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Sinister Masquerade: A Rare Case of Primary Bone Follicular Lymphoma Mimicking Chronic Osteomyelitis and Tuberculosis

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ABSTRACT

Background:
Primary bone lymphoma (PBL) is a rare extra-nodal manifestation of non-Hodgkin lymphoma (NHL), constituting less than 1% of all NHLs and approximately 7% of malignant bone tumors. While diffuse large B-cell lymphoma is the predominant subtype, follicular lymphoma (FL) rarely presents as isolated primary bone disease. Accurate histopathological evaluation is therefore pivotal for diagnosis and management.

Case Report:
We describe a 26-year-old immunocompetent male presenting with progressive pain and swelling over the left humerus. Imaging revealed a destructive lytic lesion with soft tissue extension, initially suggestive of chronic osteomyelitis. Empiric antibiotic and anti-tubercular therapies were initiated without improvement. The patient subsequently developed pathological fracture, chest wall extension, lymphadenopathy, systemic "B" symptoms, and a cavitary lung lesion. Laboratory evaluation revealed anemia, elevated inflammatory markers, and markedly raised β2-microglobulin. Definitive diagnosis was achieved by excisional lymph node biopsy and bone marrow examination, which demonstrated Grade 3A follicular lymphoma with positive immunohistochemistry for CD20, CD10, BCL-2, BCL-6, and C-Myc, and a high Ki-67 index. The patient deteriorated rapidly and succumbed before initiation of definitive oncologic therapy.

Conclusion:
Primary bone follicular lymphoma represents a rare and diagnostically challenging entity that may masquerade as chronic osteomyelitis or skeletal tuberculosis. This case highlights the need for early consideration of lymphoproliferative disorders in atypical, treatment-refractory bone lesions.

Keywords- Chronic Osteomyelitis, Follicular Lymphoma, Non-Hodgkin Lymphoma, Primary Bone Lymphoma, Tuberculous Osteomyelitis

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INTRODUCTION-

Primary bone lymphoma (PBL) is a rare form of extra-nodal non-Hodgkin lymphoma (NHL), accounting for less than 1% of all NHLs, approximately 7% of malignant bone tumours, and 4–5% of all extra-nodal lymphomas.[1,2] The vast majority of PBL cases are of the diffuse large B-cell lymphoma (DLBCL) subtype, with follicular lymphoma (FL) representing a rare variant.[3] Although FL commonly involves the bone marrow in advanced systemic disease, its primary manifestation as an isolated bone lesion is exceptionally uncommon and sparsely reported in literature. Moreover, clinical and radiological features of PBL often mimic those of chronic infections such as bacterial osteomyelitis or skeletal tuberculosis, particularly in endemic regions. Consequently, misdiagnosis is common, often leading to inappropriate and delayed management. We present a case of high-grade follicular lymphoma initially misdiagnosed as chronic osteomyelitis and disseminated tuberculosis in a young, immunocompetent male. This case underscores the importance of considering lymphoproliferative disorders in the differential diagnosis of atypical bone lesions unresponsive to standard therapies, and it emphasizes the critical role of histopathology in establishing a definitive diagnosis.

CASE REPORT

A 26-year-old previously healthy male presented to a peripheral healthcare facility with a 4-week history of progressive pain and localized swelling over the proximal third of the left humerus. Radiography revealed a lytic lesion in the meta-diaphysis with a lateral soft tissue component [Figure – 1(a)].

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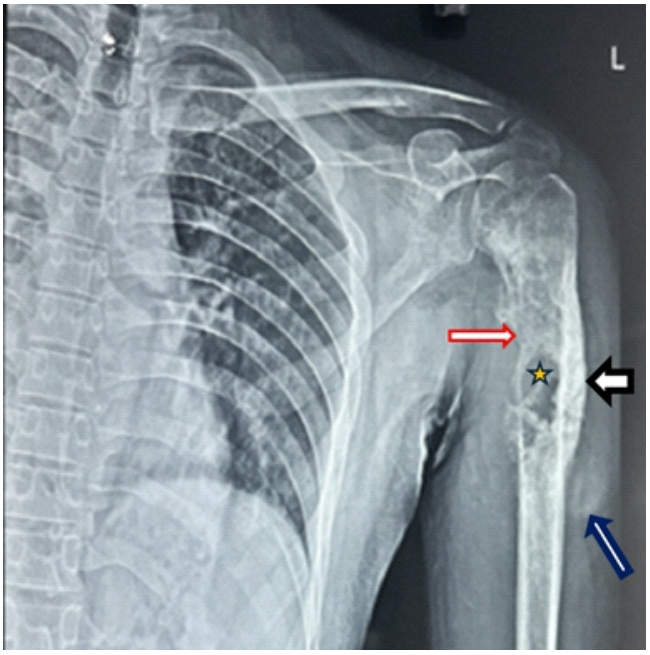

Figure 1(a) - Moth eaten pattern of bone destruction along (red border arrow); large central lucent area (yellow star) with cortical thinning on inner aspect; periosteal new bone formation (black border arrow) and subtle soft tissue mass on lateral aspect of proximal humerus (blue border arrow).

MRI demonstrated a hyperintense T2/hypointense T1 lesion with cortical breach, significant marrow edema, and a soft tissue mass measuring 6.7 × 6.3 × 4.2 cm, no regional lymphadenopathy was detected. Laboratory investigations, including inflammatory markers, were within normal limits. A provisional diagnosis of chronic osteomyelitis was made, and empiric therapy with rifampicin and linezolid was initiated. Bone biopsy and cultures were non-diagnostic.

Two months later, the patient returned with purulent discharge, worsening pain, and swelling extending to the left chest wall. Imaging revealed a pathological fracture of the left humerus [Figure-1(b)], for which external fixation was performed.

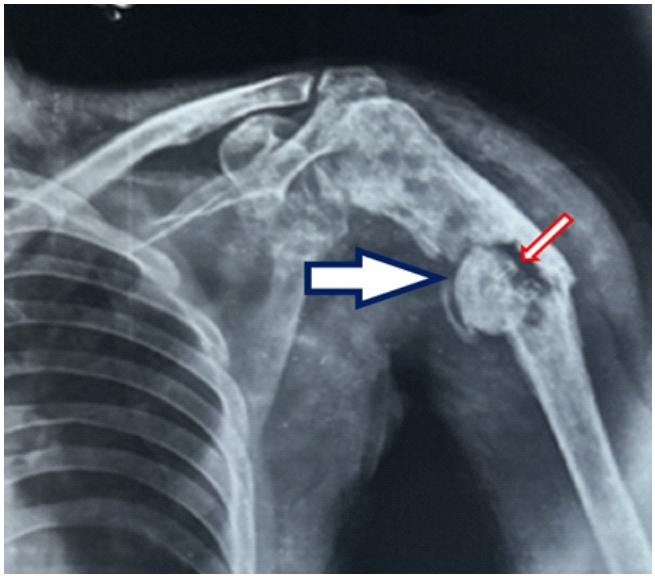

Figure 1(b) - Pathological fracture of proximal 1/3rd of left humerus (blue border arrow); post biopsy staples (red border arrow).

Despite escalation to intravenous piperacillin-tazobactam and vancomycin, there was no clinical improvement. Subsequently, he developed cervical and axillary lymphadenopathy and systemic symptoms, including anorexia and significant weight loss. Chest imaging identified a thick-walled cavitary lesion in the right lower zone [Figure – 2(a)]. CECT of the chest and abdomen [Figure – 2(b)] revealed 13 mm–walled cavitary lesion in the superior segment of the right lower lobe with retroperitoneal, mesenteric lymphadenopathy, and splenomegaly.

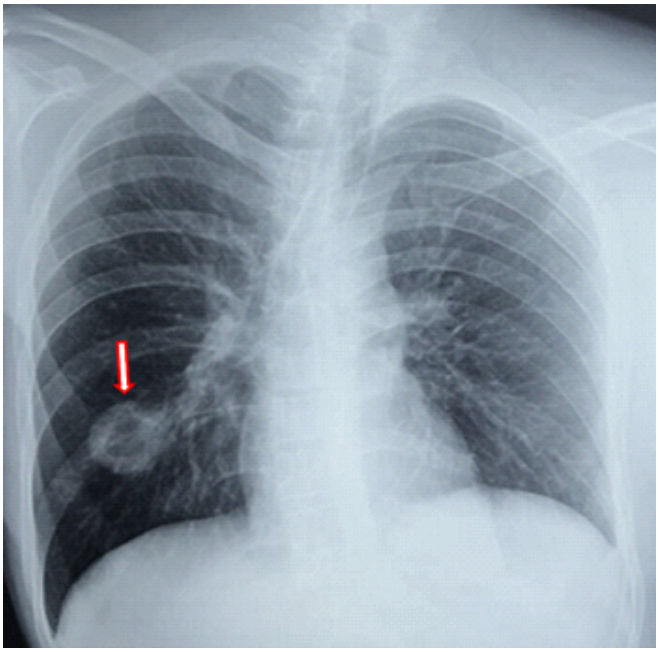

Figure 2(a) - Chest radiograph showing thick walled cavitary lesion in right lower zone (red border arrow).

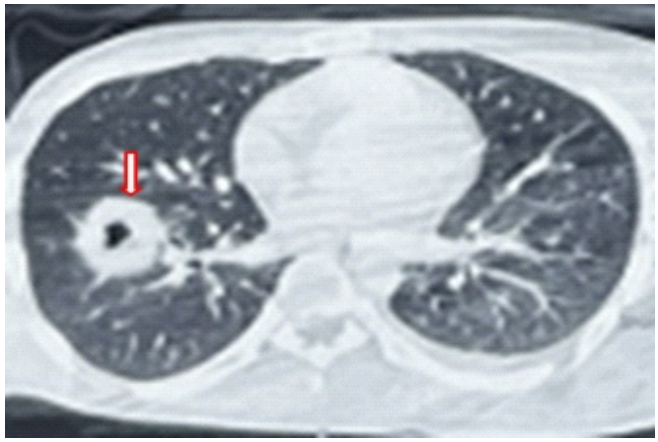

Figure 2(b) - Computerised tomography (CT) of chest showing thick walled cavitary lesion in superior segment of right lower lobe (red border arrow).

Aspiration of the chest wall collection yielded pus with no identifiable organisms. Cytology and microbiological investigations, including AFB testing and cultures, were inconclusive. A presumptive diagnosis of disseminated tuberculosis was made, and first-line anti-tubercular therapy was initiated. However, after 8 weeks, the patient showed clinical deterioration. Further evaluation at a tertiary center revealed anemia, mildly elevated ESR, CRP, LDH, and a markedly raised serum β2-microglobulin (6236 ng/mL), with negative fungal markers. Flexible bronchoscopy with BAL yielded no evidence of infection. Given the atypical course

and persistent negative microbiological findings, a lymphoproliferative disorder was suspected. Excisional biopsy of a cervical lymph node and bone marrow examination confirmed a diagnosis of Grade 3A Follicular Lymphoma, with immunohistochemistry positive for CD20, CD10, BCL-2, BCL-6, and C-Myc, along with a high Ki-67 proliferation index [Figure – 3(a), 3(b), 3(c) & 3(d)].

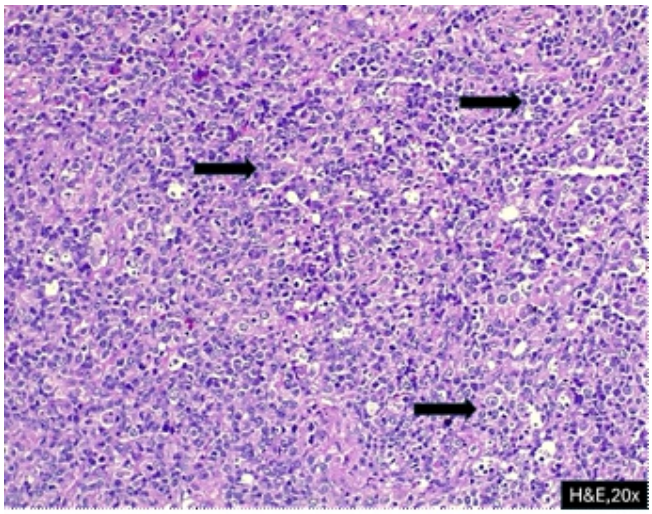

Figure 3(a) - H&E (20x) Complete effacement of nodal architecture, which is replaced by intermediate to large sized atypical lymphoid cells (black arrows).

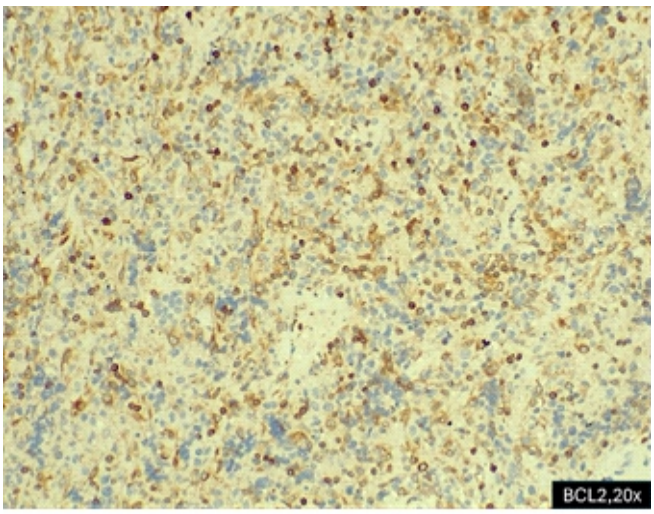

Figure 3(b) - BCL2, (20x), Immunoreactive in < 50% of tumor cells.

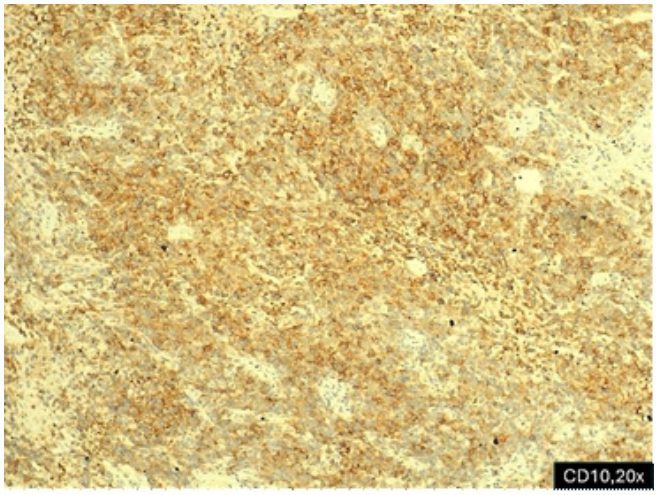

Figure 3(d) - CD10, (20x), Diffuse immunopositivity.

Despite referral for oncologic management, the patient's condition rapidly declined, and he succumbed to the disease.

DISCUSSION

The diagnostic criteria for PBL, as per WHO definitions, include one or more osseous lesions without evidence of supra-regional nodal involvement or other extra-nodal disease at initial staging. This distinction is critical in differentiating PBL from systemic lymphoma with secondary bone involvement or from primary bone marrow lymphoma (PBML), where bone marrow is infiltrated without radiographic evidence of bone lesions.[4]

In a compiled cohort of 16 patients with PB-FL, there was a slight male predominance (12 males, 4 females) with a median age of 60 years (range 25–88).[5] The most common presenting symptom is localized bone pain, often in the meta-diaphyseal region of long bones such as the femur, spine or tibia.[6] Patients may also present with soft tissue swelling or, less commonly, pathological fractures and systemic "B" symptoms such as fever, night sweats, and weight loss.[7] The clinical presentation of PBL is often insidious and nonspecific, contributing to frequent diagnostic delays, with some studies reporting a median diagnostic delay of up to eight months.[8] Radiological findings such as lytic, moth-eaten, or permeative lesions with minimal periosteal reaction are characteristic but not pathognomonic. In the case series reported by Krishnan et al, these radiologic features were often misinterpreted as metastatic disease, multiple myeloma, osteomyelitis, and other primary bone tumors such as osteosarcoma or Ewing's sarcoma (in younger patients), especially given the axial skeleton involvement and demographic overlap (typically males in their sixth decade).[9] Unlike multiple myeloma, however, patients with PB-FL or PBL typically do not present with hypercalcemia, renal dysfunction, or clonal paraprotein on serum protein electrophoresis. Similarly, pathologic fractures are less common at diagnosis, although it may occur during disease progression. MRI remains the imaging modality of choice in evaluating PBL, owing to its sensitivity in detecting marrow involvement and soft tissue extension. The typical findings include marrow replacement (low signal on T1-weighted images and high signal on T2-weighted or STIR sequences), often associated with a soft tissue mass and cortical destruction.

CONCLUSION

Primary bone follicular lymphoma is a distinct and rare presentation of FL that requires high clinical suspicion for accurate diagnosis. A multidisciplinary approach integrating imaging, histopathology, and clinical evaluation is essential to differentiate it from other mimics such as myeloma, metastases, or infectious osteomyelitis, and to initiate timely and appropriate therapy.

Conflict Of Interest : None
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