PRIMARY BONE LYMPHOMA MIMICKING AS POLYARTHRITIS

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ABSTRACT
A 17 years old boy presented with warm, tender and swollen joints of both upper and lower limbs along with inflammatory back pain and heel pain since 7 months. He had developed continuous high grade fever 3 days ago and complained of marked weight loss during the last 6 months. On examination his liver, spleen and cervical lymph nodes were palpable. X ray of the affected joints revealed osteolytic lesions in tibia, fibula, and humerus and fracture head of femur. Bone marrow examination revealed infiltration by sheets of lymphoid cells which were positive for leukocyte common antigen and CD_{20}. The bone biopsy from a lytic lesion in proximal left tibia revealed a similar picture of infiltration with sheets of CD_{20} positive lymphoid cells. Need to remember that lymphoproliferative disorders can mimic rheumatological disorders in clinical practice. The case is presented to share the experience of others.

INTRODUCTION

Primary lymphoma of bone (PLB) is an extremely rare condition that is usually confused with other primary injuries of the bone. It is characterized by the involvement of one or more bone locations, with or without involvement of regional lymph nodes and viscera.[1] PLB constitutes 3 – 7% of all malignant bone tumours and approximately 3% of all extranodal lymphomas. It is found at all ages and any part of the skeleton can be involved, but a trend exists in favour of bones with persistent bone marrow. Long bones (femurs, tibia) are the most common site of involvement. Patients with PBL may rarely present with constitutional B symptoms such as fever or night sweats. Most series also show a male preponderance. Diffuse large B-cell lymphoma is the commonest type of primary non Hodgkin's lymphoma of bone in the Pakistani population.[2] Primary bone marrow lymphomas produce mainly both hypercalcaemia and osteolytic lesions apparently due to abnormal production of osteoclast – activating factor but these findings are rare at presentation.[3]

CASE REPORT

A 17 year old boy presented with history of multiple painful joints for 7 months in the OPD. The pain started in the hip joint, soon however his heels, elbows, ankles, knees, shoulders and hands were also involved. He had significant morning stiffness and admitted to have inflammatory character back pain. On examination all the involved joints were swollen, painful, warm to touch. There was no lymphadenopathy, hepatosplenomegaly, normal cell counts with absence of any abnormal cells in peripheral blood. He was provisionally diagnosed as having spondyloarthropathy with peripheral arthritis. He was treated with oral steroids and Sulphasalazine. However his symptoms worsened and he presented after 4 weeks with excruciating pain in the involved joints on slight movement, high grade continuous fever. He had lost 4 kg weight, his inguinal lymph nodes were palpable, small, firm and rubbery. Liver, spleen were palpable 1 finger below costal margin each but no focal lesion was present on ultrasonography. On investigation he was anaemic with Hb 7.7 g/dl, with TLC 6.9×10^9/l, Absolute neutrophil count 2.4×10^9/l, Platelet count 186×10^9/l. The coagulation profile, Alkaline phosphatase, AST and ALT were normal, total bilirubin was 2.4 mg/dl, indirect bilirubin was 1.8 mg/dl. Serum urea was 23 mg/dl, Serum createnine was 0.8 mg/dl, uric acid was 9.8 mg/dl.

Radiological examination of the extremities demonstrated osteolytic lesions with bone destruction involving the meta diaphysis of tubular bones and underlying pathological fractures. No periosteal reaction was present and no adjoining soft tissue component or intraarticular extension of the lesions was noticed. In addition well defined and eccentric lucent bone lesions in metadiaphyseal tubular bones were also present suggestive of hyper-parathyroid activity (brown tumour). Chest X-ray revealed no lung pathology. He was advised peripheral smear examination, inguinal lymph node biopsy and CT scan abdomen, but patient left against medical advice.

He was readmitted after one week, with high grade fever above 102°F, drowsiness, severe generalised bone tenderness and grade I bed sore; His Blood Pressure was 100/60, Temp: 101°F, Respiratory rate 22/ min. His lab findings showed markedly high ionized calcium of 2.9 mmol/l, low intact Parathormone level, normal phosphate and alkaline phosphatase, low albumin 22 g/l, uric acid 15.4 u/l, LDH 1090 u/l, serum creatinine1.2 mg/dl.

His Hb was 5.4 g/dl, TLC 2.3 × 10^9/l, ANC 1.02× 10^9/l, platelet count 200 × 10^9/l. Red cell morphology was normochromic normocytic with microspherocytes and an occasional schistocyte. Direct Coombs test was positive. Bone marrow biopsy revealed infiltration with diffuse sheets of pleomorphic lymphoid cells replacing the normal architecture. These cells were diffusely positive for leukocyte common antigen (LCA) and CD_{20}. At the same time incision bone biopsy from left tibial tuberosity was taken from the radiologically suggested permeative lesion. The tissue obtained was soft and fleshy in gross examination. Histological examination revealed replaceoment of bone tissue by sheets of pleomorphic lymphoid cells which were LCA +ve. The diagnosis of Diffuse Large B Cell Lymphoma of the bone was established... Ki – 67 / MIB – 1 index was advised. Clinically he was placed in Ann Arbor Stage IV with B symptoms.

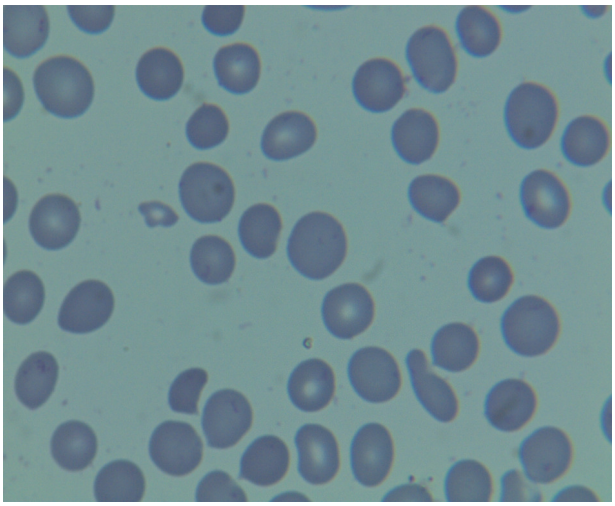

Fig. 1: *Blood smear with microspherocytes and schistocytes (Giemsa stain).*

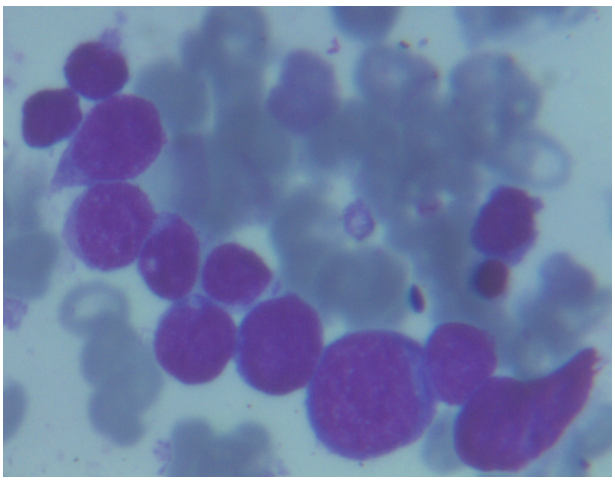

Fig. 2: *Lymphoma cells in bone marrow aspirate showing high nuclear cytoplasmic ratio, open chromatin, 1 – 3 nucleoli, scanty agranular, grey blue cytoplasm (Giemsa stain).*

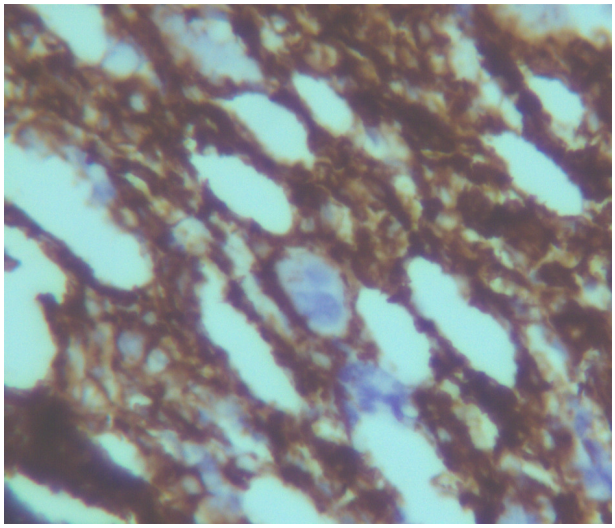

Fig. 3: *Bone marrow core. CD 20 immunostain +ve in infiltrating cell sheets.*

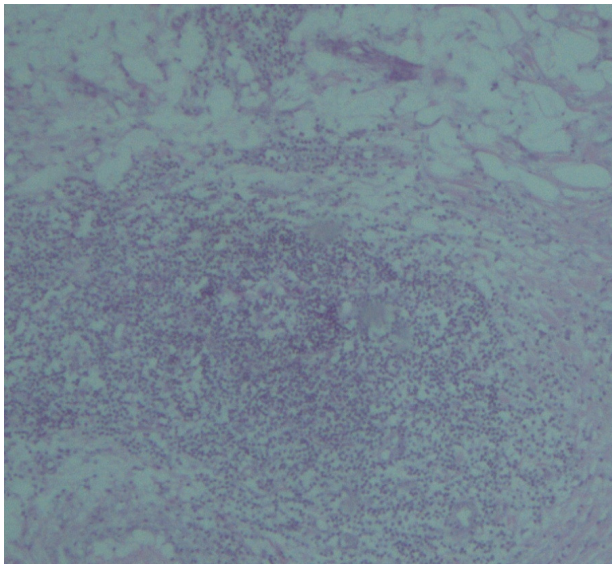

Fig. 4: *Incisional tibial bone biopsy revealing sheets of lymphoma cells on left and bone tissue right (H&E preparation).*

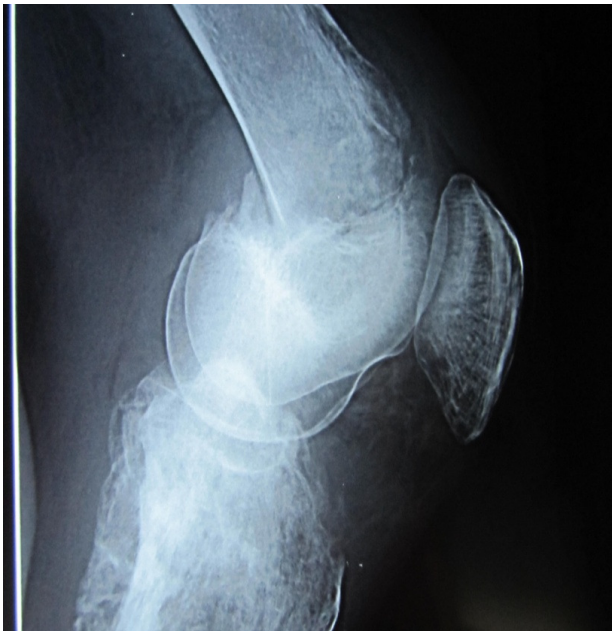

Fig. 5: *X ray Left knee joint lateral view (Lytic Lesion).*

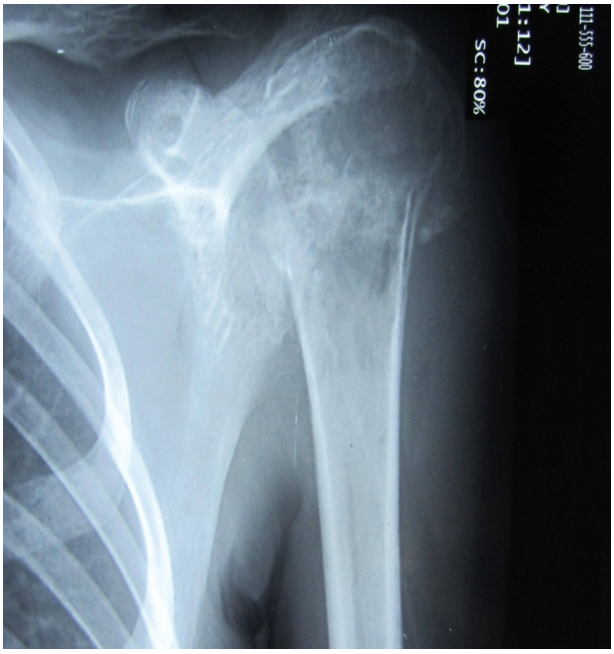

Fig. 7: *X-ray Right shoulder joint AP view (Lytic lesion).*

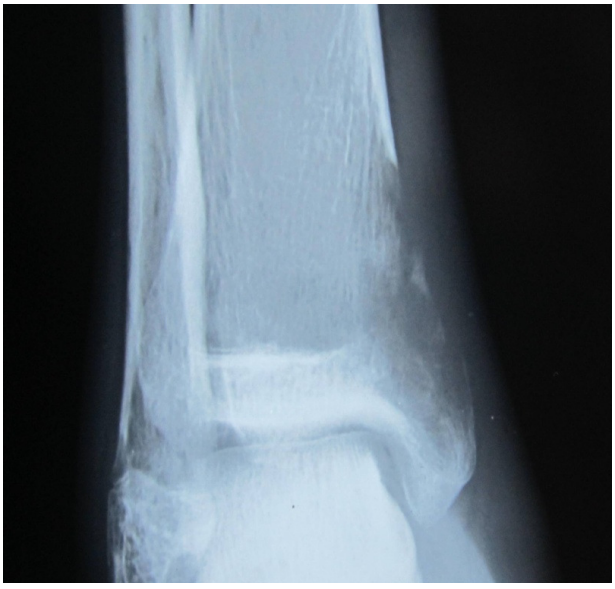

Fig. 6: *X-ray Left ankle joint AP view (Lytic Lesion Tibial malleolus).*

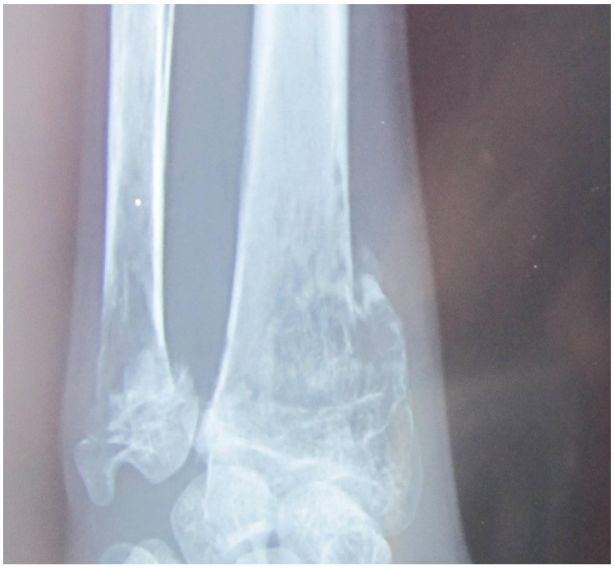

Fig. 8: *X-ray Right wrist AP view (Lytic lesion).*

DISCUSSION

We present a rare case of bone lymphoma masquerading as inflammatory arthritis, later on presenting as multiple osteolytic lesions with pathological fractures, with radiological features of both bone replacement with malignant process and brown tumor. Associated autoimmune hemolytic anemia, hypercalcaemia, low parathormone level, bone and bone marrow replacement with Diffuse Large B Cell Lymphoma suggested a bone lymphoma with ectopic parathyroid hormone like protein production.

Although acute leukaemias have been known to present with joint swelling in the absence of abnormal haematological findings, however, arthritis as a presenting sign of lymphoma, is extremely rare [4]. Equally uncommon is primary bone involvement at the time of presentation with non-Hodgkin lymphoma. Tissue diagnosis with biopsy of an adjacent lymph node or directly from the involved bone forms the foundation of the diagnosis. High grade tumors are

rare, the most common grade identified is intermediate, followed by low grade lesions.[5] Falicinia et al reported three children with non-Hodgkin's lymphoma who had joint swelling at the onset of their disease.[4] Takasaki et al reported a patient with Diffuse large B cell non-Hodgkin's lymphoma who developed multiple bone lesions and hypercalcemia. The presentation was similar to our patient with advanced disease, drowsiness, multiple bony fractures and osteolytic lesions.[6]

Osteolysis and hypercalcemia are observed in 5–15%, and 10%, respectively, of malignant lymphoma patients during their clinical course. However, both osteolysis and hypercalcemia are uncommon at onset of the disease. The secretion of osteoclast – activating factors such as MIP_1alpha, MIP_1beta and RANKL, by the tumor cells (and/or bone marrow stromal cells) have been implicated in the etiology of osteolysis and hyper-calcemia in some malignant lymphoma cases.[3] The underlying cytokines responsible for osteolysis and hypercalcaemia could not be investigated in our patient because of budget constraints. However his low normal Parathormone level suggested the possibility of a PTH like peptide secretion by tumour cells causing severe degree of osteoporosis witnessed in some of the X-rays. On conventional X-ray examination, primary NHL of bone shows variable changes, including lytic lesions or permeative lesions with bone destruction. Cortical erosion or destruction may occur, but there is usually little periosteal reaction.[1] Our patient showed similar lesions involving both upper and lower limbs as seen in figure 1 – 4. There was no soft tissue or intra-articular extension of the tumour at any site. Normal Alkaline phosphatase was suggestive of a primarily osteoclastic activity with no attempt at bone formation.

It is *concluded* that this case report highlights the fact that lymphoproliferative disorders can mimic rheumatological disorders and physicians taking care of patients with inflammatory arthritis should be aware of musculoskeletal manifestations of lymphomas.

REFERENCES

1. Pinheiro RF, Filho FD, Lima GG, Ferreira FV. Primary non-Hodgkin lymphoma of bone: An unusual presentation. J Can Res Ther 2009; 5: 52-3.
2. Qureshi A, Ali A, Riaz N, Pervez S. Primary non-hodgkin's lymphoma of bone: Experience of a decade. Indian J Pathol Microbiol 2010; 53: 267-70Non.
3. Matsuhashi Y, Tasaka T, Uehara E, Fujimoto M, Fujita M, Tamura T, et al. Diffuse large B-cell lymphoma presenting with hypercalcemia and multiple osteolysis. Leuk Lymphoma. 2004; 45 (2): 397-400.
4. Falcinia F,Bardareb M, Cimazb R, Lippia A, Coronab F. Arthritis as a presenting feature of non-Hodgkin's lymphoma. Arch Dis Child 1998; 78: 367-370.
5. Smith ZA, Sedrak MF, Khoo LT. Primary bony non-Hodgkin lymphoma of the cervical spine: a case report. Journal of Medical Case Reports. 2010; 4: 35.
6. Takasaki H, Kanamori H, Takabayashi M, Yamaji S, Koharazawa H, Taguchi J, Fujimaki K, Ishigatsubo Y. Non-Hodgkin's lymphoma presenting as multiple bone lesions and hypercalcemia. Am J Hematol. 2006; 81 (6): 439-42.