



Peripheral Primitive Neuroectodermal Tumor of the Calcaneus: A case report

by Seyed Ali Hashemi, MD ¹, Negar Azapria, MD ², Amir Reza Vosoughi, MD ³, Masoome Pourmokhtari, MD ⁴

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Ewing's sarcoma family of tumors is the second most common primary aggressive bone tumor especially in the late teenage years. We presented a 21 year-old man with swelling and pain of left heel. Imagings were in favor of osteomyelitis but no periosteal reaction was identified. Open biopsy revealed primitive neuroectodermal tumors. Finally, he underwent below knee amputation. Therefore, biopsy of lesions in calcaneus, especially without periosteal reaction, is strongly recommended.

Key words: Peripheral Primitive Neuroectodermal Tumor, Calcaneus, Ewing's Sarcoma.

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Ewing's sarcoma family of tumors (ESFT) is the second most common primary aggressive bone tumor in young patients. This entity consists of Ewing's sarcoma, Askin tumor, and peripheral primitive neuroectodermal tumors (PNET).¹ They comprise the small, highly anaplastic, round, and blue cell tumors, cytogenetically confirmed by a t(11,22) or t(21,22). This genetic alteration can be detected with RT-PCR or FISH in fresh or paraffin-embedded material.^{2,3}

They are seen more in males (60 %), especially in the late teenage years.^{4,5} The diaphysis of long bone, especially the femur, is the most common site. Foot involvement is rare and in this anatomical location, the calcaneus is the second most common site after the metatarsal bones.⁶

To our knowledge, there is no report of PNET of the calcaneus in the literature; although, we could find several cases of calcaneus Ewing's sarcoma.⁶⁻⁹ The important points in these reports were the same presentation and radiographs changes. Metastasis was the leading cause of death as described by Gupta, et al. A 19 year-old male died after 10 months due to pulmonary metastasis. Delay in diagnosis was because of treatment of the lesion as a tuberculosis infection instead of taking an open biopsy urgently.⁶ Metastasis to the tibia and fibula⁷ and meninges⁸ were also reported.

Address correspondence to: Seyed Ali Hashemi, MD,
E-mail: sahashemi1411@gmail.com. Tel/ Fax: +98 711 6234504.
Study was carried out in Research Center for Bone & Joint Diseases, Chamran Hospital, Shiraz University of Medical Sciences, Shiraz, Iran.

¹ Assistant Professor of Orthopedic Surgery, Research Center for Bone & Joint Diseases, Chamran Hospital, Shiraz University of Medical Sciences, Shiraz, Iran.

² Assistant professor of pathology, Department of Pathology, Chamran Hospital, Shiraz University of Medical Sciences, Shiraz, Iran.

^{3,4} Resident of Orthopedic Surgery, Research Center for Bone & Joint Diseases, Chamran Hospital, Shiraz University of Medical Sciences, Shiraz, Iran.



Figure 1 Axial computerized tomography scan revealed mixed osteolytic and osteoblastic changes without periosteal reaction.

Case Report

A 21 year-old man presented with swelling and pain of the left heel for seven months. The swelling had become increasingly severe since the time of admission. The patient had no history of trauma. His medical history was unremarkable. Physical examination revealed tenderness and swelling of the left heel with stretched overlying skin. There were no systemic symptoms. Laboratory tests were within normal limits.

Plain radiographs and computed tomogram (CT) showed osteolytic and osteosclerotic changes with cortical destruction in the left calcaneus without periosteal reaction. (Fig. 1) On magnetic resonance image, there was a 27 mm osteolytic lesion in the anterior aspect of the left calcaneus with cortical erosion and sclerotic change of other parts of the bone.



Figure 2 T2-weighted magnetic resonance image showed soft tissue mass with changes in bone.

It was hypointense on T1-weighted images and hyperintense in T2-weighted images. There was an obvious soft tissue mass on magnetic resonance imaging (MRI). (Fig. 2) The condition was thought to be chronic osteomyelitis versus tumor. Open biopsy was performed for final diagnosis.

On light microscopy, the tumor showed mainly a sheet of uniform small round cells with high nuclear/cytoplasmic ratios and finely dispersed chromatin infiltrated between muscle fibers. (Fig. 3) Some of the tumor cells arranged around the vessels were in a pseudorosette fashion. Areas of necrosis were also present. On immunohistochemical analysis, the cells had strong staining for CD99. (Fig. 4)

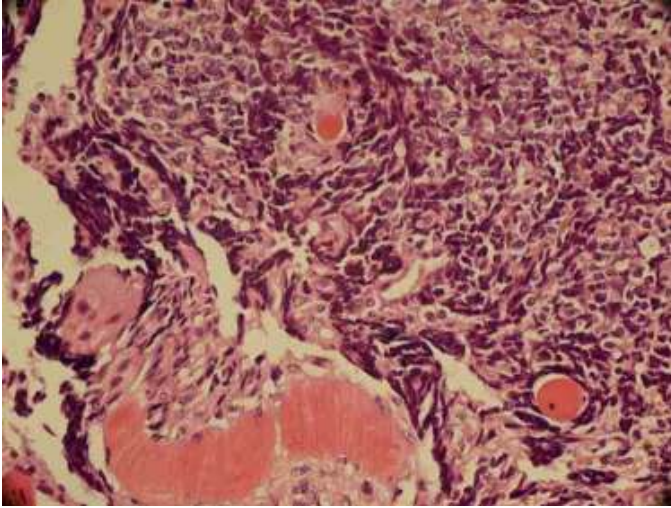


Figure 3 Infiltration of small malignant cells between muscle bundles (H&E $\times 200$).

Most cells stained positively for vimentin as well. Few clusters had some cells positive for synaptophysin and glial fibrillary acidic protein. Negative reactions with CD45, desmin and epithelial membrane antigen excluded other small round cell tumors such as lymphoma/leukemia and embryonal rhabdomyosarcoma. Overall, these findings were in favor of Peripheral Primitive Neuroectodermal Tumor. Computed tomogram study of the thorax and bone scan did not reveal any metastasis. He underwent a below knee amputation. After one year follow-up, the patient is alive with no evidence of recurrence or metastasis.

Discussion

ESFTs are malignant tumors with common histologic and molecular features but differing only in their extent of cellular differentiation.¹⁰ Its peak incidence is in patients ranging from 15 to 29 years old (2.9 per million per year). Fortunately, the incidence did not change in previous 20 years. Also, the fraction of patients with detectable metastases at diagnosis remained fairly stable at 20-25%.^{1,11}

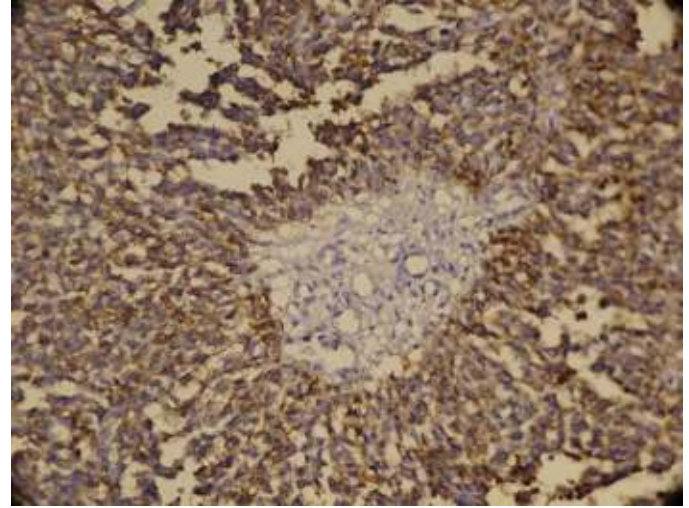


Figure 4 CD99 positive tumor cells in immunohistochemistry (IHC $\times 200$).

There are some factors showing poor prognosis, such as: adult age, female gender, Hispanic race, metastases, large tumor (> 8 cm), low socioeconomic status, pelvic primary tumor, high erythrocyte sedimentation rate, and high alkaline phosphatase.^{12,13}

The most common presenting symptom is pain; although it is not a good indicator of malignancy. Swelling and palpable mass usually are seen. Most patients have normal laboratory studies but some may have elevated ones.^{2,14} Radiographs usually shows mixed radiolucent and radiodense lesions with permeative pattern and periosteal reaction in different forms (lamellated, parallel, speculated, perpendicular or mixed). Usually ESFTs of the foot make a diagnostic challenge for orthopedics surgeons. Because: 1) These tumors are rare in the foot and delay in diagnosis is a common problem. 2) Often radiographic appearances are similar to other parts involvement (cortical erosions, lytic lesions, and soft tissue mass), but lack of periosteal reaction and other features suggesting aggression sometimes may be seen.^{15,16} 3) A great early misdiagnosis of these tumors especially in the foot is osteomyelitis due to the similarity in radiographic features. Mortality is more in patients with the initial diagnosis of osteomyelitis.¹⁷ Different parts of body may be involved by these tumors as metastases.^{7,8}

Microscopically, monotonous population of uniform small round blue cell tumors, slightly larger than normal lymphocyte, with scant cytoplasm and round nuclei are seen in ESFTs.¹⁸ PNET is differentiated from other members by more neuronal differentiation.⁹

Membrane staining for CD 99, transmembrane protein encoded by the MIC 2 pseudogene located in the short arm of chromosome X and Y, is seen in almost all cases of this tumor family.^{10,18} Lymphoblastic lymphoma/acute lymphoblastic leukemia, rhabdomyosarcoma, small cell osteosarcoma, and metastatic neuroblastoma should be considered in differential diagnosis. The most useful, though nonspecific, marker in the diagnosis of PNET is CD99, with a diffuse membranous staining pattern in these tumors. This protein is also highly expressed lymphoblastic lymphoma/acute lymphoblastic leukemia and rhabdomyosarcomas. The leukemic cells stain with terminal deoxytransferase (TdT) and clear cut matrix production by malignant cells is necessary for diagnosis of osteosarcoma. Myo D1 and desmin expression are in favor of rhabdomyosarcoma. The presence of neural markers such as such synaptophysin, S100, and chromogranin in an EFT indicates neuroectodermal differentiation (PNET).¹⁰

Although limb salvage procedures such as large frozen allogenic graft of femoral head and neck¹⁹ and distally pedicled osteomyocutaneous folded fibular flap²⁰ were introduced in recent years, amputation is recommended in a patient with a high grade calcaneal sarcoma with a large soft tissue mass without metastases beside chemoradiotherapy.¹⁴

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