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Case Report
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A Rare Manifestation of Primary Bony Non-Hodgkin's Lymphoma of the Hand: A Case Report and Literature Review

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Abstract

Background: Primary bone non-Hodgkin's B-cell lymphoma is an extremely rare especially in the hand and only four cases with Diffuse Large B-Cell Lymphoma (DLBCL) of the hand have been reported in the worldwide.

Case Report: We describe an additional case of 89-year old man with primary DLBCL of the hand with characteristic pathological fracture of the metacarpal bone of the thumb without Rheumatoid Arthritis (RA), autoimmune disease or Methotrexate (MTX) treatment and underwent the ORIF with K-wires implants with chemotherapy.

Conclusion: The preoperative diagnosis for DLBCL is very difficult. Orthopedic surgeons should be acquainted with the differential diagnosis of primary bony lymphoma. The definite diagnosis is based on histopathological with Immunohistochemical (IHC) study and imaging examination, in which other disease lesions should be excluded.

Keywords: Non-Hodgkin's lymphoma (NHL); Rheumatoid arthritis (RA); Diffuse large-B-cell lymphoma (DLBCL); Metacarpal; Immunohistochemical (IHC)

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Introduction

Primary Bone Lymphoma (PBL) is a rare type of peculiar extra nodal presentation of Non-Hodgkin's Lymphoma (NHL) and distinct histopathological entity of Malignant Lymphoma (ML) originate in bone. PBL accounts for 3% of malignant bone tumors and for only 1% of all types of NHLs [1-5]. The most common histological type of NHL is the B-cell lymphoma accounting for 80% to 90% of all cases with 30% being DLBCLs. Primary bone NHL of the hand is an extremely rare entity. Up to date and review the literature, only four cases have been reported in the English literature. We herein report an additional case with PBL-DLBCL rare manifestation of pathological fracture clinically of the metacarpal bone of the left thumb and review the pertinent literature.

Case Presentation

An 89-year-old man visited at our Emergent Department with complaining of swollen and severely painful after taking heavy goods in his left hand for 2 weeks. He was admitted with vital signs showed stable. He had hypertensive cardiovascular disease and left distal femoral bone fracture post-total hip arthroplasty for years. No history of Rheumatoid Arthritis (RA), autoimmune disorders or Methotrexate (MTX) treatment mentioned. Physical examination, his left hand revealed marked painful swelling, local tenderness, instability and deformity with range of motion limitations of the thumb. There were no lymphadenopathy and palpable mass. The laboratory evaluation, immunologic and serological findings showed within normal reference ranges. The chest X-ray revealed tortuosity of thoracic aorta with calcifications, borderline cardiomegaly and prominent hila with interstitial change of both lower lung fields, no evidence of bone destruction or malignancy change. The initial plain X-ray of the left hand showed soft tissue swelling and displayed the permeated type bone destruction with pathologic fracture of the metacarpal bone of the left thumb (Figure 1A), and degenerative joint disease of left hand also found. The Computed Tomography (CT) scan image of the left hand revealed marrow replacement and cortical destruction (Figure 1B).

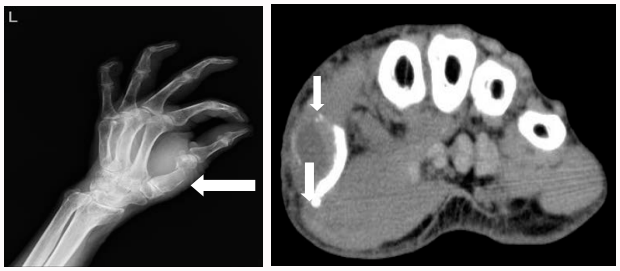

Figure 1: The plain radiography of left hand (A) shows soft tissue swelling, permeated bone destruction and pathologic fracture of the 1st proximal phalange (white arrow). The CT-scan image of the left hand (B) shows marrow replacement and cortical destruction of the 1st proximal phalange (white arrow).

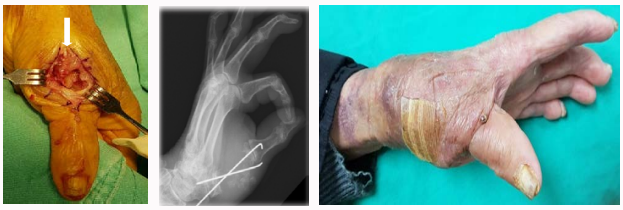

Figure 2: Photographs of the intraoperative findings (A) demonstrate malignant tumor invasion (white arrow) with pathological fracture of the left metatarsal bone of the thumb and the ORIF with K-wires implants (B) was performed. The post-operative ten days displays stable wound healing and well preserved functions of the left thumb (C).

He underwent the Open Reduction Internal Fixation (ORIF) with tumor excision with K-wires implants and bone graft (Figure 2A and 2B). The operative procedure was smooth. The stable wound healing condition after surgery and well preserved thumb anatomic functions with no complications noted (Figure 2C).

Histopathological findings

Microscopically, the excisional biopsied soft tissue and bony fragments composed of accumulation of Malignant Lymphoma (ML) cells with diffuse large B-cell type (Figure 3A and 3B). Immunohistochemical (IHC) study, tumor cells demonstrated diffusely strongly positive immunoreactivity for CD45 antigen (leukocyte common antigen) (Figure 3C), and increase positive immunostaining for Ki-67 (Figure 3D) labeling proliferating index with 70% of involved tumor cells, and diffusely strongly positive for CD20 and Bcl-2 (Figure 3E and 3F). However, lymphoma cells illustrated negative immunostaining for pan-CK, EMA, CD3, CD99, CD138, S-100 protein, NSE, TTF1, chromogranin-A, calretinin, vimentin, actin, and desmin. Taken together, based on the histopathological examination and IHC methods confirmed a diagnosis of primary bony NHL with DLBCL of the hand. The bone marrow aspiration biopsy surveillance revealed free for lymphoma cell involvement. Consequently, followed by standard chemotherapy regimen for DLBCL consisting of the courses with R-CHOP (rituximab; cyclophosphamide, doxorubicin, vincristine, and prednisone) on scheduled. The subsequently whole body bone scan images demonstrated distant multiple spinal, ribs and tarsal bone metastases. Unfortunately, he was expired with obstinate duodenal ulcer with bleeding and progressive complicated systemic multi-drug resistance bacterial infectious sepsis four months after surgery.

Discussion

PBL is a rare disease and distinct clinicopathological entity.

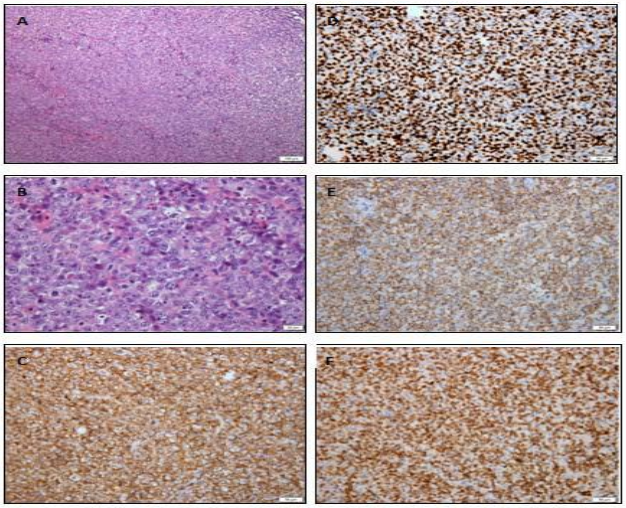

Figure 3: Photographs of the histopathological sections of the DLBCL of left thumb. The Hematoxylin and Eosin (H&E) show diffusely monotonous lymphoma cells (A, H&E, original magnification x10) and diffuse large lymphocytes infiltration (B, H&E, original magnification x40). The malignant lymphoma immunophenotype with IHC stains show diffuse strongly positive staining for CD45 (C, original magnification x20), increase positive staining for Ki-67 (D, original magnification x20), diffuse positive for CD20 (E, original magnification x20) and positive for Bcl-2 (F, original magnification x20).

Primary osseous Hodgkin's Lymphoma (HL) is a very actually uncommon tumor. The majority of PBLs are NHL, and the most common subtype is DLBCL. PBL can involve the skeletal system or as a manifestations of system disease [1,6-8]. PBLs are classed as Non-Hodgkin's Lymphoma (NHL) is the most common type, but in rare cases of osseous Hodgkin's lymphoma also identified. Primary bone NHL of the hand is relatively rare entity. Diagnosis of PBL should be identified on the combined clinical and imaging examinations, and is actually confirmed histopathological with IHC study. Because PBL is relative uncommon malignant bone tumor, the pre-operative diagnosis is very difficult. Primary bone NHL of the hand is an extremely rare histopathological entity. Up to date and review the literature, only four cases have been reported in the literature [2-5]. Here, we illustrate an additional rare case of primary bone DLBCL involving the metacarpal bone of the left thumb. Simultaneously, clinical, imaging, management and histopathological with IHC examination, and related literature also reviewed. PBL occurs in a wide spectrum of patients, aged from 1 year and 6 months to 86 years [1-6,8]. The peak age of cases diagnosed with PBL is 50-60 year of age group and is mild predominant in men than in women [8-10]. The most frequent involved sites in PBL include the axial skeleton, pelvis, femur, humerus, skull and neck, rib and the tibia [5,11-13]. The majority of cases with PBL are diagnosed initially with a single localized lesion involvement. Primary bone DLBCL of the hand is an extremely rare entity. Patients with DLBCL usually are characterized by localized bone pain, limitation of movement, soft tissue swelling, and or possibly a palpable mass in the involved site, or pathologic fracture developed. In recent investigations, primary DLBCL of the hand is the most common histopathological type [2-5]. In retrospective study and reviewing the literature, only four cases have been described in the English registered literature (Table 1). In these of three cases were patients with RA treatment with MTX [2-5], and in one case diagnosed with a needle biopsy for Epstein-Barr virus showed positive [4], and one case with no RA [5] similar as

Table 1: Summary of cases with primary bone DLBCL of the hand in the literature reported.

No. / Ref.	Sex/Age (years)	Clinical manifestation	Tumor bone	location/affected Relative characteristics	Follow-up period and outcome
Case 1. Birlik et al. [2]	F/69	Several multiple pain and swelling	joints Right hand, 4th (ring) finger	Mimics RA, septic arthritis, osteomyelitis with treatment	Unknown
Case 2. Kennedy et al. [3]	M/64	Progressive pain with palpable mass	left Right hand, 4th (ring) finger	RA with treatment	MTX NED after 6 years follow up
Case 3. Gordons et al. [4]	F/77	Progressive enlarged mass Mild swelling, painless	Left hand, 2nd metacarpal bone	EBER-positive	NED after 5.5 years follow up
Case 4. Galati et al. [5]	F/77	crepitation and instability Pathological fracture	Right hand, little finger	Nil	NED after 6 months follow-up
Present Case	M/89	Swelling and painful	Left hand, thumb, metatarsal bone	Nil	Expired after 4 months follow-up

DLBCL: Diffuse Large B-Cell Lymphoma; Ref: Reference, No.: Number; RA: Rheumatoid Arthritis; MCP: Metacarpophalangeal; EBER: Epstein-Barr Virus (EBV) -Encoded Small RNA; MTX: Methotrexate; NED: No Evidence of Disease

our present case. Birlik et al. [2] reported the first case of a 69-year-old woman with mimicking RA demonstrated direct synovial involvement of the right fourth finger joint with NHL presenting with polyarthritis. The second case, Kennedy et al. [3] presented a 64-year-old man with an 18-year history of RA that was treated with MTX. Unfortunately, a DLBCL presenting as a mass located in the left ring Metacarpophalangeal (MCP) joint with synovial involvement. The third case, Gordon et al. [4] illustrated the case of a woman with 77-year-old woman with a 20-year history of seropositive RA involving both hands presented to her primary RA who developed bone DLBCL limited to her hands. A needle biopsy revealed diffuse large B-cell lymphoma, which is positive for Epstein-Barr Virus (EBV)-Encoded Small RNA (EBER), indicating that lymphoma cells are infected with EBV, respectively. The forth case, Galati et al. [5] demonstrated the case of a 77-year-old male patient with isolated primary DLBC of the proximal phalanx of the little finger without RA or MTX treatment. To our knowledge and the reviewing of English literature, the additional case may be the fifth registered case with primary DLBCL of the metacarpal bone the hand without RA or MTX treatment shown as (Table 1). Most cases with DLBCL are solitary, but also may be polyostotic lesions limited to the skeletal system and no visceral or regional lymph node involvement. Our reported additional case firstly presented DLBCL with metacarpal bone involvement of the thumb manifested hand swelling, pain and pathological fracture developed. Subsequently whole body bone scan images demonstrated distant multiple spinal, ribs and tarsal metastases. The differential diagnosis clinically should be included PBL, bone sarcomas, metastatic cancers and other primary malignant osseous tumors. The clinical features and imaging are usually nonspecific with difficult to distinguish PBL from other primary bone neoplasms such as Ewing's sarcoma, neuroendocrine tumor, osteogenic sarcoma, and chondrosarcoma. The current reports documented initial diagnostic bony specimen suggested that could be obtained by surgical procedure and histopathological with IHC methods should be performed for PBL and for differential diagnosis. Other surgical procedures should be avoided as much as possible, especially if the lesion is extensively damaged or pathologically fractured in the bone lesion [14-17]. Although previous reports have presented an increased risk of ML with MTX treatment and others have elucidated conflicting results and suggest may be an association between NHL and RA in patients both with and without MTX treatment [3]. Birlik et al. [2] described a DLBCL with synovial involvement of the right ring finger proximal interphalangeal and MCP joints and the amputation of the affected finger was performed. RA is a common autoimmune disease inducing a systemic inflammatory disorder with chronic inflammatory change of the synovial lining. The systemic nature of RA can characterize in multiple, extra-articular variable features include immune mediated anemia, vasculitis, neuropathy, pulmonary and renal disease, and subcutaneous nodules etc. Increased rates of NHL in RA and some other chronic inflammatory conditions include Sjogren's syndrome, systemic lupus erythematosus, which is primarily associated with severity of inflammatory disease activity [4-5]. EBV infection and chronic immunosuppression or immunodeficiency plays an important role in the pathogenesis of most lymphomas that occur after solid organ transplantation or in the elderly [4]. The pathophysiology of RA and others pathogenesis of malignancies is still unclear known. RA can cause a depletion of B-lymphocytes could present a dramatic improvement of the disease. In addition, patients with RA have an increased risk of B-cell NHL [1-5]. In the setting of rheumatologic disease, tumorigenesis seems to be triggered by B-cell antigenic stimulation and chronic inflammation, which is further aided by immune dysfunction [4,18-21].

The definite diagnosis is depended on histopathological and IHC examination after biopsy examination and imaging studies assesses for other diseases to should be excluded. Histopathological features are characterized analogous to those nodal and other peculiar extranodal DCBCLs. Previously, IHC study, tumor cells are generally immunostaining for CD45 and the large majority of cases for B-cell markers CD20, CD21, and CD79a, and approximately 70% of cases are expressed Bcl-2 [15,22]. PBL is an uncommon disorder of extranodal DLBCL with a relatively favorable prognosis for patients with systemic lymphoma with bone involvement. Primary bone DLBCL shows a higher survival rates than other types of NHL [11,23]. In previously, the optimal therapeutic strategy of primary DLBCL of the hand is still uncertainty because insufficient experience in rarity of the clinicopathological features and management model results. Treatment includes conventional chemotherapy, radiotherapy and surgery. The therapy primary DLBCL of the hand suggest consists mainly of chemotherapy and immunotherapy, often in combination with radiotherapy [2-5]. The goal of current study could be to illustrate socioeconomic, demographic, and anatomic factors as prognostic indicators of increase survival rate. For pathological fractures, ischemic necrosis, spinal cord compression or weight-bearing bone injury, orthopedic intervention is usually required to impair stability or joint movement. Prognosis and survival rates are good in most cases of DLBCL of the hand. In previous case reports demonstrate that free of disease, no recurrence or metastases on short-term follow-up to more than 6 months or even for 6 years of life [2-5]. The potential for long-term survival demonstrates the use of implants and technologies with optimal long-term control opportunities. In our case, patient with advanced-stage DLBCL of the thumb and pathological fractures did occur, and we had to surgically remove the tumor, and at the same time with chemotherapy could be quickly eliminated the tumor. Unfortunately, our case expired 4 months after surgery due to refractory duodenal ulcer bleeding and

progressive complicated multi-drug resistant bacterial infectious sepsis. Therefore, future treatment of patients with DLBCL of the hand relies on rigorous staging criteria and adherence to successful published protocols using collaborative clinical trials [5]. Many investigative prognostic factors have been elucidated in earlier retrospective studies. Age, performance status, and serum lactate dehydrogenase levels, three remaining International Prognostic Index (IPI) variables, and other factors can be used to assess prognosis [15]. The diagnostic value of CT and Magnetic Resonance (MR) imaging scans is important in order to distinguish the diagnosis of the primary bone DLBCL from the tumor with the radiological evidence of the soft tissue and its origin. The diagnostic value of histopathology and IHC analysis is most important preferred.

Conclusion

DLBCL of the hand is an extremely rare entity. Until now, there are no adequate well-documented studies regarded on prognosis or morbidity. We describe an additional extremely rare case with DLBCL of the thumb with no RA, autoimmune disease or MTX treatment. To our knowledge and review the literature, the small number of presented cases elucidated and insufficient well-documented surveillance data reported. The evaluation of prognosis and recurrence rate should be still assessed.

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