follow-up is ongoing.

Fig. 6 Higher magnification image showing small round cells with less cytoplasm and proliferation with solid or partial alveolar structure

Fig. 7 Immunostaining showing positivity for MIC2

Discussion

The differential diagnosis considered for solid malignant tumors with spinal cord compression in children include neuroblastoma, Hodgkin's disease, rhabdomyosarcoma, Ewing sarcoma, and Wilms tumor [1]. Ewing sarcoma is reported to occur in 6–10 % of primary bone tumors, and 80 % of this occurrence is observed in teenagers, with a male:female ratio of 3:2. It usually occurs in the diaphysis of the long bones. In flat bones, occurrence in the pelvis is frequently observed and occurrence in the cranial bones, scapula, and vertebra is rare. Pathological findings include proliferation of homogeneous small round tumor cells and positivity for glycogen on periodic acid-Schiff (PAS) staining. Immunostaining detects CD99 (*MIC2* gene product). Gene testing shows reciprocal translocation

Fig. 8 Gene testing showed an EWS-FLI 1 chimera

involving chromosome 22 located on EWS-FL11 in ≥ 90 % of the cases.

The incidence of Ewing sarcoma in the perivertebral space is 8 %, and it is the lowest in the thoracic vertebrae compared to the other vertebrae, with the incidence in the epidural space being 0.9 % [2]. Persistent back pain and radiculopathy are common symptoms. We are only aware of 11 previous reports [2–12] in the literature of Ewing sarcoma of the epidural space in a child (Table 1), and the majority of these are reported in boys (seven cases) and at the lumbar vertebral level or thoraco-lumbar junction (eight cases). Our report of a 5-year-old girl with an upper thoracic lesion will be the first of its kind with regard to age, sex, and site of occurrence.

Factors involved in the prognosis include site of the tumor, tumor volume, age, sex, resection rate of tumor, presence of metastasis, treatment response, anemia, fever, and an increase in LDH [13–15]. For 20 years, the gold standard in the treatment of Ewing sarcoma of the limb is the combination of neo-adjuvant chemotherapy and *enbloc* resection. Radiotherapy is a consistent alternative option to surgery. In the cases in which radiotherapy is preferred, surgery can be decided at the end of the therapeutic plan. Conversely, in view of the evolution of the more frequent Ewing sarcoma of the limb, it is known that most of these sarcomas undergo a dramatic volume reduction immediately after the first chemotherapy course. However, if an

Fig. 9 An MRI taken after 2 years and 5 months showed the disappearance of the growth of the residual tumor and recurrence was not observed

Table 1 Case reports of Ewing sarcoma of the spinal epidural space in children

Reported by	Age (years)	Sex	Symptoms	Affected area	Tumor resection	Outcome (progression-free interval) (months)	Reported in
Klimo P Jr, et al. [2]	10	Boy	Right lower extremity pain	L4–5	Partial	46	2009
Dogan S, et al. [3]	13	Boy	Bilateral lower extremity pain	T11–L1	Total	6	2009
Song X, et al. [4]	4	Girl	Left lower extremity pain	T11–L4	Partial	22	2008
Kogawa M, et al. [5]	7	Girl	Tetraplegia	C2–4	Partial	60	2004
Mukhopadhyay P, et al. [6]	13	Boy	Neck pain	C3–5	Partial	11	2001
Kaspers GJ, et al. [7]	7	Boy	Leg numbness	T12–L1	Partial	40	1991
Machin VM, et al. [8]	4	Boy	Gait disorder	L1	Total	5 (demise)	1987
Spaziente R, et al. [9]	14	Girl				48	1983
Kinsella TJ, et al. [10]	10	Boy	Left lower extremity pain	L4–S	Partial	16 (demise)	1983
Simonati A, et al. [11]	12	Boy	Lower back pain	L3	N/A	15	1981
Tefft M, et al. [12]	6	Girl	Lower back pain	L4	Partial	40	1969
Case in this report	5	Girl	Back pain	T1–2	Partial	29	2012

epidural mass is compressing the spinal cord, we must perform decompressive surgery immediately like in this case [1]. Practically, though an *enbloc* resection is a standard procedure in Ewing sarcoma of the limb, the majority

of cases of Ewing sarcoma of the epidural space are treated by marginal or intralesional resection to preserve the nerve, because the tumor is often found after presentation of neurological symptoms, and an emergency operation

before definitive pathological diagnosis is performed. Therefore, resection with an insufficient tumor resection margin has already been performed when Ewing sarcoma is pathologically diagnosed after the surgery, and results in poor outcomes including high recurrence and low survival rate.

One year and 2 months postoperatively, no recurrence was seen on MRI, and after 1 year and 5 months, PBSCT with megatherapy was performed. Although PBSCT has not been proven to be effective for solid tumors, a few reports show that PBSCT is effective when performed in the state of complete response (CR) [16, 17]. However, local radiotherapy, surgical decompression, and chemotherapy have all been advocated previously, and no randomized, controlled studies or prospective studies compare their short- and long-term outcomes. Therefore, a clear indication regarding treatment for primary epidural tumors with neurological symptoms is unknown.

In this case, although the tumor had not been completely resected, we judged the symptoms as near CR because no enlargement of tumor was observed by imaging techniques. Thus, PBSCT was performed as it would possibly improve the prognosis. We expect a long disease-free interval in this case because the factors involved in poor prognosis are not present, as the patient was a girl, who was only 5 years old, and there was no metastasis was present at initial treatment, anemia was not present and the child showed a mild increase in LDH. However, careful follow-up is necessary because the average progression-free interval reported previously is 33 months after the surgery.

Conclusion

Ewing sarcoma of the epidural space tends to be found after neurological symptoms are manifested. This type of disease is rare, and definitive diagnosis in the early stage is difficult. In the majority of cases, partial resection is chosen because of its occurrence site. In this case, local recurrence had not occurred and chemotherapy appeared to have an effect. However, Ewing sarcoma of the epidural space has a higher recurrence rate compared to that in the bone; thus, long-term follow-up by physical examination, CT, and MRI is necessary.

Conflict of interest None of the authors has any potential conflict of interest.

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