Relapse to Cerebellum in a Child with Ewing's Sarcoma

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ABSTRACT

A 10-year-old girl presented with vomiting for a month. She had been in remission for 39 months after treated with surgery and chemotherapy for localized femoral Ewing's sarcoma. She had no abnormal finding on physical examination. Computed tomography and magnetic resonance imaging of the brain revealed a cerebellar mass. Metastatic work-up including positron emission tomography revealed abnormal accumulation only at cerebellar region. The tumor was totally removed surgically and the histological diagnosis was consistent with Ewing sarcoma.

Key Words: Ewing's sarcoma, Relapse, Cerebellum, Children

ÖZET

Remisyondaki Çocuk Hastada Ewing Sarkomunun Serebellar Relapsı

On yaşında kız hasta bir aydır devam eden kusma şikayeti ile başvurdu. Hikayesinden femura lokalize Ewing sarkomu tanısı ile cerrahi ve kemoterapi gördüğü, tedavisini tamamladığı ve 39 aydır remisyonda olduğu öğrenildi. Nörolojik muayenesi normaldi. Beyin tomografisi ve manyetik rezonans görüntülemesinde serebellumda kitle tesbit edildi. Pozitron emisyon tomografi ile yapılan metastatik hastalık taramasında sadece serebellumda anormal FDG18 tutulumu saptandı. Tümör cerrahide total olarak çıkartıldı. Histopatolojik incelemede Ewing sarkomu tanısı konuldu.

Anahtar Kelimeler: Ewing's sarkom, Relaps, Serebellum, Çocuk

INTRODUCTION

Although central nervous system (CNS) metastasis is frequent in adults with malignant diseases, it is infrequently encountered in childhood. CNS involvement is reported to be 2.2-6.2% and the cerebellar involvement is very rare at admission.[1] Ewing's sarcoma is a primary malignant tumor of bone and accepted in the Ewing family of tumors which were thought to originate from the neuroectodermal tissue and present distinct histology. Thus, the tumor may arise in different sites of the body and relapses often occur at lung, bone or their combination.[2] Cerebellum is an unusual and rare site of relapse in Ewing sarcoma. We describe a 10-year-old girl who had vomiting caused by a relapsing mass in the cerebellum 39 months after the treatment for Ewing's sarcoma of the left femur.

CASE REPORT

A 7-year-old girl was presented with pain and swelling at her left knee in August 2003. The only positive physical finding was pain on palpation at left femur. Her sedimentation rate was 26 mm/h, alkaline phosphatase (ALP) 305 IU/L and lactate dehydrogenase (LDH) 758 IU/L. Direct radiograms (X-ray) of the femur showed a hypodens area under epiphyseal plaque at distal part of the left femur. Magnetic resonance imaging (MRI) studies showed medullar infiltration and posterior cortical destruction causing periosteum reaction at left femur. Bone scintigraphy revealed abnormal accumulation in left femur. Histopathologically, the biopsy material composed of small, round cells with hyperchromatic nuclei. Immunohistochemistry revealed that these cells show CD99 expression. These findings were consistent with Ewing's sarcoma. She underwent surgery, the tumor was removed totally and the surgically margins were also histopathologically tumor negative. She received chemotherapy consisting of cisplatin, ifosfamide, adriamycin and vincristine. She completed her chemotherapy on May 2004. At the end of chemotherapy, the MRI and positron emission tomography (PET) scan results were normal. The biopsy from left femur revealed no neoplastic cells and good response to treatment. While she had been following for 39 months and she was on remission, she admitted with the complaint of vomiting for a month. Her physical examination including neurologic examination was normal. Because of her previous sarcoma history, computed tomography (CT) of the brain was planned. CT scan showed a mass with 4 cm in diameter at cerebellum. MRI was performed by a 1.5 Tesla scanner. Axial and sagittal T1-weighted (590/15 ms) spin-echo (SE), dual T2-weighted (2290/15-85 ms) SE and fast fluid attenuated inversion recovery (8000/100/2000 ms) images were obtained by using 5 mm slice thickness with 1 mm intersection gap. MR scans showed an extraaxial posterior fossa mass compressing the right cerebellar hemisphere, brain stem and fourth ventricle. On supratentorial images enlarged third and lateral ventricles were also noted (Figure 1). Metastatic work-up including whole blood count, liver and renal tests, cerebrospinal fluid analyses, thorax CT and PET were negative. The tumor was totally removed by surgery. The surgical margins were tumor negative. The control CT after surgery revealed no residual mass. The histopathologic findings revealed a tumor that composed of small-round cells. There were wide necrotic areas and the neoplastic cells were positive with CD99 (Figure 2). The cerebellar histopathologic findings were also consistent with her previous femoral findings. She was diagnosed as relapse of Ewing's sarcoma. She was now in remission without any additional treatment. Her vomiting resolved completely and her physical examination was completely normal. Chemotherapy was planned additional to surgery however the patient refused the treatment. She had been in complete remission for two years.

DISCUSSION

Despite intensive chemotherapy, improved surgical approaches and advanced radiotherapy techniques, 30% to 40% of patients still experience recurrent disease and have poor prognosis in Ewing's sarcoma. In the early seventies when the diagnosis was primarily based on neurologic examination and advanced imaging techniques were not on use, the rate of intracranial metastasis in Ewing's sarcoma had been reported as high as 56%.[3] In recent studies, the total incidence of CNS involvement in Ewing's sarcoma is reported to be 2.2-6.2% and the cerebellar metastasis rate was 1.2% at admission.[1,4,5] However there is no data about the incidence of relapses at cerebellum. Shuper et al. reported the mean age at

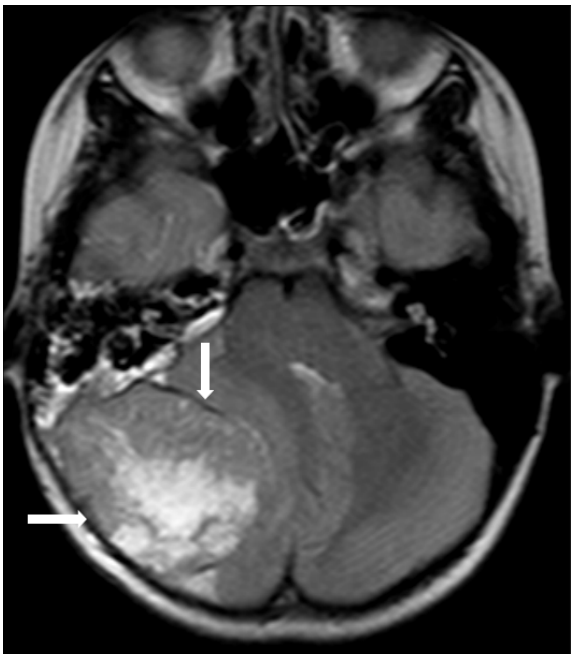

Figure 1. A T2 weighted axial MR image through the posterior fossa shows a dural-based right posterior fossa mass with heterogeneous signal intensity. The lesion also has cystic/necrotic areas. Displacement of right cerebellar hemisphere and brain stem with fourth ventricle compression were also present.

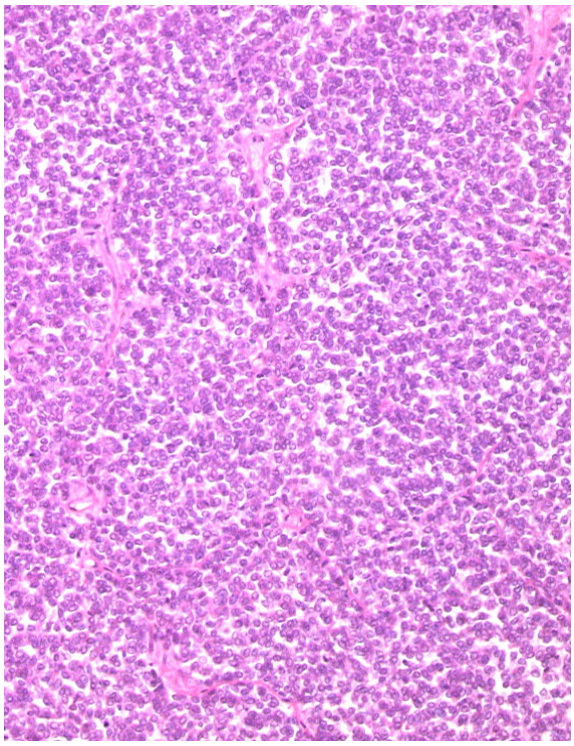

Figure 2. Tumor composed of small round cells (HE, X 100).

diagnosis of the original tumor was 12.3±8.4 years and the median time from the initial diagnosis to the finding of CNS involvement was 3 years.[1] Our patient relapsed to cerebellum 39 months later from the primary tumor treatment.

Ewing's sarcoma is known to disseminate widely, predominantly via the haematogenous route. The metastasis to the CNS indicates blood-brain-barrier destruction, possibly associated with secondary involvement of the duramater and skull. The increase in the number of brain metastasis may be due to the prolonged survival resulting from intensive systemic chemotherapy or to the inability of the chemotherapeutics in crossing the blood brain barrier.

The major symptoms of CNS involvement are headache, vomiting, congested papilla, diplopia and paresis. The onset of the symptoms is fast in children. Thus, the neurologic manifestations differ from adults. Seizures, lethargy, headache, speech disorders, hemiparesis, diplopia, and cranial nerve involvement such as facial palsy are frequent symptoms in children.[5] Although our patient had a cerebellar metastasis of 4 cm in diameter, interestingly she had no abnormal neurological finding at physical examination at the time of admission.

MRI and CT are two mostly known and recommended imaging techniques. There was an increase in detecting metastasis to the brain after the availability of CT.[6] MRI performs excellent imaging in showing the tumor manifestations in the central nervous system, allows cerebrospinal fluid examination in the detection of meningeal metastasis and detects multiple brain metastasis more accurately.[7]

Multimodal therapy consisting of radiotherapy, surgery, and chemotherapy is recommended for Ewing's sarcoma. Although Johnson and Pomeroy pointed out the necessity for preventive irradiation to the CNS during therapy for Ewing's sarcoma, Trigg et al. found that four of 10 patients with CNS metastasis had received preventive CNS irradiation.[4,8] Similarly, Simpson et al. reported no difference between patients received preventive CNS irra-

diation or not as regard to CNS metastasis.[9] In a large study including 445 patients, isolated meningeal or intra-parenchymal CNS involvement in Ewing's sarcoma is found uncommon and that routine CNS prophylaxis is considered unnecessary.[4]

The prognostic factors for Ewing's sarcoma are the age, metastatic stage and size of the tumor at diagnosis.[10] Glaubiger et al. considered that the prognosis is poor for the centrally and proximally located primary tumors compared to the distally located primary tumors.[11] Nesbit et al. found that the prognosis is poor in primary cases originating from the pelvis.[12] The estimated rate of one year survival from the diagnosis of brain metastasis was reported 23.8% ±8.5%.[13] Patients with early relapse within the first 2 years following initial diagnosis have a poorer diagnosis with 4% to 8.5% 5 year survival. Those with later recurrence experience a 23% to 35% 5 year survival. Also the patients with primary metastasis have higher risk of relapse than those with localized disease.[10]

The prognosis of patients with Ewing tumor has significantly improved to cure rates approximating 70% however the prognosis in relapse is poor. Promising response rates have recently been reported for the combination chemotherapies with topotecan and stem cell transplantation to the relapsed patients but it seems that these studies need further evaluation.

The possibility of metastasis of the primary disease to the CNS should be considered at the follow up of the long-term survivors from Ewing's sarcoma. A child who develops headache and/or vomiting and has a history of malignant disease should be investigated for brain metastasis although the patient does not have any abnormal neurologic finding.

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