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Case Report

Primary bone lymphomas—Clinical cases and review of literature

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ABSTRACT

Primary bone lymphoma (PBL) is an uncommon clinical entity and a rare presentation of non-Hodgkin's lymphoma. PBL accounts for less than 5% of malignant bone tumors, 4–5% of extra nodal lymphoma and less than 1% of all non-Hodgkin's lymphoma. Diffuse large-B-cell lymphoma (DLBCL) accounts for the majority of cases of PBL. The incidence of PBL is so rare that many of its aspects remain unknown. A number of studies have been reported from western countries but only a few reports are available from Asia. Out of 20,000 bone lesions received in our department over 5 years, only 5 cases were primary bone lymphoma; all of which were DLBCL. We report our experience on PBLs with main emphasis on two unusual presentations of this rare tumor.

1. Introduction

According to WHO classification, PBL is defined as a mono-ostotic disease with or without involvement of regional lymph nodes, or as a poly-ostotic disease affecting multiple skeletal sites without visceral- or lymph node involvement [1].

Primary lymphoma of bone is an uncommon clinical entity and accounts for less than 5% of malignant bone tumors, 4–5% of extra nodal lymphoma and less than 1% of all non-Hodgkin's lymphoma. Diffuse large-B-cell lymphoma (DLBCL) accounts for the majority of cases of PBL [2]. The varied clinical and histopathological profiles of PLB are still to be explored entirely.

2. Methods

A 5 year study (2006–2011) of all primary lymphomas of bone were undertaken retrospectively and prospectively in our department. Cases with unusual presentation were studied in detail along with their immunohistochemical profile. In all patients, staging evaluation included hematological and chemical survey, in addition to chest X-rays, abdominal ultrasonography, computed tomography of the chest and abdomen, and bone marrow biopsy. Cases were staged according to the Ann Arbor staging system [3]. Complete data on followup was not available due to either inability of patient to complete followup or referral of patient to some higher/cancer speciality center. The patients were treated with combined radiochemotherapy. The dose of radiation therapy was between 35 and 45 Gy, and CHOP chemotherapy regimen was employed. Complete Response (CR) was defined as disappearance of all evidence of lymphoma, as documented by a normal physical examination, blood tests, and radiologic imaging. When residual radiographic abnormalities were consistent with normal bone reformation, patients were considered in CR if no other possible signs of disease were present. Partial Response (PR) was defined as $>50\%$ reduction in tumor burden without CR after completion of treatment, and no response as anything else. Local failure was defined as failure in the initial bone site and/or in adjacent lymphnodes. Failure anywhere outside these confines was considered to be distant [4].

3. Observations and results

Out of 20,000 bone lesions received in our department over 5 years from 2006 to 2011, 360 (1.8%) were neoplastic out of which 11 were bone lymphomas. Of the 11 cases of bone lymphomas, 6 cases were secondary involvement by non-Hodgkin's lymphoma and 5 cases were primary bone lymphoma. All the 5 cases of primary bone lymphoma (PBL) were Diffuse large B-cell lymphoma (DBCL) type, 3 of which presented in pelvis(60%), 1 each in femur (20%) and mandible (20%). 3 cases were of usual and 2 had unusual presentation or morphology. Table 1 summarizes the clinic-pathological characteristics of the patients described in this study.

The first unusual presentation (case 4) was a 65-year-old man who presented with the chief complaints of intermittent fever,

Abbreviations: PBL, Primary bone lymphoma; DLBCL, Diffuse large B cell lymphoma; NHL, Non-Hodgkin's lymphoma.

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pain and swelling of the jaw for the past 6 months. On examination, multiple draining sinuses were present on right side of jaw. A CT scan of the jaw revealed a breach in the cortex of the mandible on the right side [Fig. 1]. A presumptive diagnosis of tubercular osteomyelitis was made and draining fluid was sent for AFB stain, results came were negative. A biopsy was sent for histopathological examination, which revealed diffuse infiltration of the skin, subcutaneous tissue and muscle with lymphoid cells [Fig. 2]. Immunohistochemistry was positive for LCA, CD20, Ki 67 (50–60%) and negative for CD3 and CD4 [Fig. 3]. Hence a diagnosis of diffuse large B cell lymphoma of the mandible was made and the patient was started on CHOP chemotherapy regimen followed by radiotherapy to which he is responding well. Additional investigations did not show any other bony lesions or lymphnode involvement.

The second peculiar presentation (case 5) was a 54-year-male who complained of pain and swelling of right hip since 5 months with increasing intensity. On examination the patient had restricted movements of left hip joint and a lump could be palpated. X-ray showed soft tissue and bony mass involving the right ileum [Fig. 4]. A presumptive clinicoradiological diagnosis of chondrosarcoma was made and biopsy was performed. Histopathological examination showed small round cell tumor cells in a sclerotic stroma [Fig. 4]. Immunohistochemistry of the lesion showed positivity for LCA, CD 20, CD10,Vimentin, Bcl-2, Bcl-6, PAX-5, MUM1, Ki-67 (70–80%) and negative for CD 99, Pancytokeratin, Desmin, CD-3, S-100, CD-5, HMB-45 [Fig. 5]. The morphology and immunophenotype was compatible with the diagnosis of diffuse large B cell lymphoma and suggest a follicle center cell origin. So a final diagnosis of diffuse large B cell lymphoma of right ileum was made. No additional bony or lymphnode involvement was found. The patient was advised CHOP chemotherapy followed by radiotherapy.

Table 1
Clinico-pathological characteristics of patients described in the study.

Sl. no.	Age	Sex	Site	Diagnosis	Stage	Followup
1	55	M	PELVIS	DLBCL	I E	Referred
2	47	F	PELVIS	DLBCL	II E	Lost
3	59	M	FEMUR	DLBCL	II E	PR
4	65	M	MANDIBLE	DLBCL	I E	CR, no. failure at 1 year
5	54	M	PELVIS	DLBCL	I E	Referred

4. Discussion

Primary lymphoma of bone is a rare disease, first described by Oberling in 1928 and he labeled it as reticulum cell sarcoma of bone because of the presence of characteristic reticulin fibers within the lesion [5]. This work was followed by Parker and Jackson and later by Ivin and Boston who, eventually established the distinct entity of this lesion and labeled it as the malignant lymphoma of bone [6,7]. The use of immunohistochemistry in highlighting the cellular origin of these lymphomas was described by Vassallo in 1987 [8]. Even till today, the diagnosis of these lesions remains challenging and requires the help of immunohistochemical markers along with histopathology to lead to the final diagnosis.

The definition of PLB varies throughout the literature. Generally, this entity is defined as malignant lymphoma arising within the medullary cavity of a single bone without concurrent regional lymph node or visceral involvement [9]. In contrast, Shoji and Miller permitted regional lymph node metastases but stipulated that the interval between the onset of symptoms of the primary focus and the appearance of distant metastases should be greater than 6 months [10]. The vast majority of these lymphomas are non-Hodgkin lymphoma (NHL), the common subtype being diffuse large B cell lymphoma. In addition to DLBCL, other lymphoid malignancies may manifest with primary bone presentation, including

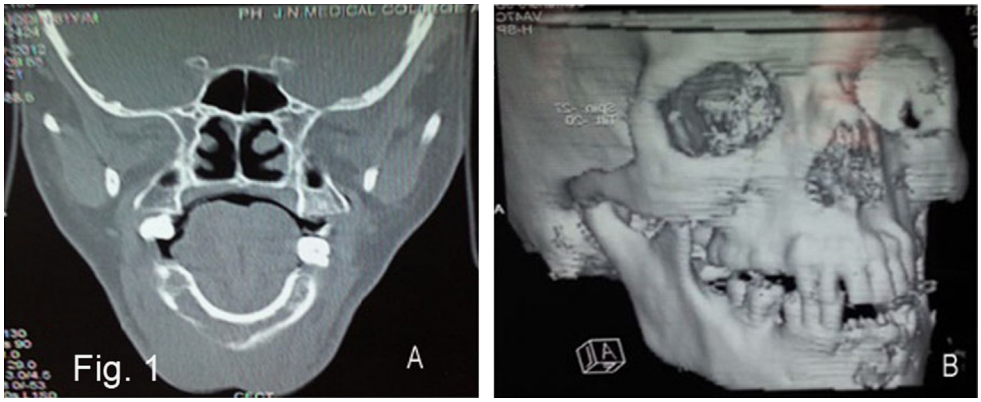

Fig. 1. CT scan revealed breach in mandibular cortex.

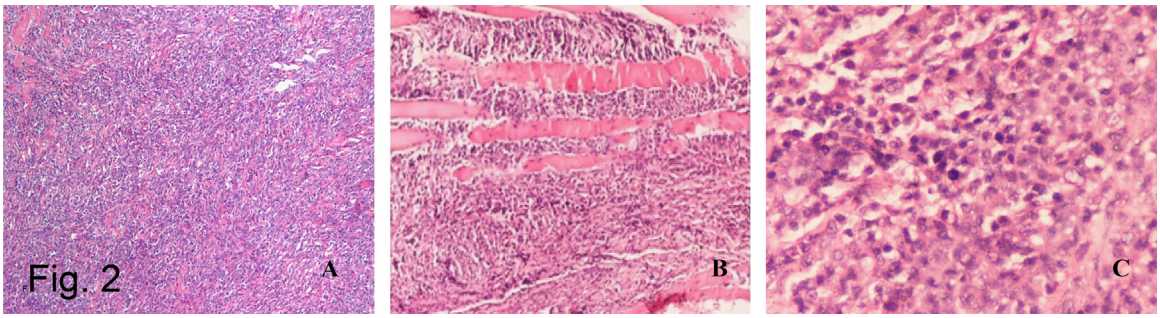

Fig. 2. Diffuse infiltration of large B-cells. (H&E).