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Case Report

The enigma of xanthogranulomatous osteomyelitis: report of a rare case with review of literature

Arushi Gupta, Nehal Ahmad, Sabina Khan*, Rubeena Mohroo, Aneesha Kataria

Department of Pathology, Hamdard Institute of Medical Sciences and Research, New Delhi, India

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***Correspondence:**
Dr. Sabina Khan,
E-mail: drsabina1@gmail.com

ABSTRACT

Xanthogranulomatous osteomyelitis (XO) is a rare chronic inflammatory condition histopathologically characterized by foamy macrophages, lymphocytes, plasma cells and fibrosis. It primarily affects organs like gallbladder and kidney but rarely involves bone. To date, only 21 cases of bone XO have been documented. XO mimics neoplastic bone lesions, creating diagnostic challenges necessitating a comprehensive approach that includes a thorough clinical history, detailed radiographic evaluation and definitive histopathologic examination. Hereby, we report a rare case of 25-year-old male presenting with pain, swelling and fever in the left forearm. Imaging revealed features suggestive of osteomyelitis and histopathological examination showed sheets of foamy macrophages, chronic inflammatory cells and fibrosis, thus clinching the diagnosis of XO. Through the case report we wish to highlight the importance of considering XO in the differential diagnosis of bone lesions so to avoid misdiagnosis of malignancy.

Keywords: Osteomyelitis, Foamy macrophages, Bone lesions, Neoplastic condition

INTRODUCTION

Xanthogranulomatous Osteomyelitis (XO) is a rare chronic inflammatory condition first described by Cleto Cozzutto in 1984.[1] It is histopathologically characterized by the accumulation of histiocytes or foamy macrophages. These macrophages, often periodic acid-Schiff (PAS)-positive are a hallmark of XO and are accompanied by other inflammatory cells like lymphocytes, plasma cells and sometimes polymorphonuclear leukocytes along with areas of fibrosis and calcification within the affected tissue.[2]

This condition mostly seen in gallbladder, kidney, urinary bladder, fallopian tube, ovary, vagina, prostate, testis, epididymis, colon, and appendix. However, it is exceptionally rare in the lungs, brain or bone.[3] Delayed-type hypersensitivity reaction may be implicated in its pathogenesis.[4] To date, only about 21 cases of XO have been documented in the literature.

We present a rare case of a 25-year-old Nigerian male who experienced pain and swelling in the left forearm, with clinical suspicion of chronic osteomyelitis. This case is notable due to the extreme rarity of XO affecting bone, highlighting its significance in the broader context of inflammatory and neoplastic bone disorders.

CASE REPORT

A 25-year-old Nigerian male was referred to orthopaedic OPD with the chief complaints of pain, swelling and fever in the left forearm for the previous 2 months. On physical examination, the patient had tenderness, swelling, and erythema in the forearm. Investigation showed an elevated erythrocyte sedimentation rate (ESR) of 28 mm/hr (normal range, 0-15 mm/hr) and a hs-C-reactive protein (hs-CRP) level of 47.58 mg/l (normal range, <1 mg/l). Hemoglobulin, total leukocyte count and differential count were within normal ranges. Renal and liver function tests were normal.

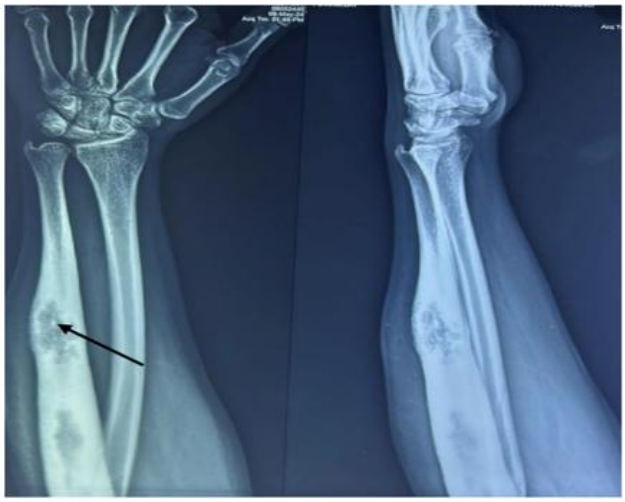

Figure 1: X-ray shows mixed density, periosteal reaction and cortical disruption with soft tissue swelling in diaphysis of ulna.

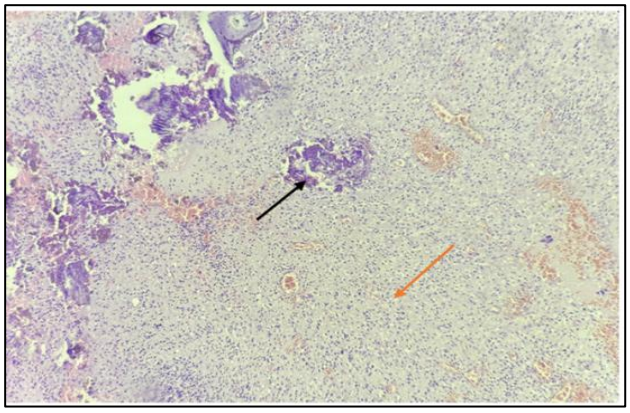

Figure 2: Microphotograph of a fragment of dead bone (black arrow) surrounded by histiocytes (orange arrow), plasma cells, lymphocytes and eosinophils (H and E stain, 10x).

X-ray of the left forearm showed a periosteal reaction and bulging of the bone with a questionable destruction of the cortex (Figure 1). Magnetic resonance imaging revealed intramedullary heterogenous altered signal intensity involving proximal and mid shaft of the ulna. Overlying cortical irregular thickening and well defined hyperintense collection is seen circumferentially around lesion along with gross myofascial edema most likely osteomyelitis. The lesion was biopsied and sent for histopathology. Grossly, multiple grey, brown soft to firm bony fragments was received measuring 1.5×0.7×0.3 cm.

The entire tissue was processed for examination. Microscopy showed predominantly small spicules of dead bone surrounded by chronic inflammatory cells comprising of sheets of foamy macrophages, plasma cells, lymphocytes, histiocytes and occasional eosinophils. (Figures 2 and 3). Areas of fibrosis were also seen. Based on these histopathological features, a diagnosis of XO was rendered. Tissue was also sent for culture; however, no organism was seen.

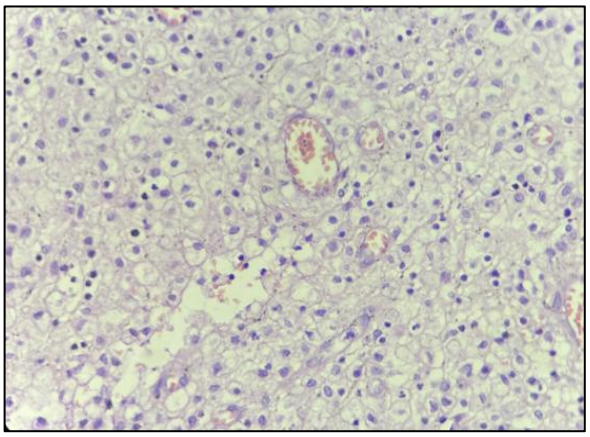

Figure 3: Microphotograph of sheet of foamy macrophages along with diffuse infiltration of mixed inflammatory cells comprising of lymphocytes, plasma cells and eosinophils (H and E stain, 40x).

DISCUSSION

Xanthogranulomatous inflammation is a well-documented phenomenon in various organs, where it typically forms mass-like lesions that can easily be mistaken for tumors. XO represents a unique and challenging condition due to its rare occurrence and its potential to closely mimic neoplastic bone lesions. This rarity can lead to significant diagnostic dilemmas, as the condition shares many clinical and radiological features with malignant processes. This inflammation is histologically characterized by the infiltration of chronic inflammatory cells, particularly foamy histiocytes.[5] These histiocytes are notable for their large size and abundant, granular, eosinophilic cytoplasm, features that are often seen in both neoplastic and non-neoplastic lesions, further complicating the diagnostic process.

The earliest documented cases of XO were reported by Cozzutto and Carbone, who described two instances involving the first rib and the epiphysis of the tibia.[1] These cases highlighted the difficulty in distinguishing Xanthogranulomatous inflammation from malignant conditions, given the mass-like presentation of the disease.

A review of the 21 reported cases of XO, in addition to the case presented here, offers some insights into the epidemiology and presentation of this rare condition (Table 1).[5-21] The review suggests a higher prevalence of XO in males, with 16 out of 21 cases occurring in male patients. Interestingly, there does not appear to be a characteristic age distribution, indicating that it can affect individuals across a broad range from 5-65 years of age. Most cases were unifocal (18 out of 21), with lesions predominantly affecting long tubular bones, such as the femur, tibia, and ulna. This pattern is consistent with the case presented here.

Table 1: Review of literature of 21 cases of XO.

Author/ year of publication	No. of cases	Patients age (in years)/ sex	Location
Cozzutto, 1984[1]	2 cases	5/male	First rib
		14/male	Proximal metaphysis of tibia
Vankalakunti et al, 2007[6]	1 case	50/ male	Diaphysis of ulna
Cennimo et al, 2009[7]	1 case	41/male	Index finger and wrist
Mehdinezhad-Kashani et al, 2010[8]	1 case	22/male	Mid-diaphysis femur
Kamat et al, 2011[5]	1 case	13/male	Distal tibia
Borjian et al, 2012[9]	1 case	14/male	Humeral head, fibular diaphysis
Nunes at al, 2012[10]	1 case	56/Male	Distal metaphysis of humerus
Holmes et al, 2013[11]	1 case	44/Male	Distal tibia
Lee et al, 2013[12]	1 case	59/male	Distal ulna
Wang et al, 2014[13]	2 cases	45/male	Third rib
		46/male	Fifth rib, eighth rib
Rathi et al, 2014[14]	1 case	50/male	Distal tibia
Gupta, 2014[15]	1 case	20/female	Peritrochonteric region of femur
Sapra et al, 2015[16]	1 case	34/male	Medial malleolus, talus, cuboid
Singh et al, 2015[17]	1 case	65/female	Peritrochonteric region of femur
Arul et al, 2016[19]	1 case	20/male	Femur
Baisakh et al, 2016[20]	1 case	21/female	Distal femoral epiphysis, proximal tibial metaphysis
Kaneuchi et al, 2017[18]	1 case	36/female	Distal metaphysis of tibia
Cheema et al, 2017[21]	1 case	5/female	Humerus
Solooki et al, 2019[3]	1 case	15/male	Proximal metaphysis of tibia
Present study	1 case	25/male	Diaphysis of ulna

Radiologically and grossly, XO manifests as mass-like lesion which leads to suspicion of malignant process. This pseudo-neoplastic presentation makes it critical to differentiate XO from true malignancies, as the treatment strategies for these differ significantly. The differentiation requires a comprehensive approach that includes a thorough clinical history, detailed radiographic evaluation and definitive histopathologic examination. In the presented case, the patient had a history of chronic osteomyelitis and radiological studies revealed periosteal reaction, cortical destruction, and intramedullary heterogeneous signal intensity, all features that could be seen in both infectious and neoplastic processes.

The histological differential diagnosis for XO is broad and includes conditions such as Langerhans cell histiocytosis, Erdheim-Chester disease (ECD), chronic recurrent multifocal osteomyelitis (CRMO), xanthoma, infiltrative storage disorders, malakoplakia, fibrohistiocytic tumors, and metastatic renal cell carcinoma.[22-26] Each of these conditions has its own distinct clinical and histological features, but the overlap with XO can make differentiation challenging. For instance, Langerhans cell histiocytosis also involves the proliferation of histiocytes and can present with bone lesions, while ECD is a rare non-Langerhans cell histiocytosis that similarly involves foamy histiocytes and systemic manifestations.

Given that XO, there is no established, standardized treatment protocol. The management of XO generally involves surgical intervention, with most cases being treated with curettage and bone grafting to address the localized bone destruction. Antibiotics are often prescribed in conjunction with surgical procedures, particularly in cases where there is a suspicion of or confirmed infection. However, the exact role of antibiotics remains unclear, as XO is not always associated with active bacterial infection.[4] In the case presented here, tissue culture was negative for organisms, reinforcing the notion that XO can occur without clear infectious etiology.

CONCLUSION

The case is being presented here as it underscores the importance of considering XO in the differential diagnosis of bone lesions, particularly in cases where the clinical and radiological findings suggest a neoplastic process. While XO is a benign condition, its ability to mimic malignant bone lesions altogether require diligent diagnostic workup to ensure timely and appropriate management. The definitive diagnosis of XO relies on histopathological examination, which remains the gold standard for diagnosing this condition and differentiating from other aggressive pathologies including malignancies.

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