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Case Report

A Rare Case of Primary Non-Hodgkin's Lymphoma of The Bone in a Female Patient Admitted To Dubrovnik Hospital in 2013 - @

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ABSTRACT

Primary Non-Hodgkin's Lymphoma of The Bone (PLB) is rare entity [1,2,3]. Patients generally present with localised bone pain, soft-tissue swelling or palpable mass. Pathological fracture of the proximal femur and humerus secondary to soft-tissue tumors is well documented in the literature. Lymphomas presenting primarily at these sites with pathological fracture is unusual. A review of the world literature shows that the incidence of the skeletal manifestations from NHL is less than 5%, and in all these cases, bony involvement was reported many years after presentation of the primary cancer. Histopathologically, PLB usually represents diffuse large B-cell lymphoma. We report 56-year-old female patient case report of Primary non-Hodgkin's lymphoma of proximal femur and proximal femur with pathological fracture and management. In January 2014. A 56-year-old woman was diagnosed with stage IV B primary large-cell diffuse primary non-Hodgkin's lymphoma. After one year of initial diagnostic procedures and chemotherapy with rituximab together with cyclophosphamide, vincristine, procarbazine, and prednisolone she achieved a total response.

Keywords: Primary Non-Hodgkin's Lymphoma of Bone; Pathological Fracture; Chemotherapy

INTRODUCTION

Primary Lymphoma of The Bone (PLB) is a rare extranodal presentation of Non-Hodgkin's Lymphoma (NHL) Jacobs Kurosawa. It was first described by Oberling in 1928 [4,5]. It accounts for approximately 3% of the malignant bone neoplasms and is comprised of less than 5% of all extranodal non-Hodgkin's lymphomas. An osseous involvement of a lymphoma is generally seen as a part of a multi-system dissemination. Primary lymphoma of the bone can be defined as a lymphoma which occurs in the bone without any evidence of a distal nodal or an extra-nodal tissue involvement [5,6]. PLB can involve any part of the skeleton, but a trend exists in favour of the bones with persistent bone marrow. The femur is the most common site and it is affected in 29% of the cases. The other sites include the pelvis, humerus, head and neck, and the tibia [4-7]. The clinical presentation depends upon the rate of the tumor cell proliferation and the initial localisation. The patients generally present with localized bone pain, and less frequently, with a soft-tissue swelling or a palpable mass. On conventional radiology, PLB has a widely variable imaging manifestations which consists of either „lytic destructive pattern“ or a „blastic sclerotic pattern“ [8]. Pathological fractures may be present in approximately one quarter of the cases, as were seen in our patients.

Diagnostic testing typically include: Complete Blood Cell Count (CBC); peripheral blood smear; routine serum chemistries; serum Lactate Dehydrogenase (LDH) level; bone marrow aspirate and biopsy; bone biopsy; chest radiography; plain films; bone scan; Computed Tomography (CT) scanning; Magnetic Resonance Imaging (MRI). When detectable, primary NHL of bone can have a heterogeneous appearance with lytic, blastic, and mixed lesions reported [6,9,10]. Additional imaging features include periosteal reaction, soft-tissue extension, pathologic fracture, and cord compression [6]. The radiologic differential diagnosis includes benign (reactive conditions, osteomyelitis) and malignant entities (Hodgkin lymphoma, sarcoma, neuroblastoma, metastatic disease).

MATERIALS AND METHODS

A 56-year old female patient presented in December 2013. with pain in the chest, thoracic spine, epigastric and right scapular region for one month duration. Clinically, the patient had history of 3 kg weight loss and fatigue. On examination, she was found to be hypertensive (160/90 mmHg) and had no palpable hepatosplenomegaly or lymphadenopathy. In past the patient had arterial hypertension, she takes no therapy. In 2009. The patient underwent gastroenterologist examination: Ezophagogastrosocopy showed a moderate gastroesophageal reflux into the distal oesophagus, with hyperemic, vulnerable mucosa. Diagnosis: Sy Gerd gr 2. EKG: QS in V1-V3.

Antihypertensive and analgetic therapy was ordered and the difficulties have been reduced. After twenty days the patient was examined by Neurologist because of the sudden pain in the thoracic spine which spreaded into the sternal region and in the right leg as well. She uses anti-pain drugs, but with no improvement. Neurologically, there were signs of hypoesthesia in the L4, L5 dermatoma on the right. Lasegue test terminally positive [Figure 1].

The MR of the thoracic and LS spine was recommended.

Leukocytes: 4,80. (Ref. 3,40-9,70); Haemoglobine (g/L): 135, (Ref. 119-157), Trombocytes(10e9/L): 227 (Ref. 6,80-10,40): CRP (mg/L) 14,48 (0,00-5,00), Alkal-phosphatase (U/L) 124 (64-153): Troponine (ng/ml) > 0,01 (Ref. 0,000-0,100): Amilase (U/L) 345 (Ref. <400).

X Ray of the thoracic spine: less calcified body and arches of thoracic spine, with subchondral osteosclerosis surface plate with signs of partial degenerative spondylitis. The height of the thoracic spine corpus was normal. Intervertebral space between TH 7 - 8 was slightly reduced.

The chest radiograph and the ultrasound of the abdomen were normal as was her full blood count and biochemical profiles.

Gynaecological examination, esophagogastrosocopy and colonoscopy, MMg, ophthalmological, dermatological examination were negative.

The patient was immobilised with Jewett orthosis.

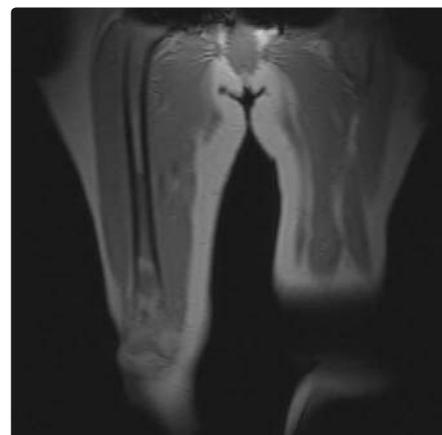


Figure 1: Coronal T1-weighted image reveals few low signal lesions in the marrow of the mid and distal right femoral shaft which contrasts with areas of high signal intensity of normal marrow fat.

One month after the initial examination by Internal medicine specialist and two months of the duration of pain, the patient was reported to our Orthopedic and traumatology department with a pathological fracture of the TH 5 and L 2 spine corps, proved with MRI diagnostics.

Ca (mmol/L) 2,39, Ca-dU (mmol/L) 6,1.

Computerised tomography (CT) scan of the right femur showed small lytic destructions of bone corticalis 10 cm of length in the mid-shaft of the right femur. There were no signs of bone compacta destruction or bone expansion. Pathologic substrate which infiltrated medullary narrow was also presented. According the radiomorphological characteristics, differential diagnostically the femoral lesion points on low-grade chondrosarcoma.

MRI findings revealed a large expandible lytic infiltrative lesion of the medullary canale with very discrete diffuse bone compacta destruction at the level of the mid and distal shaft of the right femur, for 16 cm of craniocaudale diameter was recorded. There was absence of bone corticalis lytic lesion. There were no pathological findings of extraosseal soft tissue or periosteal reaction. Radiomorphological characteristic were suggestive of metastasis or an osteogenic tumor.

The first biopsy of the vertebral body showed no signs of tumor tissue. The new intramedullary biopsy of the right femur was performed after seven days: the seven samples were positive on vimentine and LCA, negative on pancreatokeratine, S-100 and CD 3. Histologically examination showed diffuse large B-cell NHL (high gradus).

The biopsy report was suggestive of a lymphoproliferative disorder which involved the bone.

The tissue was sent for a histopathological examination. The final pathological diagnosis was a primary lymphoma-NHL, diffuse large B-cell type (non-GC subtype) of the shaft of the femur.

Imunohistochemically the cells were positive for CD20+, BCL6+, BCL2+,CD10 focal+(less than 30% cells), MUM1+, CD5-, CD3-, EBV-LMP1-. Clinical stady IV E [Figure 2].

The patient recived chemotherapy which consisted cyclophosphamide, adriamycin, vincristine, and prednisone (CHOP).

Total body scintigraphy was performed with 99m-Tc MBq 740. After 12 months of the diagnosis, there has been no relapse either clinically or radiologically.

Two month after the initial examination, the patient suffered pain in the right femur. She denides pain at the spine. She was verticalised with Jewett orthosis and walker. The primary tumor site was not founded.

A three months after the final diagnosis, the treatment with chemotherapy is performed: 4+4 cyclus.

She achieved a partial response with rituximab together with cyclophosphamide, vincristine, procarbazine and prednisolone.

Three years after the first symptoms and initial examination the patient still suffered cervical and lumbal spine pain with rare cases of vertigo. She used cervical collar, Jewett orthosis and analgetics.

PET-CT didnt recognised any signs of malignant disease or metabolic activity. The conclusion: the remission of disease has been achieved [Figure 3].

DISCUSSION

Most cases of primary lymphomas of the bone are the NHL type and the Diffuse Large B-Cell Lymphoma (DLBCL) subtype. Primary NHL of the bone (primary bone lymphoma) is a rare condition, accounting for less than 1-2 % of adult NHL, and less than 7-10 % primary bone tumors [1,2]. The majority of the cases are limited disease by the Ann-Arbour staging system and occurs in adults of age 45-50 and it shows a male preponderance with a male to female ratio of 3:2. [4, 8-13].

Primary Lymphoma Of Bone (PLB) accounts for 3% to 7% of primary neoplasms of bone and must be distinguished from more common bone tumors in the pediatric population such as osteosarcoma, Ewing sarcoma, and other small round blue cell tumors. In this study, pathology databases from 4 institutions were queried for PLB in individuals 1 to 21 years old [14].

The femur (29%) is the most common site, followed by the pelvis (19%), humerus (13%), skull (11%) and the tibia (10%) [15].

Some series have found that the long bones and the flat bones are equally affected [12].

The clinical presentation includes local pain, swelling and a pathological fracture. The diagnosis is established by biopsy. CT scan of the abdomen and the chest to assess the lymph node involvement and serum LDH estimation are done as a part of the staging procedure. [16].



Figure 2: Sagittal T1 –weighted image reveals few low signal lesions in the marrow of the mid and distal femoral shaft without extraosseal soft tissue mass or periosteal reaction.

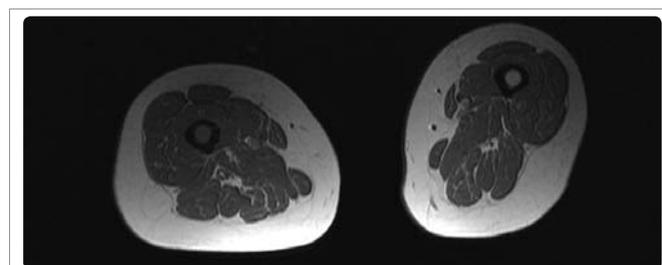


Figure 3: Axial T1-weighted image shows low signal intensity lesion intramedullary in the right femoral shaft. The lesion is confined within the marrow of the affected side.

The most common pathology subtype is diffuse large B-cell lymphoma [12,16].

A pathological fracture of the long bones, which are secondary to the soft-tissue tumors had been well documented in the literature: lymphomas which present primarily at these sites with pathological fractures are unusual.

The most common pattern „the lytic destructive pattern“ , presented as permeative, moth-eaten or focal lyses with well-defined margins is reported in 70% of the cases [8] [Figure 4].

Pathological fracture in bone lymphoma is uncommon. In a large series of 131 patients with primary bone lymphoma over 22-year period, one third had lymphoma involvement of the long bones with pathological fracture occurring in nine patients [12]. In contrast, in a retrospective analysis of 36 patients with primary (n=17) and secondary (n=19) bone lymphoma surgically treated at an orthopaedic center over a 15-year period, pathological fracture of the proximal femur of humerus was observed in three patients only [5]. Our patient illustrated pathological fracture secondary to lymphoma involvement of the femur, which is uncommon even in patients with lymphoma involvement of the long bones.

In a study of sixteen patients with primary NHL in the vertebrae of the spine, who were treated between 1994 and 2006 (10) 5 of them had radicular pain. Our patient had also radicular pain, but no motor signs of neurological deficit [18] [Figure 5 a,b].

The overall 5-year survival rate is 49.6%, with a 10-year survival rate of 30.2%. Median overall survival is 4.9 years (95% CI: 3.9, 6.1). In multivariable analysis, age ($p < 0.0001$), marital status ($p = 0.006$), and appendicular vs. axial tumor location ($p = 0.004$) is found to be independent predictors of survival [19].

Anaemia, elevated lactate dehydrogenase (LDH), Alkaline Phosphatase (ALP), Erythrocyte Sedimentation Rates (ESRs), platelet counts, and calcium levels have been reported with primary non-Hodgkin lymphoma of bone [6,11].

Our patients has no elevated laboratory tests values [Figure 6].

The treatment for primary NHL of bone includes chemotherapy, the optimal sequence of treatment is CHOP-R 8 (Cyclophosphamide, doxorubicin, vincristine, prednisolone, rituximab) regimen [4,11-13,17]. As necessary, stabilisation of a pathologic fracture will occur before the initiation of other therapies [6,12].

The patient received chemotherapy which consisted cyclophosphamide, adriamycin, vincristine, and prednisone (CHOP). After 12 months of the diagnosis, there has been no relapse either clinically or radiologically [Figure 7]. Here presented case agreed with

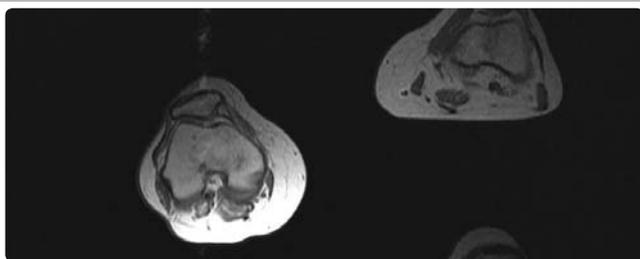


Figure 4: Axial T1-weighted image reveals some focal low intensity signals in distal femoral part in the affected side.

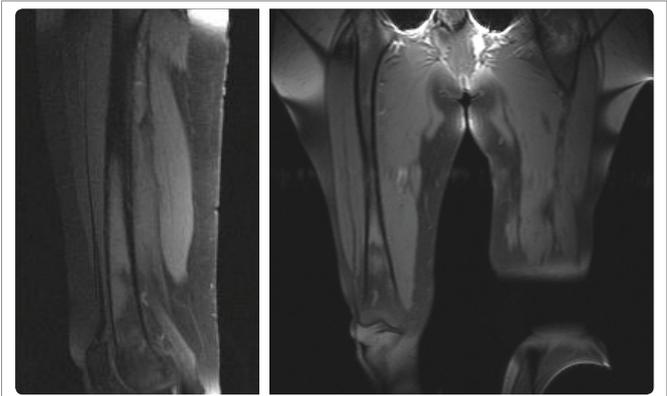


Figure 5a,b: Sagittal T2 FS (a) and coronal T2 FS (b) images show high signal intensity of the lesions in central and distal part of the femur and linear abnormalities within the cortical bone in the mid part of the femoral shaft.

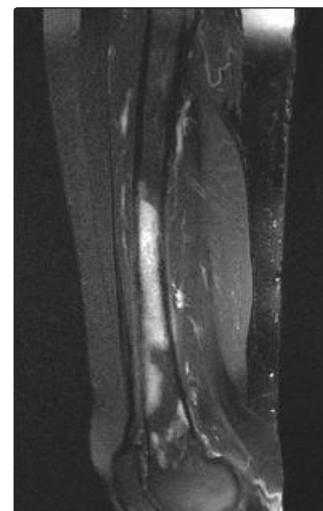


Figure 6: STIR T2-weighted sagittal image shows high signal intensity of the lesions in central and distal part of the femur.

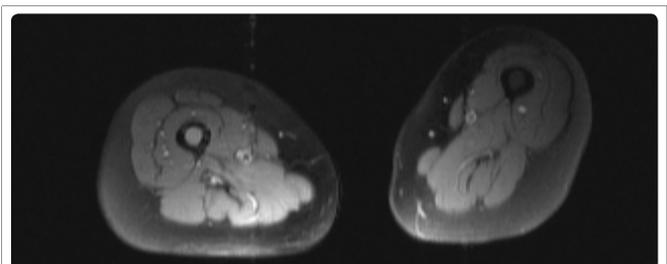


Figure 7: STIR T2 weighted image shows high intensity signal of the intramedullary lesion in the femoral shaft in the affected side with discrete linear abnormalities within the cortical bone.

the literature on primary bone lymphoma, in which the diagnostic problem and an excellent prognosis of a malignant tumor have been emphasized [15].

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