MULTICENTRIC BONE INVOLVEMENT AND COMPLETE RESPONSE TO CHEMOTHERAPY: A CASE REPORT

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ABSTRACT

***Introduction**: Primary lymphoma of the bone (PLB) is a rare clinicopathological disease. PLB accounts for approximately 3% of all malignant tumors. It frequently affects the femur and pelvis, and the spine is affected only in 1.7% of all cases. Because it is a rare disease, the optimal treatment strategy has not yet been established.*

***Case presentation**: We present a case of a 36-year-old male who had complaints of back pain, leg pain and fatigue that did not affect his daily tasks. The positron emission tomography (PET) also showed multifocal lesions of bones. An excisional biopsy of osteolytic lesions in the left scapula revealed diffuse large B-cell Non-Hodgkin Lymphoma. Chemotherapy was administered and complete response was observed.*

***Conclusion**: Multifocal PLB is an exceptional situation. The diagnosis is challenging because of the low incidence and unspecific radiological features. Studies should be carried out to identify the optimal treatment in the future. Here, we want to emphasize the complete response with chemotherapy of a multicentric involvement primary bone lymphoma.*

***Key words**: Non-Hodgkin Lymphoma, multicentric involvement, diffuse large B-cell lymphoma.*
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Introduction

Primary lymphoma of bone (PLB) is defined as lymphoma localized to the bone not involving any lymph nodes or any other tissues at diagnosis[1]. Bone involvement is common complication in advanced stage lymphomas, but PLB is a rare disease, accounting for approximately 3% of malignant bone tumors, less than 2% of all lymphomas and less than 5% of all extra nodal lymphomas in adults[1-3]. Diffuse large B-cell lymphoma is the most common pathological type and represents over 80% of primary lymphomas of the bone[4]. The most common localizations for PLB are reported to be the femur or the pelvis (50%), the long bones of the upper limbs (20%) and in other sites (30%) such as the ribs, mandible or scapula[5].

According to the World Health Organization (WHO) classification, lymphoma involving bone had been separated into four groups; 1) single skeletal site (regional lymph node involvement present or not); 2) multiple-bone involvement without visceral or lymph node involvement; 3) bone lesion with involvement of visceral sites or multiple lymph nodes at multiple sites; and 4) patient with known lymphoma and bone biopsy confirms involvement of bone. Groups 1 and 2 are considered primary lymphoma of the bone[4].

Case presentation

We report a case of 36-year-old male who complained of back and leg pain with fatigue that does not affect his daily tasks for several months.

The patient had fever and night sweats. Medical or surgical history was unremarkable. He had 15-year smoking history and no alcohol usage. On clinical examination, a bad oral hygiene, absent teeth and dental caries were observed. Skin and conjunctivas were pale. Bilateral respiratory sounds were rugged and expiratory rhonchi were present. There was no evidence for lymphadenopathy or other mass lesions.

Computerized tomography showed decreased density consistent with osteoporosis in all bone structures and heterogeneous hypodense lytic images were shown causing cortical irregularity in superior-posterior part of the left scapula. A thoracolumbar magnetic resonance imaging (MRI) revealed an infiltrating mass spreading from left scapula. There were also pathologic findings on bilateral humeruses and left lower thoracic vertebra. Positron emission tomography (PET) also showed multifocal sites (Figure 1).

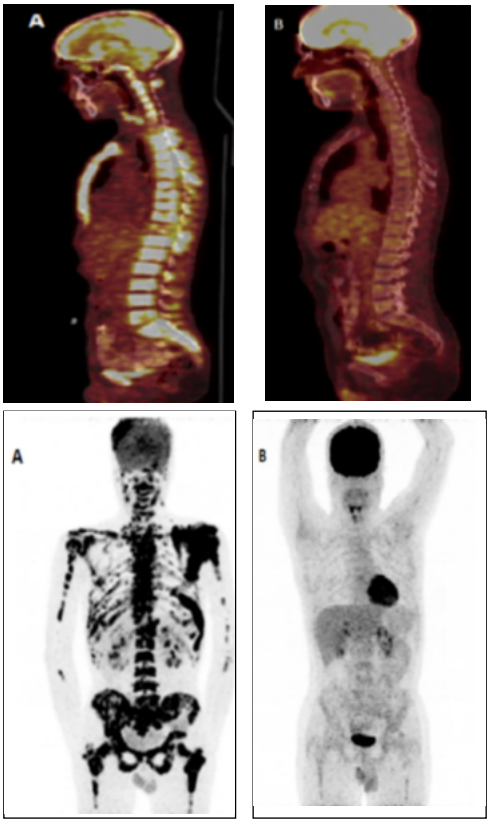

Figure 1: Maximal-intensity projection images obtained with 18F-FDG1 PET/CT2. The abnormally high uptake of 18F-FDG1 in the skeletal system of the patient was seen in figure 1/A. After six cycles of chemotherapy, there was no uptake of 18F-FDG1 in the skeletal system of the patient as seen in figure 1/B.

1: Fluorodeoxyglucose

2: Positron emission tomography/computerized tomgraphy

Laboratory investigations demonstrated a hemoglobin level of 7.2 g/dL [13.6-17.2 g/dL] , a hematocrit level of 22% [39.5-50.3%], an LDH level of 2521 U/L [1-247 U/L], and a uric acid level of 6.2 mg/dL [3.5-7.5 mg/dL]. Before bone marrow aspiration, an orthopedic excisional biopsy for diagnosis was performed. The procedure was performed without complications. The pathology exam revealed a diffuse large B-cell lymphoma. According to the clinical manifestation and pathological results, the diagnosis was established to be stage IV diffuse large B-cell lymphoma. We gave six cycles of chemotherapy of rituximab, doxorubicin, cyclophosphamide, vincristine and prednisolone (R-CHOP). Complete response was obtained in our patient.

Discussion

With this report, we recognized a rare PLB presenting with back pain and fatigue. He gave similar history and symptoms of Non-Hodgkin Lymphoma (NHL), but results showed that he had only multiple bone involvement without regional lymph node metastases.

PLB was first defined in 1939 by Parker and Jackson and it was named as 'Primary reticulum cell sarcoma of bone'[7]. Later in 1950, Coley et al[6] suggested that definition of PLB should be as 'a tumor presenting in an osseous site and involving bone marrow with metastases only to regional lymph nodes or with no evidence of disease elsewhere for at least six months after diagnosis'. In primary multifocal osseous lymphoma (PMOL), multi-focal bones are affected and there is no evidence of visceral or distant nodal disease. In the WHO classification of neoplasms of the hematopoietic and lymphoid tissues published in 2001 and updated in 2008, PBL is recognized as an independent disease[7]. The diagnoses criteria of PLB are regarded as primary involvement site of the bone, no evidence of extra bone lesion according to the clinical and radiographic examination, no evidence of any other extra bone lesion six months after bone lesion is diagnosed; the diagnosis is confirmed by both pathological morphology and immunohistochemistry[4].

It accounts for approximately 5% of all NHL and 3% of all primary bone tumors[8]. It is a rare disease and for this reason modalities of diagnosis, management and prognosis remain controversial. The most common histopathological type is the dif-

fuse large-B cell lymphoma which accounts for about 80% of PLBs[3,8,9].

PLB occurs in a broad range of patients, aged from 18 months to 86 years[10], median age at diagnosis ranges from mid 40s to mid-60s (generally aged over 30 years) with a peak incidence at fifth to sixth decades[11,12,13]. Disease is slightly more common in males. Published series slightly differ in the most common location for PBL, but although any bone can be involved, the most reported sites are femur and pelvis, followed by other long bones in upper extremities[1,2,8]. Primary vertebral location is very uncommon, usually arising from the thoracic and lumbar spine[2,14]. Involvement of more than one bone is seen in approximately 10 to 40% of cases[15].

The most frequent symptoms of PLB are bone pain, a palpable mass or both[1,8]. Back pain becomes the most common symptom when the spine is affected. Systemic 'B' symptoms such as fever, night sweats or weight loss exceeding 10% of body weight six months prior to diagnosis are comparatively uncommon[1].

Differential diagnosis should be made with metastatic disease of the affected bone[2]. Difficulty in identifying such lesions may result in delayed diagnosis of the process[16]. When PLB is suspected, MRI is the preferred technique for the diagnosis. Areas of bone marrow replacement can be observed. Also the soft tissue extension and spine involvement can be evaluated[12,13,16]. The differential diagnosis should include diseases destructing bone such as lymphoma, plasmacytoma, metastases, myeloma and osteomyelitis[5,17]. Once the diagnosis is established; polyostotic, metastatic or regional lymphatic disease involvement should be discarded[18]. PET scan can accurately localize the lesions and may help staging of PLB[1].

In the past years, several chemotherapy regimens have been used and in 2001 the rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (RCHOP) was introduced. Today, standard treatment is based on systemic chemotherapy and local radiotherapy[3,13,18]. Five-year survival rates are ranging from 62% to 88%[1,3,8].

PLB has a favorable prognosis over patients of systemic lymphoma with bone involvement. Age is a prognostic factor. The majority of the reports indicate better survival for patients younger than 60 years and a few others show better survival in patients younger than 40 or 50 years[11]. Jawad et al. analyzed 1,500 adult patients with PBL, and pointed out that younger age and localized disease were independent predictors of survival[19].

In conclusion, PLB is a very rare disease and multicentric involvement is a much rarer situation. Because of these reasons, the optimal treatment options are not clear. In this case, we presented a primary bone lymphoma with multicentric involvement who had a complete response with chemotherapy. Future treatments will be dependent on strict staging criteria and successful protocols. Further studies are needed to establish the standard strategy for PLB.

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