Ewing’s Sarcoma of the Calcaneus: A Case Report

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Abstract

Ewing’s sarcoma is rarely found occurs in the bones of the hands and feet. We report a case of Ewing’s sarcoma of the left calcaneus in a 15-year-old girl who complained of left heel pain and swelling. An open biopsy was performed and histological examination showed the proliferation of uniform small round cells. Immunohistochemical staining for CD99 showed diffuse strong positivity in the cytoplasmic membrane of the tumor cells. After preoperative chemotherapy, a below knee amputation was performed.

Key Words: Ewing’s sarcoma, Calcaneus

INTRODUCTION

Ewing’s sarcoma is a primary osseous neoplasm composed of small, round, relatively uniform cells with no microscopic evidence of matrix production. It comprises 6–8% of all malignant bone tumors in Mayo Clinic files. The majority of patients are in the second decade of life. It shows a predilection for males with ratio of 1.4 to 1. Many portion of the skeleton may be involved, but more than half of tumor involve the long bones, usually diaphysis. The skull, vertebra, scapula, and short tubular bones of hands and feet are rarely involved. To our knowledge, Ewing’s sarcoma of the calcaneus have not been reported in Korean literature.

We report a case of Ewing’s sarcoma that arose in the left calcaneus of a 15 year-old girl, and review the literatures.

CASE REPORT
A 15-year-old girl presented with pain and swelling in the left heel for 8 months. The pain had become increasingly severe 2 months before admission. Physical examination revealed tenderness in the left heel. Her medical history was unremarkable. Laboratory tests were within normal limits. Plain radiographs demonstrated osteolytic and osteosclerotic change in the left calcaneus (Fig. 1). There was no periosteal reaction.

On MR image, the left calcaneus was seen as low signal intensity on T1WI and high signal intensity on T2WI (Fig. 2). Soft tissue adjacent to the left calcaneus showed no abnormal finding. The radiologic impression included osteomyelitis, stress fracture and uncommon neoplasm. Open biopsy was

Fig. 1. Plain radiograph shows a mixed osteolytic and osteosclerotic lesion in the left calcaneus.

Fig. 2. Sagittal T1-weighted MR image scan of left calcaneus shows intramedullary low signal intensity.

Fig. 3. Monotonous small round cells are diffusely proliferated among trabeculae of bone(Hematoxylin-eosin stain, x40).

Fig. 4. Tumor cells have uniform, round nuclei with scanty cytoplasm (Hematoxylin-eosin stain, x200).
performed. The specimen consisted of multiple fragments of red–tan soft tissue and bone. Microscopic examination showed uniform small round cell proliferation among trabeculae of bone (Fig. 3). The tumor cells have uniform round nuclei and scanty cytoplasm (Fig. 4). The nuclei contained finely dispersed chromatin. Mitotic figures were occasionally seen. Rosettes formation was not present. On the immunohistochemical stain, the tumor cells showed diffuse strong cytoplasmic membrane positivity for CD99 (12E7; Dako Corp., USA) and negativity for leukocyte common antigen (CD45RB; Dako Corp., USA) (Fig. 5). The pathologic diagnosis of Ewing’s sarcoma was made. After preoperative chemotherapy, below knee amputation was performed. The resected left calcaneus was replaced by grayish fibrous tissue with necrosis (Fig. 6). Chemotherapy–induced tumor necrosis was 90% of total tumor volume. The cortex was intact. Soft tissue extension was not found. The patient remained free from recurrence or metastasis over a period of 22 months.

**DISCUSSION**

Ewing’s sarcoma is a malignant neoplasm constituted by a uniform proliferation of small round cells without extracellular matrix, with partial or overt neuroectodermal differentiation. It was previously designated as Ewing tumor, peripheral neuroepithelioma, peripheral neuroblastoma, and Askin tumor. Ewing’s sarcoma, although the second most common malignant bone tumor of children and young adults, occurs only rarely in the bones of hands and feet. The most common clinical symptoms are pain and a mass in the involved area. Fever, anemia, leukocytosis and increase in erythrocyte sedimentation rate are often seen.
The histogenesis of Ewing’s sarcoma is unknown. A neuroectodermal origin has been proposed based on variable expression of neuronal immunohistochemical markers, ultrastructural features, and the ability of Ewing tumor cell lines to differentiate along a neural pathway in vitro.\(^9\) However, Ewing’s sarcoma can exhibit some epithelial and mesenchymal characteristics, and can appear in tissues or organs not related to the neural crest–like soft tissues of the limbs or in the kidney. Therefore, other histogenetic possibility can not be discarded.\(^9\)

Radiographically, Ewing’s sarcoma of the long tubular bones show an ill defined osteolytic lesion, Permeative or moth–eaten bone destruction often associated with onion–skin like multilayered periosteal reaction is characteristic.\(^4,\)\(^10\) Ewing’s sarcoma in the bones of the hands and feet range from the classic, aggressive appearance to atypical lesions mimicking benign entity.\(^11\) In the present case, osteomyelitis was regarded as a differential diagnostic possibility. These two entities often may not be distinguishable without biopsy.

Grossly, Ewing’s sarcoma is tan–gray and often necrotic and hemorrhagic. Necrotic yellowish and semi–fluid tissue obtained from intramedullary or subperiosteal lesion at open biopsy might grossly be erroneously interpreted as pus by surgeons.\(^4\) Histologically, most cases are composed of uniform small round cells with round nuclei containing fine chromatin, scanty clear or eosinophilic cytoplasmic membranes, whereas in others, the tumor cells are larger, have prominent nuclei, and irregular contours.\(^1,\)\(^4\) The cytoplasm of the tumor cells frequently contains PAS (periodic acid–Schiff) positive glycogen.

CD99 is a cell surface glycoprotein, the product of the \(MIC-2\) gene. CD99 is widely expressed in different tissues at a low level, but diagnostically useful is the consistent, high expression in Ewing’s sarcoma, which typically show a distinctive membrane staining.\(^12\) The present case showed diffuse strong cytoplasmic membrane positivity for CD99. On the electron microscopic study, glycogen aggregates and occasional neurosecretory granules are present.\(^1,\)\(^4\)

The present case is histologically typical of Ewing’s sarcoma. To our knowledge, this case is the first case report of Ewing’s sarcoma arising in the calcaneus in Korean literature.

The histologic differential diagnosis for Ewing’s sarcoma includes small cell osteosarcoma, mesenchymal chondrosarcoma, lymphoma, metastatic neuroblastoma, and primitive neuroectodermal tumor (PNET). Distinction of Ewing’s sarcoma from small cell osteosarcoma and mesenchymal chondrosarcoma is based primarily on the demonstration of the corresponding matrix in close association with and apparently produced by otherwise nondescript small
blue cells. In the present case, because of the absence of malignant osteoid and cartilage, we can rule out small cell osteosarcoma and mesenchymal chondrosarcoma. Lymphoma have mixture of small and large lymphocytes with prominent nuclear convolutions and clefts, unlike the smooth contours of Ewing sarcoma cells. In our case, malignant lymphoma can be excluded because of negative staining for CD45RB. Metastatic neuroblastoma generally shows rosette formation and the presence of the neurofibrils. In our case, rosette formation and neurofibrils were not found. Neuroblastoma lack CD99 immunoreactivity. Ewing’s sarcoma and PNET are closely related and now known as the Ewing family of tumors. Ewing’s sarcoma and PNET show a common characteristic t(11;22)(q24;q12) chromosomal translocation. PNET is the differentiated form of Ewing family of tumors. Homer Wright rosettes comprise the major light microscopic criterion for the diagnosis of PNET. In our case, Homer Wright rosettes were not present.

The prognosis in Ewing’s sarcoma has improved in the modern era of treatment and current survival rate is estimated to be 41%. Important prognostic factors include the stage, anatomic location, the size of the tumor, chemotherapy-induced necrosis and treatment. The calcaneal lesions appear to be worse than lesions in other hands or feet locations. In our case, the patient showed no evidence of recurrence or metastasis during 22 months follow-up. In the treatment of Ewing’s sarcoma, Wilkins et al. stated that patients with surgically accessible lesions should undergo treatment consisting of surgery, chemotherapy, and in selected cases, radiation. Casadei et al. concluded that Ewing’s sarcoma of the foot should be treated with neoadjuvant chemotherapy, radiotherapy, and surgery.

요 약

유임육종은 소아와 청소년기에 발생하는 악 성 골종양으로 주로 건 뼈의 골간에 발생한다. 손과 발에 발생하는 유임육종은 매우 드물다. 저자들은 왼쪽 발꿈치뼈에 발생한 유임육종 1 예를 경험하였기에 문헌 고찰과 함께 보고한다. 15세 여자가 왼쪽 발꿈치의 동통과 부종을 주소로 내원하였다. 방사선 소견에서 왼쪽 발꿈치뼈에 골용해성 및 골경화성 병변이 관찰되었다 수술 전 시행한 생검에서 종양세포들은 균일한 동근 모양의 종양세포로 구성되어있었다. CD99에 대한 면역조직화학염색에서 대부분의 종양세포의 세포질이 강한 양성반응을 보였다. 유임육종으로 진단을 하고 화학요법을 한 후 무릎밑절단을 시행하였다.

REFERENCES