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

Sitanshu Barik¹, Nikhil Goyal¹, Souvik Paul¹, Vivek Singh¹, Shobha Arora¹

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 extradonal 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.
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 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

### Table 1: Differentials for causes of foot swellings

|                                | Lipoma                  | Periosteal chondroma   | Fibroma                |
|--------------------------------|-------------------------|------------------------|------------------------|
| **Benign lesions**             |                         |                        |                        |
| **Malignant lesions**          | Chondrosarcoma          | Ewing sarcoma          | Osteosarcoma           |
| **Bone lesions**               |                         |                        |                        |
| **Soft-tissue lesions**        | Metastatic lesions      | Synovial sarcoma       | Epithelioid sarcoma    |
| **Infections**                 |                         |                        | Clear cell sarcoma     |
| **Acute osteomyelitis**        | -                       |                         | Pleimorphic sarcoma    |
| **Chronic osteomyelitis**      | Tuberculosis            | Brucellosis            | Leiomysarcoma          |
| **Fungal**                     |                         |                        | Liposarcoma            |

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 lateral malleolus was not separately palpable from swelling. Tendoachilles could be separately palpable. Ankle motion was restricted and painful with no distal neuro deficits.
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 team.

| Authors          | Year | Sex | Age | Duration | Diagnosis                  | Bone involved                                                                                      | IHC                        | Treatment                | Follow-up |
|------------------|------|-----|-----|----------|----------------------------|---------------------------------------------------------------------------------------------------|----------------------------|--------------------------|-----------|
| Yang et al. [9]  | 2018 | M   | 16  | 8 months | Left iliac, D11, L1-4 and Sacrum | Excision biopsy of Left Ilium and Sacrum                                                          | CD30, ki67, ALK-1, EMA     | DHAP                    | -         |
| Narla et al. [10]| 2018 | M   | 31  | 1 month  | Core biopsy from Vertebrae  | Ribs, Iliac bones, D-L Vertebral, Sacrum and Right Femoral Neck                                 | CD30, ki67 and ALK-1       | CHOP                    | Lost to follow-up       |
| Noh et al. [11]  | 2018 | M   | 34  | 20 days  | Bone                        | Right Ilium                                                                                      | CD30, ALK-1, EMA and CD3   | Right Hemipelvectomy     | Death      |
| Mundada et al. [12]| 2017| M   | 38  | 20 days  | Bone                        | Vertebral bone, left humerus, Ribs, Iliac bones, D-L Vertebral, Sacrum and Right Femoral Neck | EMA, LCA, CD30 and ALK-1   | CHOP                    | Death      |
| Hue et al. [13]  | 2017 | M   | 3   | 6 months | Left Proximal femur        | Core biopsy from Femur                                                                            | CD99, CD30 and ALK-1       | DHAP                    | -         |
| Kim et al. [14]  | 2016 | F   | 52  | 2 months | Ribs, Right Scapula, Sacrum, Proximal femur and L2 Vertebral | 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                                                                           | ALK-1 Chemotherapy+Radiation+Surgery | CD30        | CDVP                   |
| Chen et al. [16] | 2016 | M   | 12  | 8 months | LN, Bone, Hepatomegaly, Splenomegaly, Multiple Vertebral | Incisional biopsy from soft tissue around vertebrae                                               | CD30                      | Hyper CVAD/MA            | 24 months              |
| Al-Asaad et al. [17]| 2015| F   | 35  | 35 days  | Bone                        | Multiple Vertebral, Right Ilium and Ribs                                                          | USG guided biopsy from Rib | ALK-1                    | R-CHOP Death           |
| Chen et al. [18] | 2015 | F   | 40  | 4 months | LN, Bone, Hepatomegaly, Splenomegaly, and ALK-1 | Right Ilium                                                                                      | Bone Biopsy                | CD30                    | Hyper CVAD/MA          | 24 months              |
| Gujartr et al. [19]| 2015| F   | 14  | 2 months | LN, Bone, Splenomegaly, Multiple Ribs | LN Biopsy                                                                                       | LN Biopsy                 | CD30                    | CHOP                   |
| Nayak et al. [20]| 2013 | M   | 50  | 3 months | Bone                        | Multiple Ribs, DL Vertebral                                                                       | CT guided biopsy of vertebrae | ALK-1                    | CDVP                   |
| Mika et al. [21] | 2012 | M   | 13  | 6 months | Bone                        | Right Ilium                                                                                      | Core biopsy from Ilium     | EMA, CD30 and ALK-1     | -         |
| Khor et al. [22] | 2012 | F   | 26  | 6 months | LN, Bone, Splenomegaly, Left Ilium and Ribs | Core Biopsy                                                                                      | CD30                      | -                       | -         |
| Smith et al. [23] | 2010 | M   | 23  | 2 months | LN, Bone, Splenomegaly, Right Scapula | Core Biopsy                                                                                      | CD30, ki67 and ALK-1       | CHOP                    | 12 months              |
| Rahman et al. [24]| 2007| M   | 26  | 2 months | LN, Bone                    | Left Jaw                                                                                         | Core Biopsy                | CD30                    | -         |
| Ng et al. [25]   | 2007 | M   | 13  | 1.5 months | LN, Bone                    | Left Scapula                                                                                     | CD30, ALK-1               | ALCL199                | 20 months              |
| Mounasamy et al. [26]| 2006| M   | 8   | 3 months | Bone                        | Right Humerus                                                                                   | Soft-Tissue Biopsy around Humerus | CD30, ki67 and ALK-1   | -         |
| Bakshiet al. [27] | 2006 | M   | 9   | 0.3 months | Bone                        | Left ischium                                                                                     | Soft-Tissue Biopsy        | CD30                    | VPC                   |
| M   | 14  | LN, Bone | 40 | -     | LN, Bone                    | Bone biopsy                                                                                      | CD30                      | DECCl                   | Death                  |

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

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-neoplastic 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 monostotic disease [11].

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.

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.

References
1. Freeman C, Berg JW, Cutler SJ. Occurrence and prognosis of extranodal lymphomas. Cancer 1972;29:252-60.
2. Bansal S, Dharra N. Primary malignant non-hodgkin lymphoma of the talus. J Cancer Res Ther 2015;11:649.
3. Singh DP, Dhillon MS, Sur RK, Sharma SC, Radotra BD. Primary lymphoma of the bones of the foot: Management of two cases. Foot Ankle 1991;11:314-6.
4. Blume P, Charlot-Hicks F, Mohammed S. Case report and review of primary bone diffuse large B-cell lymphoma involving the calcaneus. J Foot Ankle Surg 2013;52:666-72.
5. White LM, Siegel S, Shin SS, Weisman MH, Sartoris DJ. Primary lymphoma of the calcaneus. Skeletal Radiol 1996;25:775-8.
6. Santini-Araujo E, Kalil RK, Bertoni F, Park YK. Tumors and Tumor-Like Lesions of Bone. Verlag, London, United Kingdom: Spinger; 2015. p. 385-411.
7. Gustafson S, Medeiros LJ, Kalhor N, Bueso-Ramos CE. Anaplastic large cell lymphoma: Another entity in the differential diagnosis of small round blue cell tumors. Ann Diagn Pathol 2009;13:413-27.
8. Tian C, Wang Y, Zhang Y. ALK-positive anaplastic large cell lymphoma with prominent bone involvement. Br J Haematol 2015;170:443.
9. Yang Y, Xie Q, Liu Y, Chen Y, Yin G. ALK-positive anaplastic large cell lymphoma with multifocal bone involvements: A case report and review of the literature. Int J Clin Exp Med 2018;11:2745-51.
10. Narla SL, Kurian AJ, Subramanyan A, Parameswaran A. ALK-1 positive anaplastic large cell lymphoma presenting as extensive and exclusive osseous involvement: Report of a rare association and review of literature. J Clin Diagn Res 2018;12:ED01-3.
11. Noh BJ, Han CS, Park JS, Lee J, Kim YW, Park YK, et al. ALK-positive anaplastic large-cell lymphoma with primary bone involvement: A rare case and review of the literature. Malays J Pathol 2018;40:161-7.
12. Mundada M, Ahmed F, Santa A. A challenging case of anaplastic large cell lymphoma with primary bony presentation. Asian J Oncol 2017;3:155-7.
13. Hue SS, Iyer P, Toh LH, Jain S, Tan EE, Sittampalam K, et al. Primary bone anaplastic large cell lymphoma masquerading as Ewing sarcoma: Diagnosis by anchored multiplex PCR. J Pediatr Hematol Oncol 2017;40:e105-7.
14. Kim KH, Jung YH, Han CW, Woo IS, Son JH. A case of primary bone anaplastic large cell lymphoma. Am J Case Rep 2016;17:734-8.
15. Abrego G, García J, Gilbert B, Forseen S, Toscano M. ALK positive anaplastic large cell lymphoma of the thoracic spine. J Radiol Case Rep 2016;10:1-2.
16. Tian C, Yu Y, Yang H, Zhu L, Wang Y, Zhang Y, et al. ALK-positive anaplastic large cell lymphoma with prominent bone involvement in a 13-year-old boy. Onco Targets Ther 2016;9:265-8.
17. Al-Asaadi Z, Fatin S, Patel K, Chetty N, Dubrey S. Anaplastic large cell lymphoma with axial skeletal lesions portends a poor prognosis. Br J Hosp Med (Lond) 2015;76:606-7.
18. Gajendra S, Sachdev R, Lipi L, Goel S, Misra R. ALK positive anaplastic large cell lymphoma presenting as extensive bone involvement. J Clin Diagn Res 2015;9:XD04-XD05.
19. Nayak HK, Nishant R, Sinha NK, Daga MK. Anaplastic large T-cell lymphoma presenting as an isolated osseous involvement: A case report and review of the literature. BMJ Case Rep 2013;2013:bcr2013009308.
20. Mika J, Schleicher I, Gerlach U, Adler CP, Uhle M, Knoeller SM, et al. Primary bone lymphomas thought to be osteomyelitis urgently demand a rapid diagnosis in bone pathology. Anticancer Res 2012;32:4905-12.
21. Khor LK, Wang S, Lu SJ. Anaplastic large cell lymphoma of the vertebra masquerading as tuberculous spondylitis: Potential pitfalls of conventional imaging. Intern Emerg Med 2012;7:573-7.
22. Smith ZA, Sedrak MF, Khoo LT. Primary bony non-hodgkin lymphoma of the cervical spine: A case report. J Med Case Rep 2010;4:35.
23. Rahmat K, Wastie M, Abdullah B. Primary bone lymphoma: Report of a case with multifocal skeletal involvement. Biomed Imaging Interv J 2007;3:e52.
24. Ng A, Hobson R, Williams D, Morland B. Anaplastic large cell lymphoma of bone is it a bad tumor? Pediatr Blood Cancer 2007;48:473-6.
25. Mounasamy V, Berns S, Azouz EM, Giusti V, Knapp DR. Anaplastic large cell lymphoma presenting as an epiphyseal lytic lesion: A case report with clinico-pathologic correlation. Skeletal Radiol 2006;35:619-23.
26. Bakshi NA, Ross CW, Finn WG, Valdez R, Ruiz R, Koujok K, et al. ALK-positive anaplastic large cell lymphoma with primary bone involvement in children. Am J Clin Pathol 2006;125:57-63.

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