Primary Bone Lymphoma: A Rare Case of Anaplastic Large Cell Lymphoma in Calcaneus in a Child

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Learning Point of the Article:

Aggressive fungating lesions which start as swelling over foot in a child can be a very unrelated hematological malignancy instead of any local neoplasm or infection.

Abstract

Introduction: Primary bone lymphomas are rare, and primary anaplastic large cell lymphomas (ALCLs) of bone in a child are even rarer. A case of primary ALCL of calcaneus in a 7-year-old child is presented.

Case Report: Child aged 7 years presented with fungating swelling over his right heel which was associated with fever. The diagnosis was established by immunohistochemistry (CD30, ALK) of the biopsied specimen. Treatment was done by chemotherapy and subsequent radiotherapy. At 12-month follow-up, the child was ambulant with complete resolution of the swelling.

Conclusion: Masses arising from the foot and ankle can be a diagnostic challenge, and both infection and neoplasm should be considered in its differentials.

Keywords: Bone, lymphoma, anaplastic MeSH terms: Lymphoma, large cell, anaplastic, calcaneus.

Introduction

Lymphomas are a heterogeneous group of neoplasms arising from lymphocytes which can be nodal as well as extranodal. Osseous extranodal lymphoma is a rare entity which comprises around 5% of all primary bone tumors [1]. The femur, tibia, and pelvis are the most common sites of primary bone lymphoma (PBL). A few case reports of PBL in the foot have been described in adults which are histologically diffuse B-cell lymphoma [2, 3, 4, 5]. We present a rare case of anaplastic large cell lymphoma (ALCL) affecting the calcaneus in a 7-year-old child.

Case Report

A 7-year-old male child presented with swelling and pain in the outer aspect of the right heel for past 1 month. Mother of the child correlated the swelling with a history of trivial trauma. The swelling was gradually progressing. A history of incision and drainage of swelling by a local practitioner after 5 days of onset of swelling was noted. There was an associated history of high-grade fever of insidious onset, intermittent in nature with chills and without any diurnal variation. Constitutional symptoms such as significant weight loss, loss of appetite, and malaise were present for the past 2 weeks. He was unable to walk or weight bear due to pain in right lower limb for the past 1 week. The patient was febrile and having tachycardia at presentation. No lymphadenopathy was detected clinically.

A swelling of 5*4*2 cm size which was tender was present over the posterolateral aspect of heel extending anteriorly covering lateral malleolus, posteriorly extending to the area of tendoachilles insertion to the calcaneus, superiorly 5 cm above whole of the lateral malleolus, and inferiorly 2 cm above the heel

Access this article online

Website: www.jocr.co.in

DOI: 10.13107/jocr.2019.v09.i04.1458

Author's Photo Gallery


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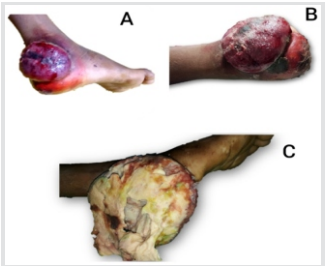

Figure 1: (a and b) Showing swelling at presentation and (c) showing swelling fungating with sloughing of skin after 2 weeks.

(Fig. 1). It had an irregular surface, well-defined round margins with loss of skin cover in more than 50% of the surface area with reddish brown color. There was active oozing of blood from the superior and inferior edge of the swelling. Temperature around swelling was raised. Lateral malleolus was not separately palpable from swelling. Tendoachilles could be separately palpable. Ankle motion was restricted and painful with no distal neuro deficits.

X-ray showed large soft-tissue shadow over heel with loss of soft-tissue planes and a lytic lesion over the posterior aspect of the calcaneus with destruction of the posterior tuberosity of calcaneus (Fig. 2a). Magnetic resonance imaging showed a lobulated well-defined mass of size 5*3.5*6 cm in the posterolateral aspect of the ankle with hyperintensity in T2 and T1 images (Fig. 2b-e). The mass invaded calcaneus posteriorly with encasement of tendoachilles. Peroneal tendons were free. Diagnosis of soft-tissue sarcoma was made.

The initial two core biopsies were non-confirmatory, one of which showed features of acute inflammation with no evidence of malignancy. Aerobic, non-aerobic, or fungal cultures were negative. The swelling increased in size and turned into a fungating mass with sloughs hanging from the surface within 2-week duration after the presentation (Fig. 1). An excisional biopsy of the swelling finally showed features suggestive of non-Hodgkin's lymphoma. The tumor mass was found to be eroding into the posterior aspect of calcaneum with the involvement of

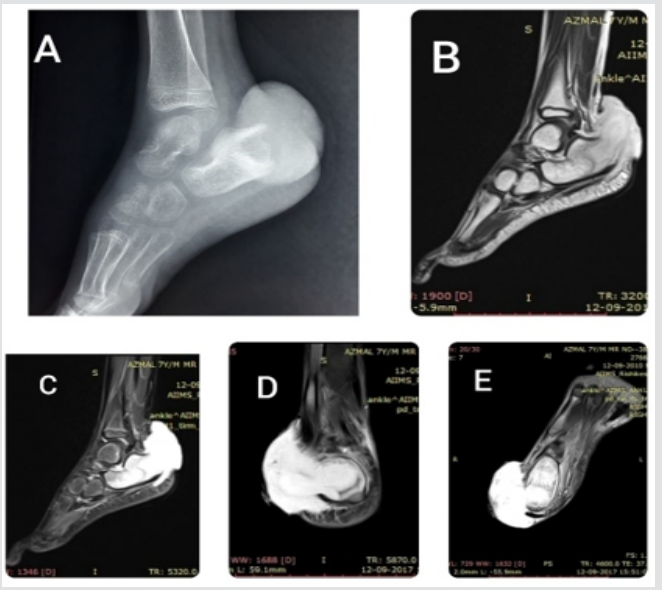

Figure 2: (a) X-ray showing soft-tissue mass on posterior aspect of calcaneum with a lytic area. (b-e) Magnetic resonance imaging showing hyperintense lesion in T1 as well as T2-weighted images in posteroinferior aspect of calcaneum.

Table 1: Differentials for causes of foot swellings

Benign lesions	Lipoma
	Periosteal chondroma
	Fibroma
	Neurofibroma
	Schwannoma
	Hemangioma
	Giant cell tumor
Malignant lesions	
Bone lesions	Chondrosarcoma
	Ewing sarcoma
	Osteosarcoma
	Lymphomas
	Metastatic lesions
Soft-tissue lesions	Synovial sarcoma
	Epithelioid sarcoma
	Clear cell sarcoma
	Pleiomorphic sarcoma
	Leiomyosarcoma
	Liposarcoma
Infections	
Acute osteomyelitis	-
Chronic osteomyelitis	Tuberculosis
	Brucellosis
	Fungal

the insertion site of tendoachilles (Fig. 3). The swelling was curetted out till the healthy-looking bone was noticed along with partial excision of the encased tendoachilles. Intraoperatively skin closure could not be achieved. The wound gradually decreased in size with 5 days of continuous vacuum-assisted closure therapy at 125 mmHg (Fig. 4), and it healed with secondary intention with regular dressing within 4 weeks. The range of motion of the ankle and subtalar joint was reduced compared to the unaffected side. Gradual range of motion exercises was started for ankle and foot. In microscopy, the tumor showed sheets of tumor cells intermediate to large cells with moderate amount of amphophilic to eosinophilic cytoplasm and the nuclei appeared to be vesicular with multiple conspicuous nucleoli with some cells showing eccentrically

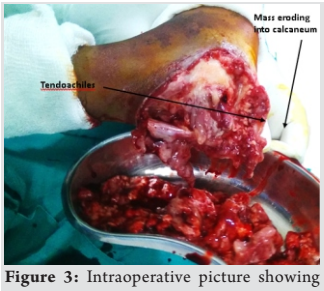

Figure 3: Intraoperative picture showing mass eroding into calcaneum.

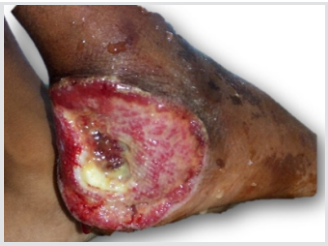

Figure 4: Granulation tissue covering calcaneum after 48 h of vacuum-assisted closure therapy.

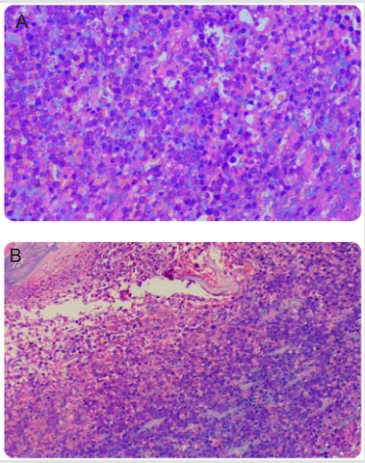

Figure 5: (a) At lower power, numerous pale tangible body macrophages are seen, producing a "starry sky" appearance (b) At high power, tumor cells have multiple small nucleoli and high mitotic index.

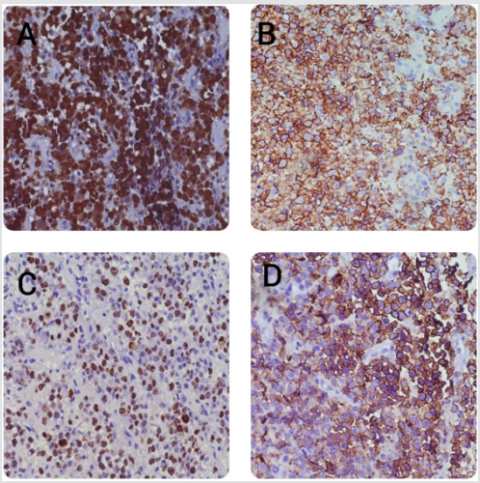

Figure 6: Immunohistochemistry panel, (a) ALK positive, (b) CD30 positive, (c) ki67 positive, and (d) leukocyte common antigen positive.

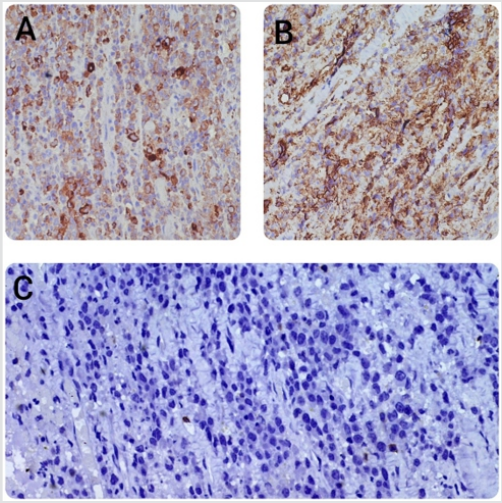

Figure 7: Immunohistochemistry panel, (a) EMA positive, (b) CD99 positive, (c) CD3 negative.

located nuclei and nuclear membrane irregularities (Fig. 5). Immunohistochemistry showed ALK, CD30, CD99, EMA, ki67, and leukocyte common antigen positivity (Figs. 6 and 7).

Staging of the patient was done by ruling out any synchronous or metachronous disease elsewhere by doing CT scan of chest and abdomen and bilateral bone marrow biopsy. Hence, a diagnosis of PBL with a histological diagnosis of ALCL was made. Treatment was carried out as advised by the oncology

Table 2: Summary of cases from 2006 to 2018 reporting ALK-positive ALCL

Authors	Year	Sex	Age	Duration	Diagnosis	Bone involved	Diagnosis	IHC	Treatment	Follow-up
Yang *et al*. [9]	2018	M	16	8 months	LN, Bone, Splenomegaly	Left Iliac, D11,12, L1-4 and Sacrum	Excision biopsy of Left Iliac Bone	CD30, ki67, ALK-1, GB and EMA	DHAP	-
Narla *et al*. [10]	2018	M	31	1 month	LN, Bone	D7-10, Ribs and Sternum	Core biopsy from Vertebrae	CD30, ki67 and ALK-1	CHOP	Lost to follow-up
Noh *et al*. [11]	2018	M	34	-	Bone	Right Ilium	Right Hemipelvectomy	CD30, ALK-1, EMA and CD3	Right Hemipelvectomy	Death
Mundada *et al*. [12]	2017	M	38	20 days	Bone	Parietal bone, left humerus, Ribs, Iliac bones, D-L Vertebrae, Sacrum and Right Femoral Neck	Tru-Cut biopsy from right iliac bone	EMA, LCA, CD30 and ALK-1	CHOP	Death
Hue *et al*. [13]	2017	M	3	6 months	LN, Bone	Left Proximal femur	Core biopsy from Femur	CD99, CD30 and ALK-1	DHAP	-
Kim *et al*. [14]	2016	F	52	2 months	LN, Bone	Ribs, Right Scapula, Sacrum, Proximal femur and L2 Vertebrae	Incisional biopsy from soft tissue around ribs	CD30	CHOP	5 months
Abrego *et al*. [15]	2016	F	24	2 months	Bone	D11,12 and L2 vertebrae	CT guided biopsy of D12 vertebrae	ALK-1	Chemotherapy+Radiotherapy+Surgery	-
Chen *et al*. [16]	2016	M	12	8 months	LN, Bone, Hepatomegaly, Splenomegaly	Multiple Vertebrae	Incisional biopsy from soft tissue around vertebrae	CD30	Hyper CVAD/MA	24 months
Al-Asaadi *et al*. [17]	2015	F	35	-	Bone	Multiple Vertebrae, Right Iliac Bone and Ribs	USG guided biopsy from Rib	ALK-1	R-CHOP	Death
Chen *et al*. [14]	2015	F	40	4 months	LN, Bone, Hepatomegaly, Splenomegaly	Right Ilium	Bone Biopsy	CD30	Hyper CVAD/MA	24 months
Gajendra *et al*. [18]	2015	F	14	2 months	LN, Bone, Splenomegaly	Multiple Ribs	LN Biopsy	CD30	CHOP	
Nayak *et al*. [19]	2013	M	50	3 months	Bone	Multiple Ribs, DL Vertebrae	CT guided biopsy of vertebrae	ALK-1	CDVP	
Mika *et al*. [20]	2012	M	13	-	Bone	B/L Iliac bones and Left Tibia	Core biopsy from Ilium	EMA, CD30 and ALK-1		
Khor *et al*. [21]	2012	F	26	6 months	LN, Bone, Splenomegaly	Left Ilium and Ribs	Core Biopsy	CD30		
Smith *et al*. [22]	2010	M	23	2 months	LN, Bone	C7 Vertebrae	LN Biopsy	CD30, ki67 and ALK-1	CHOP	12 months
Rahmat *et al*. [23]	2007	M	26	2 months	LN, Bone	Left Jaw	Core Biopsy	CD30		
Ng *et al*. [24]	2007	M	13	1.5 months	LN, Bone	Right Scapula	Core Biopsy	CD30, ALK-1	ALCL199	20 months
Mounasamy *et al*. [25]	2006	M	8	3 months	Bone	Right Humerus	Soft-Tissue Biopsy around Humerus	CD30, ki67 and ALK-1		
Bakshi *et al*. [26]	2006	M	3	0.33 months	Bone	Left ischium	Soft-Tissue Biopsy	CD30	VPC	
		M	9	NG	Bone	Right Proximal Femur	Bone Biopsy	CD30	DECCL	Death
		M	14	1	LN, Bone	Ribs	LN Biopsy	CD30	CMOP	132 months

ALCL: Anaplastic large cell lymphomas, LCA: Leukocyte common antigen

team, with 3 cycles of chemotherapy (CHOP – cyclophosphamide, doxorubicin, vincristine, and prednisone) followed by 5 cycles of localized radiotherapy. Supportive treatment in terms of prevention of anemia and infection was given. He did not have any presentation of any diseased lymphadenopathy or organomegaly during the course of treatment. At the last follow-up at 12 months, the wound over the posterior aspect had healed with the patient being ambulatory.

Discussion

Diagnosis of a swelling or fungating growth of the foot in a child can be a diagnostic challenge. Acute as well as chronic osteomyelitis along with benign and malignant lesions can present with such a scenario which can be ruled out by clinical features, laboratory investigations, and confirmed by a tissue diagnosis. The differentials for the malignant and benign conditions are presented (Table 1).

PBL is defined as (1) a single bone lesion, with or without the involvement of regional lymph nodes and (2) multiple bone lesions without lymph nodal or visceral diseases [6]. The case presented is rare in terms of the age of presentation, the location of the mass as well as the histological diagnosis. The PBLs of foot and ankle that have been reported in the literature were in adults [2, 3, 4, 5]. The histological peculiarity of this case was in terms of ALCL which was ALK positive.

ALCL is the most common T-cell neoplasm in children and adolescents. ALCL primarily involves lymph nodes with extranodal involvement of skin, soft tissue, or lung with primary involvement of bone being rare. ALCL has been divided further by the WHO into – (1) ALK-positive, (2) ALK-negative, and (3) primary cutaneous ALCL. Most of the ALCL presenting in children are ALK-positive. They also mimic as non-lymphomatous lesions. Case reports of being initially diagnosed as neuroblastoma or rhabdomyosarcoma are present [7]. They usually present at an advanced stage of disease with frequent extranodal involvement. Cases of primary bone ALCL have been reported [8]. The diagnosis is primarily based on immunohistochemistry with CD30 positivity. In a review of literature of ALK-positive ALCL with bony involvement, none of the cases reported were involving hand or foot (Table 2) [9-26]. The common sites involved were spine, pelvis, and femur. To date, the most effective treatment has been chemotherapy using CHOP regimen. Surgery is indicated for a destructive lesion in a weight-bearing bone or any pathological fracture. Irradiation therapy alone or in conjunction with chemotherapy has not shown improvement of overall survival in a mono-ostotic disease [11].

Conclusion

PBL and more precisely, primary ALCL in bone is rare in younger age group. The common site involved is axial skeleton. A high degree of suspicion with good pathological support is required to make a diagnosis of ALCL at uncommon sites. ALK-positive ALCL has shown to have good remission rates to chemotherapy.

Clinical Message

Fungating mass over the heel with lytic expansile lesion over the calcaneum is an enigma in pediatric population. Neoplastic as well as infective conditions both typical and atypical should be considered in the differentials in the workup of such a case. Histopathological examination holds the key in such cases.

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Conflict of Interest: Nil
Source of Support: Nil

Consent: The authors confirm that Informed consent of the patient is taken for publication of this case report

How to Cite this Article

Barik S, Goyal N, Paul S, Singh V, Arora S. Primary Bone Lymphoma: A Rare Case of Anaplastic Large Cell Lymphoma in Calcaneus in a Child. Journal of Orthopaedic Case Reports 2019 Jul-Aug; 9(4): 14-18.