

CASE REPORT**EWING SARCOMA WITH UNUSUAL SKULL METASTASIS IN A FOUR-YEAR-OLD ETHIOPIAN CHILD**Dori Woldu, MD², Daniel Zewdneh, MD^{1*}, Yocabel Gorfu, MD¹, Daniel Admasie, MD¹**ABSTRACT**

Ewing sarcoma is malignant round cell tumor, which is the second most common primary malignant bone tumor in pediatric patients. It presents with pain and swelling but some patients may present with signs and symptoms due to metastasis. The imaging modality preferred for diagnosis is conventional radiography. We report a four-year old female child from Tikur Anbessa Specialized Hospital in Addis Ababa, who had a locally advanced left tibial Ewing sarcoma with skull, scapula, pleura and pulmonary metastasis. This is, to our knowledge, the first case of Ewing sarcoma to be reported from Ethiopia.

Key words: Ewing sarcoma, metastasis, conventional radiograph, CT, MRI

INTRODUCTION

Ewing sarcoma is the second most common primary malignant bone tumor in children and adolescents accounting for 3% of all pediatric malignancies. It was first described by James Ewing in 1921 (1,3), as “diffuse endothelioma of bone”. It is one of the two malignant round cell tumors (primitive neuroectodermal tumor) with varying degrees of neuroectodermal differentiation. It exhibits similar imaging features and on cytogenetic analysis showing specific constant reciprocal translocation between chromosomes 11 and 22. It commonly occurs in long bones but can develop in flat bones especially in children less than six years of age and older adults. Metastasis characteristically involves the lungs and bones, but other systems may also be involved. It presents with signs and symptoms mimicking infection and the imaging modality for diagnosis is conventional radiography. Computed tomography (CT) and magnetic resonance imaging (MRI) are useful in determining lung metastasis and local extent respectively. Prognosis depends on size, location, local extent and presence of metastasis at presentation. Treatment includes surgery, radiotherapy, and both pre-operative and post-operative chemotherapy.

CASE REPORT

In October 2015, a two-year-old female child presented with complaints of left proximal leg swelling and pain with inability to move of one-month duration. Physical examination revealed minimal swelling on the left proximal leg with tenderness. Laboratory data showed moderate anemia.

Plain radiograph showed a lytic permeative lesion of the proximal metaphysis of the left tibia with a wide zone of transition, a Codman type of periosteal reaction, focal cortical breach and soft tissue mass suggesting Ewing sarcoma (Figure 1). Chest radiograph was normal (Figure 2). Histology from tissue taken with incisional biopsy confirmed the diagnosis.



Figure 1: Left knee x-ray (AP and lateral view): Lytic permeative lesion of the left proximal metaphysis of the left tibia with wide zone of transition, codman type periosteal reaction (\curvearrowright), focal cortical breach (\rightarrow) and minimal soft tissue component ($\cdots\rightarrow$).

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Figure 2: Chest x-ray: Unremarkable.

She was put on chemotherapy but defaulted after five cycles. Two years after initial diagnosis, she presented with progressive worsening of the leg swelling and development of new swelling on the head of one-month duration. On examination, she was acutely sick looking and irritable with pale conjunctivae and lobulated tender swellings of the left leg and fixed deformity of the knee joint at $\sim 110^\circ$ (Figure 3A). There was also a small scalp swelling on left parietal region firmly attached to the underlying skull vault. Laboratory data showed moderate anemia.

A radiograph of left leg showed destruction of the whole tibia with extension to the distal femur and an associated huge soft tissue mass



Figure 3: Photograph (A) and oblique radiography (B) of left leg: diffuse swelling of the left leg with scar on anterior aspect - from previous incisional biopsy (A) and x-ray shows destruction of the left tibia with extension to the distal femur and associated huge soft tissue mass. There is also scalloping of the proximal fibula (B).

as well as scalloping of the left proximal fibula (Figure 3B). Chest CT showed bilateral lung nodules and multiple fissural nodules of varying sizes, and bilateral nodular pleural thickening of the costal and mediastinal pleural borders and fissures (Figure 4), and a lytic permeative lesion with soft tissue component in the inferior angle of the right scapula. Brain CT showed a lytic permeative lesion involving the left parietal and posterior left frontal bones with soft tissue mass overlying the scalp and underlying extra axial extension. The greater wing of the sphenoid bone showed a lytic lesion with an extra axial soft tissue mass extension (Figure 5).

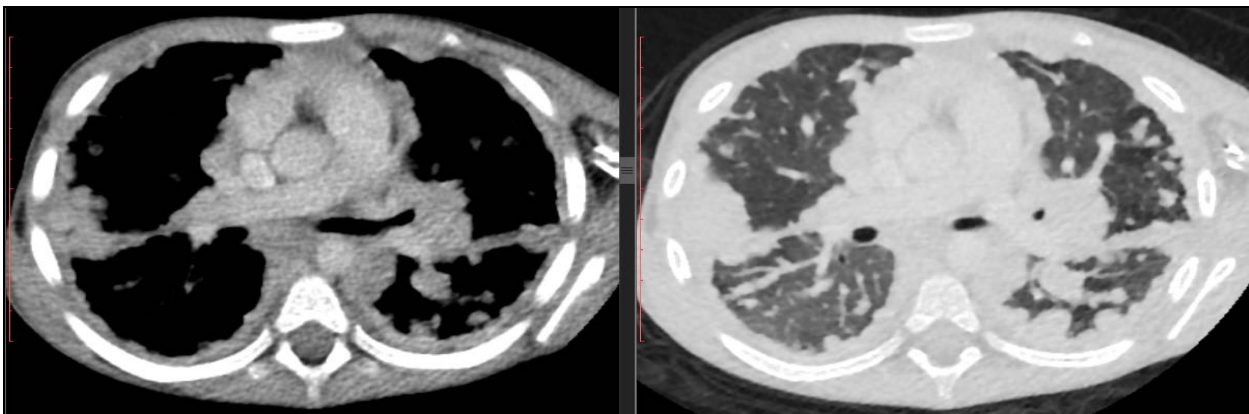


Figure 4: Chest CT scan: diffuse different size bilateral lung nodules and multiple fissural nodules. There is also bilateral nodular pleural thickening involving both the costal and mediastinal pleura, and fissures.

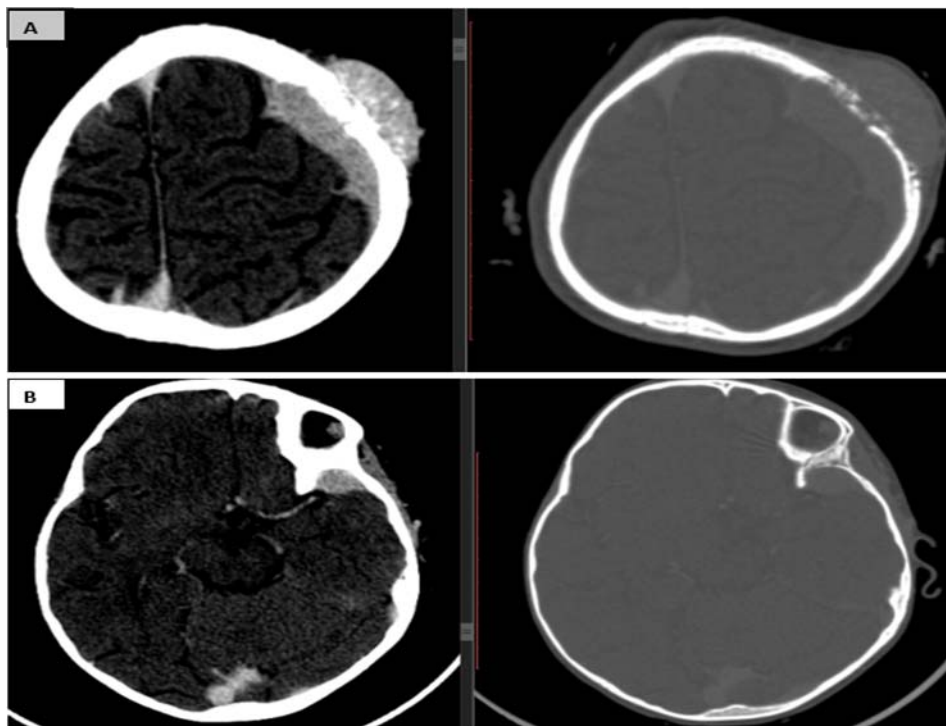


Figure 5: Contrast enhanced head CT (A & B): lytic permeative lesion involving the left parietal and posterior left frontal bones with associated heterogeneous soft tissue mass overlying scalp soft tissue swelling as well as underlying extra axial soft tissue mass (A). There is also lytic permeative lesion on the greater wing of the sphenoid bone adjacent to the left superior orbital fissure with associated extra axial soft tissue mass (B).

DISCUSSION

Ewing's sarcoma accounts for 3% of all pediatric malignancies, representing the second most common primary malignant bone cancer in children and adolescents following osteosarcoma. The incidence varies significantly with age, has a peak incidence in the second decade of life and is rare in children under five years and adults above the age of 30 (3,4). Approximately 15% of cases occur in children under 10 years. In one study the median age of diagnosis in patients less than six years of age was 42 months, 82% of which were older than 24 months (5-7).

The long bones are favored sites for primary tumor occurrence, although the axial skeleton, and extra osseous sites are common compared to osteosarcoma. In cases less than six years, axial primary tumors predominate. Ewing sarcoma arising from skull bones is rare (3,6). Ewing sarcoma usually presents as a solitary bone lesion. Multiple bone involvement has been shown to occur in the advanced stages of Ewing sarcoma, usually after pulmonary and visceral metastases manifest. On rare occasions, it involves multiple bones at the time of diagnosis (7,8).

Pain and swelling are the most common symptoms at onset. Other findings include local hot, red and tender swelling, walking disorder, neurologic impairment, respiratory symptoms, fever, and anorexia (6).

Radiographs show a classic permeative lesion with a wide zone of transition in the diaphysis or metaphysis of the long bone with reactive new bone formation that gives the lesion a sclerotic or "patchy" appearance with a soft tissue mass but no cortical breakthrough or matrix formation. There is an onion-skin type of periostitis, but can also have sunburst or amorphous types (5,11).

CT scan is better for tumor characterization in the axial skeleton for staging of lung metastasis. MRI shows low to intermediate signal intensity on both T1W and T2W images, about 32% are hyperintense on T2W images, with inhomogeneous but vivid enhancement. MRI is used for preoperative evaluation of smaller tumors (the distance between the tumor and the proximal and distal ends of the bone, whether it crosses through the growth plate or if there is involvement of the joint space, whether the tumor encases or displaces the adjacent neurovascular bundle, and if there is invasion of the adjacent muscles) and for follow-up (5,9-11). Radionuclide bone scan demonstrates a high technetium photon uptake. Similarly, it displays a high ^{18}F -fluorodeoxy glucose (^{18}F -FDG) uptake on Positron emission tomography (PET) (9).

Imaging differential diagnosis includes osteomyelitis; Langerhans cell histiocytosis, metastatic neuroblastoma, and malignant lymphoma of the

Metastasis is clinically detectable in up to 34% of the patients at the time of initial diagnosis. Even in those patients with apparently localized primary tumors, the median time from initial treatment to the development of detectable metastasis ranges from only four to 12 months when treatment is confined to the primary site. Metastasis characteristically occurs to the lung and skeletal system with equal frequency, other sites being involved in less than 10% of cases. Metastasis to skull bones, brain and dura is rare and is seen in approximately 9% of cases. Primary involvement of the skull bones is seen more commonly than metastasis to the skull (5,8). Central nervous system spread is rare as patients do not survive long enough except where early treatment has been instituted (8).

Prognostic factors include age at diagnosis, site and size of the tumor, presence of metastasis, and general condition. Skeletal site of origin is a major outcome predictor; centrally and proximally located tumors, particularly the pelvis, have poor survival while distal extremity lesions show better prognosis.

Age >15 years at diagnosis and metastasis are also poor prognostic factors but tumor size has minimal correlation with local treatment failure. Patients with exclusive lung metastasis have better outcome than those with metastasis to other systems (with or without the lung metastasis).⁽¹⁰⁾ Treatment includes resection for those with a wide margin, tumor resection followed by radiotherapy for tumors with a narrow margin, and radiotherapy for inoperable tumors. Preoperative chemotherapy helps to eradicate any micro metastases at the time of diagnosis, reduces tumor bulk facilitating excision, and in the selection of anti-tumor drugs for postoperative chemotherapy. Aggressive multidrug chemotherapy and radiotherapy, after definitive surgery, have significant roles in preventing local recurrences or systemic metastasis (8-10). Conventional radiographs are adequate to monitor progress of primary bone lesions and to screen lung metastases (11).

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