Primary Bone Lymphoma of Humerus Diagnosed by FNAC- A Rare Case Report

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Introduction

Primary lymphoma of bone (PLB) is an uncommon bone tumour with a relatively homogenous morphology and unusual clinical behaviour [1, 2]. It is defined as lymphoma arising from bone without evidence of any extraskkeletal involvement at the time of presentation. An interval of 4–6 months from the time of the osseous lesion to the development of the extraskkeletal disease is required to consider a PLB by some investigators [1–3]. This is one of the rare cause of primary osteolytic lesion [1].

Primary non-hodkins lymphoma (NHL) of bone comprises approximately 4–5 % of all extranodal NHL. Since, PLB is a curable disease, it should be differentiated from other lytic bone lesions such as secondaries and other primary bone tumours [2–4]. Due to its rarity, only a few retrospective studies have been published addressing the prognosis and treatment of PLB. Most of the studies had small patient numbers retrospectively collected over a long time span, resulting in a heterogeneous group of patients with different staging methods and a great diversity of treatment approaches [1, 3, 4]. Diagnosis of nodal lymphomas on Fine needle aspiration cytology (FNAC) has been well established. However, cytodiagnosis of primary lymphoma of bone has not been well documented because of its rarity [3]. We report a case of primary bone lymphoma involving proximal humerus in a 31-year old male diagnosed by FNAC, later confirmed by histopathology and immunohistochemistry.

Case Report

A 31-year old male, presented with pain and swelling in right shoulder since 5 months, which was aggravated since past 3 weeks. There was trivial trauma 4 months ago. Past and personal history was unremarkable. Local examination revealed diffuse swelling in right midarm to pectoralis major anteriorly and scapula posteriorly. Veins over the swelling were dilated and prominent. Haematological and biochemical parameters were within normal limits. Erythrocyte sedimentation rate was 5 mm at the end of 1 h. Serum calcium and phosphorus were within normal limits. X-ray showed complete destruction of upper end of humerus. (Figure 1) Prior X-ray done 6 months back, revealed osteoporotic change in proximal humerus. (Figure 2) FNAC done showed highly cellular smear with dispersed monotonous cells having scant cytoplasm and pleomorphic nuclei. (Figure 3) Nucleoli were prominent and multiple. Few osteoclast like giant cells were also seen. (Figures 4 and 5) Correlating with clinical findings, the possibility of malignant lymphoma, nonhodkins type was made. Confirmatory biopsy showed small fragments of bony trabeculae with cellular tumour comprising cleaved and noncleaved cells. (Figures 6, 7 and 8) Foci of necrosis and crush artifacts were also seen. Tumour cells were immunoreactive for CD 45, CD 20, CD79a and bcl-2, and negative for CD3, CD 5, CD10 and CD23. (Figure 9) Further evaluation showed no lymphadenopathy or organomegaly and bone marrow examination was unremarkable. Hence, final diagnosis of PBL-diffuse large B cell type of the humerus was made. Patient was treated with cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) regime with rituximab (6 cycles), followed with local radiotherapy of 50Gy in 25 fractions over 5 weeks. After 3 years of follow up, patients is doing well with no evidence of local recurrence and systemic involvement.

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Fig. 1 X-ray right arm showing lytic lesion and complete destruction of upper end of humerus with soft tissue extension

Discussion

Primary bone lymphoma is rare accounting for less than 1 % of all Non-Hodgkin's lymphoma [4–7]. The criteria for diagnosis of PLB is suggested by Coley are as follows: 'Lymphoma presenting in an osseous site with no evidence of disease elsewhere for at least 6 months after diagnosis' [7–9]. The presence of regional lymph node involvement does not exclude a diagnosis of PLB, but a histological examination of the lymph node is necessary [4, 6, 9, 10]. Although the original criteria of Coley implied the involvement of solitary bone. Ostrowski et al., subclassify osseous lymphoma into four groups, i.e. Group 1 consists of solitary primary bone lymphoma and Group 2 encompasses cases in which more than one bone is affected but no nodal or visceral disease is

Fig. 2 X-ray right arm showing osteoporotic change in proximal humerus. (6 months back)

Fig. 3 FNAC showing highly cellular smear with dispersed monotonous cells having scant cytoplasm and pleomorphic nuclei. (Pap, $\times 100$)

present. Group 3 includes cases with distant nodal disease and Group 4 with visceral disease [6, 7, 9, 10].

PLB occurs in patients from 1 to 86 years with a peak prevalence in the 6th and 7th decade. The femur (29 %) is the most common site of predilection, followed by pelvis (19 %), humerus (13 %), skull (11 %) and tibia (10 %). Vertebral involvement is not unusual [3, 7, 9]. In the long bones, lymphoma is usually metaphyseal or diaphyseal in location, rarely involving the epiphysis [6, 8, 10].

Extensive fibrosis, crush artifacts and necrosis contributes inadequate sampling both in biopsy and cytology [2]. To overcome this, thinner needles (e.g., 25-gauge), multiple passes of FNA, sampling different areas and avoiding necrotic centre should be done. A core biopsy is recommended for cases in which FNA fails to provide good aspirates. Most primary lymphoma of bone are either diffuse large B-cell lymphoma or mixed large cell and small cell lymphoma, although other types of lymphoma, including small lymphocytic lymphoma, anaplastic large cell lymphoma, Burkitt's lymphoma and Hodgkin's lymphoma are described [1, 5, 7, 9]. Immunocytochemical studies, including antibodies to CD20, CD3, CD45 are sufficient to establish a definitive diagnosis. If a low-grade or intermediate-

Fig. 4 Cytology with cells having prominent and multiple nucleoli. (Pap, $\times 400$)

Fig. 5 Dispersed monotonous cells having scant cytoplasm, admixed with osteoclast like giant cells. (Pap, $\times 400$)

grade lymphoma is suggested, additional markers, such as CD5, CD10, CD23 are needed. Molecular studies for specific chromosomal translocations may be useful, especially when follicular lymphoma, mantle cell lymphoma, anaplastic large cell lymphoma, and Burkitt's lymphoma are suspected [1, 2, 8–10]. Differential diagnosis include (1) hematopoietic neoplasms such as multiple myeloma, eosinophilic granuloma and myeloid sarcoma. Myeloma can be differentiated with plasma cells tend to show more abundant cytoplasm, a lesser degree of nuclear membrane irregularity, and many binucleations or multinucleated forms. Myeloid sarcoma will have neoplastic cells with high nuclear-cytoplasm ratio, fine blastic chromatin and scattered eosinophilic myeloblasts. (2) Non-hematopoietic small round cell tumors including ewings sarcoma, metastatic rhabdomyosarcoma, neuroblastoma, small cell undifferentiated carcinoma, poorly differentiated carcinoma and melanoma, (3) mastocytosis, and (4) osteomyelitis are rare differential diagnosis for PBL [2, 6, 7, 9, 10].

Primary lymphoma of bone usually responds well to a combination of radiotherapy and chemotherapy with an overall response rate of 94 % in some series and a 5-year survival rate, better than that achieved with most other primary osseous malignancy [1, 2, 4, 5]. CHOP regime is the standard

Fig. 6 Bone biopsy showing cellular tumour with fragments of bone tissue. (Haematoxylin and Eosin, $\times 400$)

Fig. 7 Biopsy showing cellular tumour comprising cleaved and noncleaved cells with fibrous septa. (Haematoxylin and Eosin, $\times 400$)

Fig. 8 Biopsy showing cellular tumour comprising cleaved and noncleaved cells. Few tumour giant cells are also seen. (Haematoxylin and Eosin, $\times 400$)

Fig. 9 Tumour showing strong immunoreactivity for Leucocyte common antigen. ($\times 400$)

first-line treatment [1, 6, 8, 9]. If CD20 antigens are positive, rituximab should be added. Radiation therapy to bulky sites of disease may be necessary after completion of chemotherapy [1, 2, 7–9]. From the clinical and radiological point of view, lymphoma of bone should be considered as a differential diagnosis especially in a young adult presenting with single or multifocal osseous involvement.

Conflict of Interest None declared.

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