

Primary Bone Lymphoma: Case Report and Review of Literature

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ABSTRACT

Primary bone lymphoma (PBL) is a rare extranodal lymphoma accounting for less than 5% of all primary bone malignancies. Most of these lymphomas are of diffuse large cell type with age group of 20-50 years. We present a case of Primary bone lymphoma- precursor B cell lymphoblastic type in a paediatric female patient. Correct diagnosis is extremely important because PBL usually is curable in the pediatric age group with appropriate therapy

Keywords: Primary Bone Lymphoma, Extranodal Lymphoma And Precursor B Cell Lymphoblastic Type

Introduction

Malignant bone lymphoma is an uncommon entity. They are classified as primary or secondary bone lymphoma (SBL). Primary bone lymphoma is a rare disease, first described by Oberling in 1928 and was termed as reticulum cell sarcoma of bone. Further studies by Parker and Jackson and later by Ivin and Boston eventually labeled it as the malignant lymphoma of bone. Vassallo in 1987 emphasized on use of immunohistochemistry in highlighting the cellular origin of this entity.^[1] It accounts for less than 1 % of all non Hodgkin lymphoma, 5% of extra nodal lymphomas and 7% of bone tumors. Most of the PBL are diffuse large B cell lymphoma histopathologically. Primary lymphoma of bone has an excellent prognosis and therefore it is very important to differentiate it from the other lytic lesions of bone.^[2] Here we report a case of PBL- diagnosed and treated in our institution.

Case Report

A 10 year old female presented with pain and swelling around the right knee since 4 months, which was progressively increasing in size. Patient also had a history of difficulty in walking, low grade fever and weight loss. Radiological examination (X RAY and MRI) revealed lytic destruction of cortex of lower end of femur with periosteal reaction and surrounding soft tissues collection. A presumptive diagnosis of an infective etiology was made and biopsy of soft tissue and bone was performed. Histopathological examination of the biopsy revealed malignant small round cell tumor (fig 1A and 1B). A panel of immunohistochemical (IHC) markers was applied for typing of this tumor. Primary IHC panel included CD 99, vimentin, desmin, myogenin, S100

and LCA. Examination revealed positivity for CD 99 and LCA suggestive of a hematolymphoid malignancy. Further IHC of the lesion showed positivity for CD79a, HLA DR, Tdt, CD10, CD 43 and negative for other B and T cell markers like CD 20, CD 3, CD5 and CD117 suggestive of Precursor Lymphoblastic B-cell lymphoma/leukemia. Further clinical and radiological workup was normal with no lymphadenopathy or organomegaly. Peripheral blood and bone marrow smears had no atypical cells. Final diagnosis was Primary lymphoma of femur- Precursor B-cell Lymphoblastic type. Patient is on treatment and regular follow up since last 6 months.

Review of Literature

The literature has defined PBL in numerous different ways. According to the WHO classification, lymphoma involving bone can be classified into four groups: Group 1, lymphoma with a single bone site with or without regional lymph-node involvement; Group 2, lymphoma with multiple bones involved, but no visceral or lymph-node involvement; Group 3, bone tumor with involvement of other visceral sites or lymph nodes at multiple sites; and Group 4, lymphoma involving any other sites and found by bone biopsy which was done to rule out possible involvement. Most of the studies have included Group 1 and Group 2 in the diagnostic criteria of primary bone lymphoma.^[3] Primary lymphoma of bone is an extremely rare tumor localized to bone without any lymph node or other tissue involvement. It primarily arises from the medullary cavity with only few cases reported in the literature. The cause of bone lymphoma is not well-known, however, immunodeficiency, organ transplantation, viral infection,

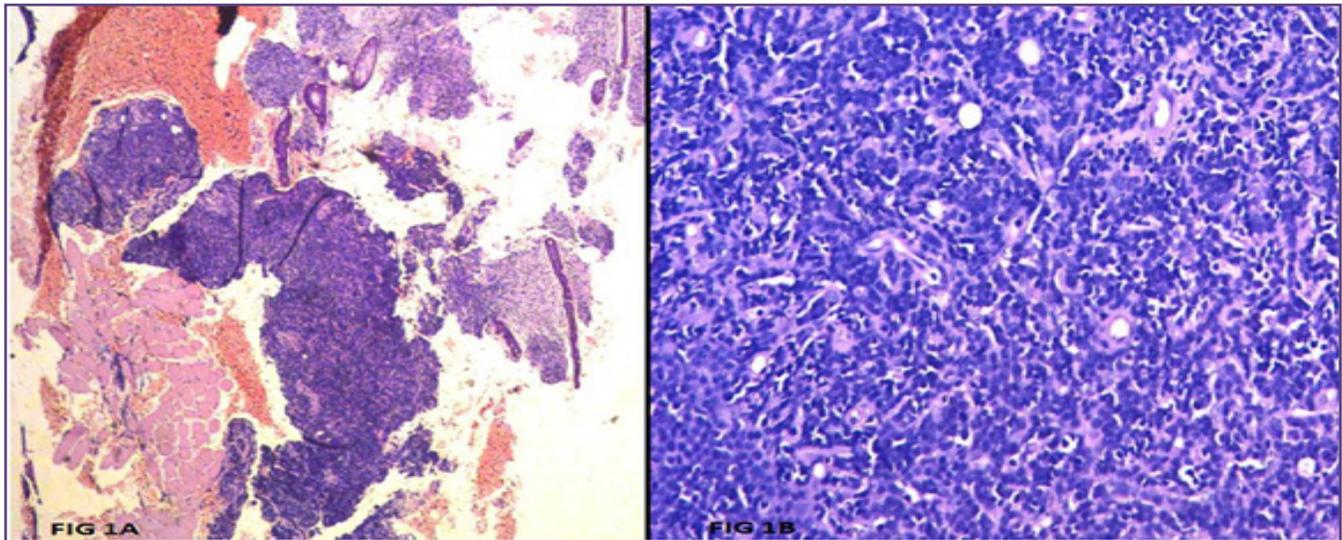


Fig. 1A and 1B :sheets of small round cell consistent with malignant small round cell tumour, [H & E, 4X AND 20X].

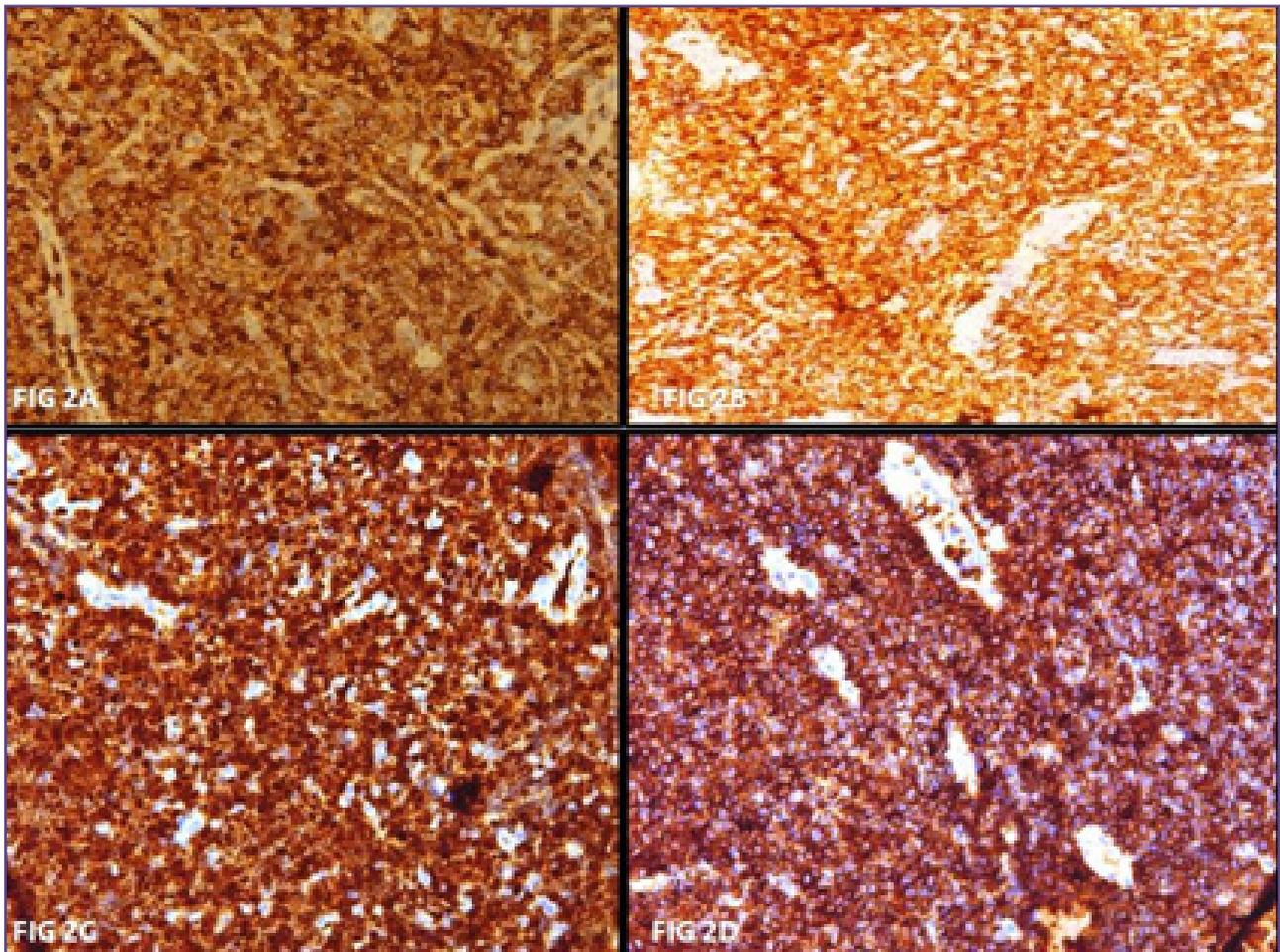


Fig. 2: Tumor cells are positive for LCA (2A), CD 79a (2B), Tdt (2C) & CD 10 (2D).

Paget's disease of the bone and inherited factors have been identified as possible causes in some of the retrospective studies.^[4] Most common age of presentation is between 20 and 50 years with a slight male preponderance (M:F ratio of 3:2). Femur (29%) is most commonly affected followed by pelvis (19%), humerus (13%), skull (11%) and tibia (10%). PLB differs from secondary lymphoma of the bone, where the axial bones are the most common sites of presentation.^[5]

To be diagnosed as primary bone lymphoma there should be (i) histological diagnosis, (ii) a primary focus in a single bone, and (iii) no evidence of distant lymph node or distant soft tissue involvement. PBL may involve multiple bones, as long as the other two criteria are met the diagnosis can be made. According to the Ann Arbor system, currently the most widely accepted staging system, PLB is divided into the following four stages: i) Stage I, single lesion in the bone with or without soft tissue infiltration; ii) stage II, more than two lesions beside one side of the diaphragm, or a single lesion in the bone with soft tissue infiltration; iii) stage III, lesions beside two sides of the diaphragm; and iv) stage IV, infiltration of the central or peripheral nervous system, or bone marrow, as determined by staging biopsy at different times.^[6]

Patient usually presents with swelling and pain which is progressively increasing in size and intensity. Radiological features of Primary bone lymphoma are non-specific resembling any other lytic lesion. There is a wide spectrum of findings ranging from a normal appearing bone to extensive lesions. The destructive lesions are patchy, radiolucent, mottled and occasionally exhibit complete loss of the outline. This may be accompanied by cortical bone thickening and destruction along with soft-tissue extension. X Ray often underestimate the extent of the lesion. CT scan is useful for disease staging and MRI is helpful in demonstrating bone marrow and soft tissue involvement. Other investigations include bone scan, skeletal survey, bone marrow biopsy, CT scan of whole abdomen and chest to assess lymph node involvement.^[7]

In contrast to adults, PBL in children is regarded as all together different clinical entity that is distinct from its adult counterpart. Like many other pediatric malignancies, PBL is considered a systemic disease in children. Paediatric PBL is characterized by rapid progression, a higher incidence of micrometastasis, and a propensity for spread to the central nervous system, yet children have a

better prognosis. Final diagnosis is established by biopsy. On routine histopathology, primary bone lymphoma appears as a malignant small round cell tumor with varied differential diagnosis. Immunohistochemistry is the main tool of differentiating it from other small round blue cell tumors, especially Ewing's Sarcoma in children. A limited panel of antibodies can lead to an erroneous diagnosis because of frequent overlap of antigenic expression in many small blue cell tumors. Tdt is the most specific and sensitive marker of lymphoblastic lymphoma/leukemia, expressed both in T and B lymphoblasts. Other useful marker includes: CD10, CD34, CD43, CD79a, CD99, HLADR.^{[8],[9]} Prognosis is excellent with overall reported survival at 5 years of 58 to 88%.^[10]

Conclusion

Thus, primary bone lymphoma should be considered in the differential diagnosis of bony tumors. Correct diagnosis is extremely important because PBL usually is curable in the pediatric age group with appropriate therapy. Chemotherapy followed by radiotherapy is the treatment of choice.

References

1. Wu H, Bui M M, Leston D G, Shao H, Sokol L et al. Clinical Characteristics and Prognostic Factors of Bone Lymphomas: Focus on the Clinical Significance of Multifocal Bone Involvement by Primary Bone Large B-Cell Lymphomas. *BMC Cancer* 2014:900.
2. Singh T, Satheesh C T, Lakshmaiah K C, Suresh T M, Babu G K et al. Primary bone lymphoma: A report of two cases and review of the literature. *J Can Res Ther* 2010:296-8
3. Jain A, Alam K, Maheshwari V, Khan R, Nobin H, Narula V. Primary bone lymphomas—Clinical cases and review of literature. *Journal of Bone Oncology*. 2013;2:132-6.
4. Heyning FH, Hogendoorn PC, Kramer MH, Hermans J, KluinNelemans JC, Noordijk EM and Kluin PM: Primary nonHodgkin's lymphoma of bone: a clinicopathological investigation of 60 cases. *Leukemia* 1999:2094-8.
5. Zhou H Y, Gao F, Bu B, Fu Z, Sun X J, Huang C S et al. Primary bone lymphoma: a case report and review of the literature. *Oncol. Lett.* 2014:1551–6
6. Coley BL, Higginbotham NL, Groesbeck HP. Primary reticulum cell sarcoma of bone; summary of 37 cases. *Radiology* 1950:641-58.
7. Maruyama D, Watanabe T, Beppu Y, et al Primary bone lymphoma: a new and detailed characterization of 28 patients in a single-institution study. *Jpn J Clin Oncol* 2007:216–23.

8. Bhagavathi S, Fu K. Primary bone lymphoma. Arch Pathol Lab Med 2009;1868-71.
9. Qureshi, A., Ali, A., Riaz, N., Pervez, S. Primary non-Hodgkin's lymphoma of bone: experience of a decade. Indian J Pathol Microbiol 2010;267-70.
10. Li X, Xu-Monette ZY, Yi S, et al. Primary Bone Lymphoma Exhibits a Favorable Prognosis and Distinct Gene Expression Signatures Resembling Diffuse Large B-Cell Lymphoma Derived From Centrocytes in the Germinal Center. Am J Surg Pathol 2017;1309.

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