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Rare Multifocal Primary Bone Lymphoma in a Young Male: A Case Report

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Abstract

Primary bone lymphoma (PBL) is a rare form of bone malignancy that usually presents as localized bone pain at one or multiple sites. Due to its vague clinical presentation, at times without overt swelling or palpable mass, diagnosis can often be delayed. We present a case of a young male patient who presented with unilateral thigh and shoulder pain initially thought to be musculoskeletal pain; however, later found to be PBL. This otherwise healthy patient was subsequently diagnosed after a dental visit to have a mandibular mass consistent with PBL on biopsy. This case illustrates the difficulty with diagnosing PBL, as the clinical presentation can mimic other diagnoses, such as dental and musculoskeletal concerns, such as in our patient, leading to a delay in diagnosis and treatment.

Categories: Hematology, Oncology, Internal Medicine
Keywords: diffuse large b cell lymphoma (dlbcl), hip pain, mandibular lesion, primary bone lymphoma, r-chop therapy

Introduction

Primary bone lymphoma (PBL) is a rare primary bone malignancy that arises within bone and typically lacks lymph node involvement; it can affect one bone or multiple skeletal sites. It represents fewer than 5% of all primary bone cancers, 4-5% of all extranodal lymphomas, and accounts for under 1% of all non-Hodgkin lymphomas (NHL) [1,2]. Diffuse large B-cell lymphoma (DLBCL) is the predominant histologic subtype, comprising approximately 80% of cases, followed by follicular lymphoma, while other subtypes are exceedingly uncommon [3]. According to the 2020 World Health Organization (WHO) classification of soft tissue and bone tumors, PBL is a type of NHL that produces one or more lesions within bone with no regional lymph node or extranodal involvement [1]. While NHL can commonly have secondary skeletal system involvement as the disease progresses, primary skeletal involvement is extremely rare [2].

The most common presenting symptom of PBL is localized bone pain in the affected region, often accompanied by soft tissue swelling or a palpable mass. Although “B” symptoms may be present at diagnosis, they are usually not the initial presenting feature. Diagnosis is frequently delayed for several months because of nonspecific clinical manifestations and inconclusive imaging findings, with an average diagnostic delay of approximately eight months [4].

We describe a case presentation of a 23-year-old male patient who initially presented at his primary care clinic with left thigh pain and left shoulder pain initially thought to be musculoskeletal in etiology. He then visited his dentist for left jaw pain and was found to have a left mandibular mass diagnosed as PBL through biopsy. We highlight the insidious clinical presentation which mimics other diagnoses, leading to difficulty and delay in diagnosing PBL. We also explore diagnostic and treatment options, which if treated promptly can be highly successful, such as our patient who underwent chemotherapy and had successful remission of his PBL.

Case Presentation

A 23-year-old male patient with no significant previous medical history presented to his primary care clinic, endorsing left thigh pain for one week that comes and goes with exercise and intermittent left shoulder pain now resolved. He denied any trauma or injury.

Vital signs were unremarkable; the patient was afebrile and normotensive. Initial laboratory tests were within normal limits, as shown in Table *1*.

Laboratory test	Patient value	Reference range
White Blood Cell Count	4.5 K/cumm	4.5–10.0 K/cumm
Hemoglobin	14.4 g/dL	13.5–16.5 g/dL
Platelet Count	268 K/cumm	160–360 K/cumm

TABLE 1: Initial laboratory findings at presentation

Exam was unremarkable for any tenderness or mass in left groin or hip flexor area. The left shoulder had full passive and active range of motion, no tenderness upon palpation or notable swelling, as well as full, intact strength and sensation of his left upper extremity. Given the concern for possible muscular strain to his left thigh area, the patient was treated conservatively with topical diclofenac gel. At his one month follow-up phone visit, the patient stated that his left thigh pain was worsening and more constant. He was then referred to physical therapy for further treatment.

At this same visit, the patient also endorsed left lower facial swelling for six months. He had recently visited his dentist and was found to have a lesion in left mandibular area with recommendation for referral to oral maxillofacial surgery (OMFS) for further evaluation and management.

This patient was then referred and seen by OMFS with core needle biopsy done of 3 x 5 cm radiolucent lesion on the left side of the mandible, extending from tooth #20 to #27. Pathology of lesion showed aggressive diffuse large B cell lymphoma and he was referred to hematology/oncology (heme/onc) for further management (Figure *1*).

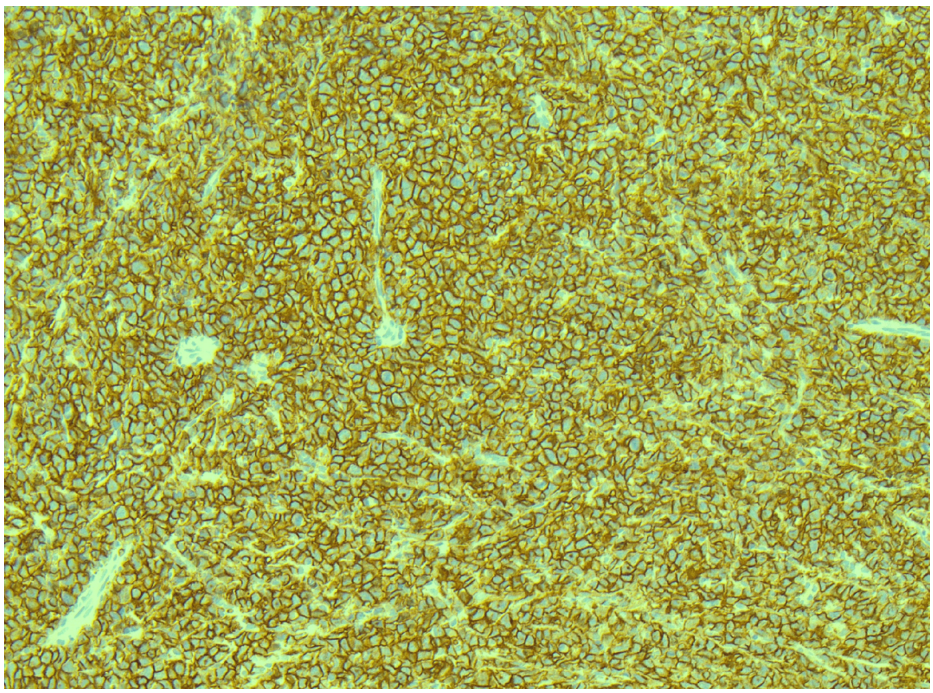


FIGURE 1: CD20 immunohistochemical staining of the mandibular lesion demonstrating diffuse positive expression

This was consistent with diffuse large B-cell lymphoma (DLBCL) of primary bone origin (10× magnification).

Further imaging with X-ray of left hip showed no acute fracture in pelvis or left hip. Expansile osteolytic lesion at left acetabulum was noted (Figure *2*).

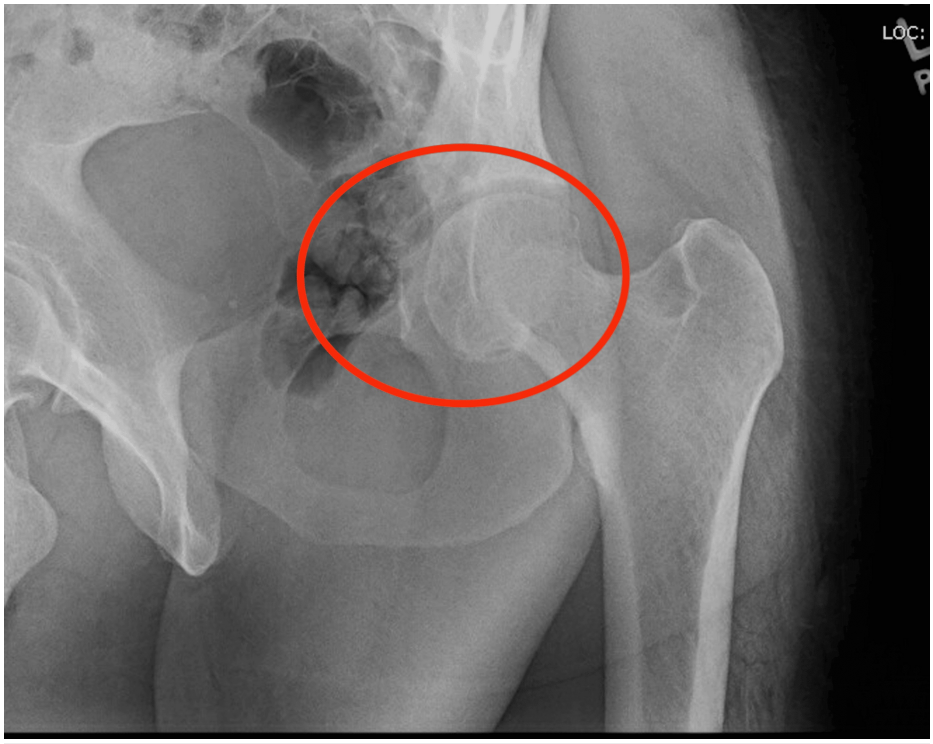


FIGURE 2: X-ray of left hip showing osteolytic lesion involving left acetabular roof and anterior column

Fluorodeoxyglucose (FDG) Positron Emission Tomography (PET)-CT scan showed osteolytic lesion of left side of mandible, left acetabulum with cortical breakthrough and left humeral head (Figure *3*).

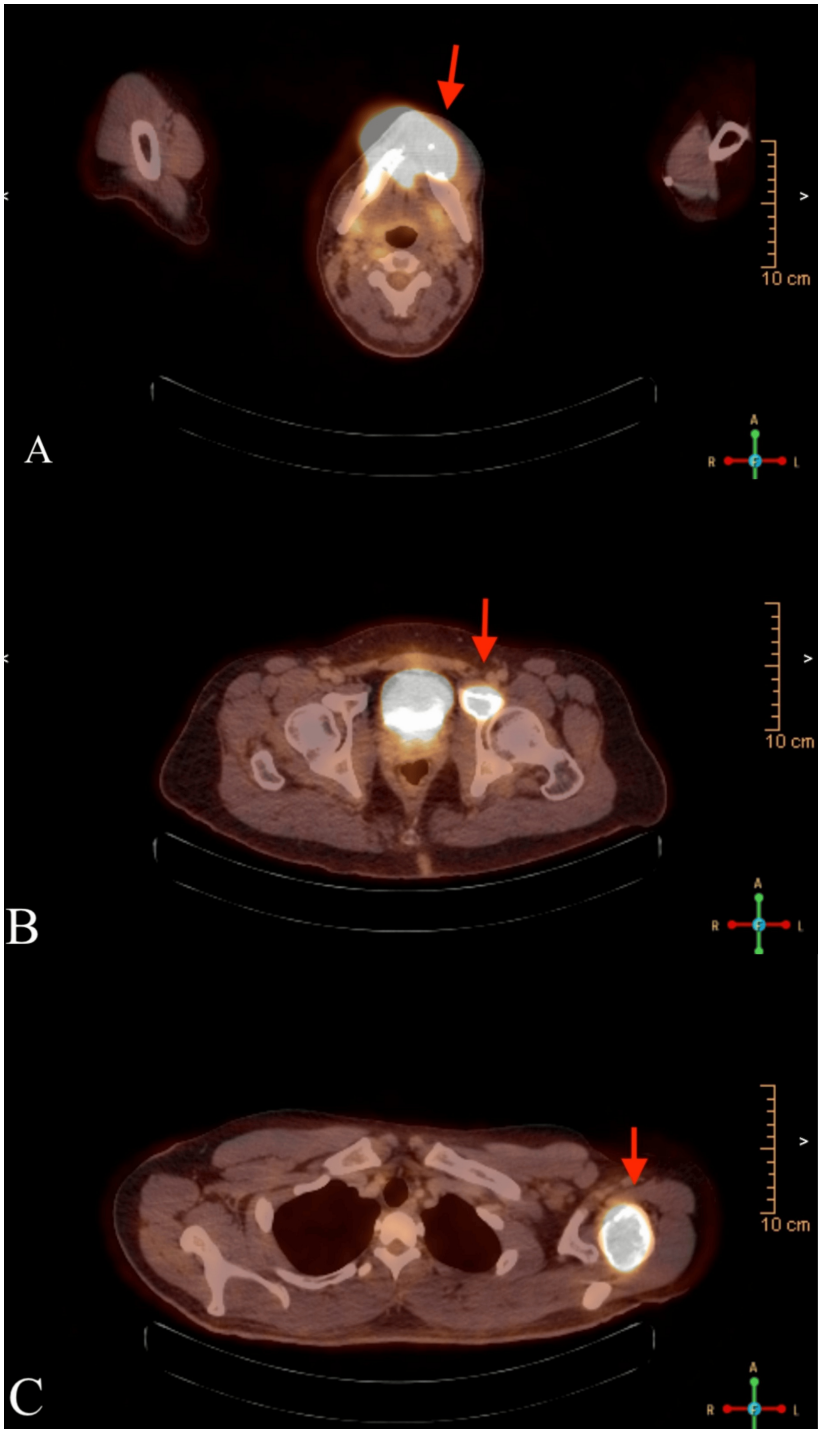


FIGURE 3: FDG PET-CT scan showing hypermetabolic osteolytic lesions

A. Left mandible B. Left acetabulum C. Left humeral head

FDG: Fluoroxdeoxyglucose, PET: Positron Emission Tomography

Per heme/onc, patient was diagnosed with primary bone DLBCL due to multiple bone involvement without lymphadenopathy. Initial lactate dehydrogenase (LDH) level was 165 U/L (reference range: 135-225 U/L). The patient underwent six cycles of Rituximab-Cyclophosphamide Hydroxydaunorubucin Oncovin Prednisone (R-CHOP) chemotherapy with remission. His left thigh pain resolved after the first cycle of chemotherapy; patient did not have any further jaw or shoulder pain on subsequent follow-up visits.

Discussion

PBL is one of the rarest primary bone malignancies and is a lymphoma that affects skeletal tissue. The most

common subtype is DLBCL, a type of NHL, which usually presents as a rapidly growing mass from one or more lymph nodes. Although NHL can affect bone with disease progression, primary involvement of skeletal tissue is very rare [2].

In a retrospective analysis by Liu et al. of over 2500 PBL patients from the Surveillance, Epidemiology, and End Results (SEER) cancer registry database from 1973 to 2016, the most commonly involved site was the vertebral column (30%), followed by long bones of the lower limb (23%) and upper limb (10%); mandibular involvement was rare, found in only 3.64% of cases [3]. Our patient presented with left acetabular involvement as well as a left mandibular lesion, with the former site more common than the latter. He also had left humeral involvement, although the patient was asymptomatic on initial presentation. The average age of those with PBL was a median of 50 years, with a similar predominance among men and women [3], although some other reports show a predominance in men [5]. Our patient was 23 years old at the time of diagnosis, which as per Liu et al., was in the age category of 20- 40 years, representing a small percentage (18.1% of total) of patients with PBL [3].

As per Liu et al., PBL generally has a favorable prognosis, with an overall five-year survival rate of 65% [3], better than systemic lymphoma with secondary bone involvement (44%) [6]. It is considered to have the most favorable prognosis of all malignant primary bone tumors. Overall survival prognosis depends on several factors, with age being one of the most important determinants. One report found that patients younger than 60 years had a five-year disease-free survival rate of 90%, compared with 62% in patients older than 60 years [5].

Poor prognostic factors include advanced disease stage according to the Ann Arbor classification, higher Eastern Cooperative Oncology Group (ECOG) performance score, elevated LDH levels, and International Prognostic Index (IPI) greater than one [4,5]. The IPI index includes age >60 years old, Ann Arbor Stage III or IV, elevated LDH, ECOG greater than one, and greater than one extranodal site of involvement [4]. In addition, lesions involving the axial skeleton rather than the appendicular or craniofacial bones, multifocal disease, and adjacent soft tissue involvement are associated with poorer survival outcomes [3,5]. Our patient had multiple factors for a favorable prognosis with being of younger age <60 years old, low ECOG status zero, normal LDH levels upon initial diagnosis, as well as appendicular and craniofacial involvement rather than axial involvement. However, he did also have a few unfavorable prognostic factors, including IPI index score of two due to being Ann Arbor Stage IV and having multiple extranodal sites of involvement.

The most common presenting symptom of primary bone lymphoma is localized bone pain in the affected region, often accompanied by soft tissue swelling or a palpable mass. The pain is typically persistent and not relieved by rest [4,5]. As the disease progresses, some patients may develop pathological fractures, although it occurs in less than 15-20% of patients [3]. In cases involving the spine, neurological symptoms may occur due to spinal cord compression [5]. Although “B” symptoms may be present at diagnosis, they are usually not the initial presenting feature [4].

Diagnosis is frequently delayed for several months because of nonspecific clinical manifestations and inconclusive imaging findings, with an average diagnostic delay of approximately eight months [5,7]. Our patient presented with localized jaw and thigh pain that progressed to become more persistent, without any B symptoms or pathological fractures. However, he had also intermittent, resolving pain in the left shoulder with an unremarkable exam, contributing to less clinical suspicion of a pathologic process. Diagnosis was delayed for months contributed by the vague insidious onset of symptoms without significant palpable findings on exam.

Plain radiographs are typically the first imaging modality used in the diagnostic workup, although findings may initially be normal or equivocal. When present, PBL often appears as a solitary lytic lesion with ill-defined, “moth-eaten” borders [5]. Associated findings may include adjacent soft tissue swelling, cortical breakthrough, pathological fractures or bony deformity secondary to tumor expansion [7]. When the jaw is affected, primary bone lymphoma can initially resemble dental pathology, such as symptoms of jaw swelling, regional tooth mobility and paresthesias, often delaying recognition until later in the disease course [1]. In our patient, an X-ray of left hip revealed an expansile osteolytic lesion at the left acetabulum suggesting that an X-ray can be a helpful and quick tool for aiding diagnosis.

Magnetic resonance imaging (MRI) and computed tomography (CT) provide detailed visualization of tumor-related destruction. MRI is particularly useful for demonstrating marrow infiltration and identifying involvement of adjacent regions or tissues, enabling earlier detection of PBL. CT is commonly used for staging both before and after treatment, as well as for ongoing surveillance. It can show soft tissue extension, bone marrow involvement and cortical disruption. Positron Emission Tomography (PET)/CT is generally the imaging modality of choice for excluding secondary bone lymphoma, and for staging, follow-up and treatment response of PBL [5]. Our patient’s PET-CT scan assisted in ruling out secondary bone lymphoma and showed no lymph node involvement, which helped in assessing the final staging.

Bone biopsy, through fine-needle, core-needle or open biopsy, remains the gold standard for diagnosing

PBL. Careful collection of tissue or bone is essential to ensure sufficient material for diagnostic testing due to tissue necrosis while also avoiding the risk of pathological fractures [5]. In our patient, the core needle biopsy of the mandibular bone obtained sufficient tissue specimen to make the definitive diagnosis of PBL.

The current preferred treatment for PBL is with the chemotherapy regimen of R-CHOP usually for six to eight cycles [5]. Radiotherapy is not recommended as a single therapy because several studies have reported a relapse rate of at least 50%. The benefit of adding radiotherapy to chemotherapy remains uncertain [7,8]. Surgical management is reserved for patients presenting with neurological complications and/or fractures; otherwise, it is not considered necessary for the treatment of PBL [4]. It is primarily used for the biopsy, fixation, and stabilization of bone lesions [3,7]. This patient achieved remission with six cycles of R-CHOP without additional radiotherapy or requiring surgical treatment.

Conclusions

We present the case of a young, otherwise healthy male patient who initially presented with left thigh and shoulder pain diagnosed as musculoskeletal strain, and a mandibular mass concerning for a dental lesion, which was confirmed on mandibular core biopsy to be PBL. Subsequent imaging, including X-ray and PET-CT scan, revealed osteolytic lesions of the left acetabulum, humeral head, and mandible, characteristic of PBL findings. This case highlights the difficulty of diagnosis given vague, insidious symptoms, such as localized pain without B symptoms or palpable physical exam findings, which can lead to a delay in diagnosis for months. It is important to consider imaging to help attain the diagnosis, especially when symptoms become more severe or constant, which could result in a sooner diagnosis. Untreated PBL can lead to greater bony involvement, pathological fractures, and poorer prognosis due to advanced staging. When treated quickly, patients can achieve favorable outcomes and high five-year survival rates and remission with six to eight cycles of R-CHOP chemotherapy.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Jennifer J. Price, Dieu-Thu Nguyen

Acquisition, analysis, or interpretation of data: Jennifer J. Price, Dieu-Thu Nguyen

Drafting of the manuscript: Jennifer J. Price, Dieu-Thu Nguyen

Critical review of the manuscript for important intellectual content: Jennifer J. Price, Dieu-Thu Nguyen

Disclosures

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