

# Primary B Cell Non-Hodgkin's Lymphoma Presenting With Multiple Osteolytic Bony Lesions In Skull

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## ABSTRACT

**Background:** Head and neck is a common site of extra-nodal NHL. However primary bony NHL is a rare presentation of an extranodal NHL. We are presenting a rare and a typical case of primary lymphoma of bone in a six year old male child presenting as low back ache, fever and difficulty in walking since two months. He had multiple osteolytic lesions in skull. Vertebral transpedicle biopsy revealed B cell lymphoma with morphologic and immunophenotypic features of immunoblastic type.

**Discussion & Conclusion:** We discussed NHL with an emphasis on extranodal bony manifestations. Primary bone NHL has a favorable outcome when treated with a combined modality therapy and regular follow up. To the best of our knowledge, this is one of the rare primary NHL of the bone being reported in the Indian literature.

**Key Words:** NHL, Osteolytic lesion, Transpedicular biopsy, Immunohistochemistry

## KEY MESSAGE

- Physician dealing with bone, back pain in children should also consider and exclude the possibility of haematological malignancy in those children who are not responding to conventional treatment.

## INTRODUCTION

Lymphomas are the third most common group of cancers in children and adolescents [1]. Non-Hodgkin's lymphomas (NHL) represent approximately 60 percent of these and Hodgkin's lymphoma account for the remainder. NHL are categorised as low, intermediate and high grade on the basis of aggressiveness. NHL only rarely present as a primary osseous lesions [2]. Clinical presentation in children is varied and depends upon the histologic subtype, the extent of the disease and primary site of the tumour. Children typically have extranodal disease involving the mediastinum, abdomen, or the head and neck region. Up to 40 percent of these are extra nodal [2],[3],[5],[7]. Most primary lymphomas of the bone, are classified as diffuse large B cell lymphomas (DLBCL) [5].

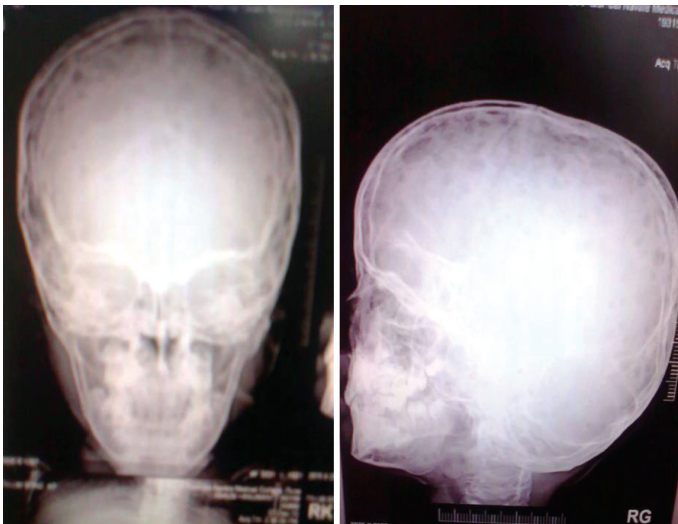
Histopathology diagnosis of NHL is not always easy as in childhood most malignant tumours other than lymphomas are composed of small cells that appear undifferentiated. There is a definitive role of immunohistochemistry in these tumours [7]. High grade NHL comprise three histologic subtypes mainly, small non-cleaved, lymphoblastic and the large cell lymphoma [2],[3],[8],[9]. DLBCL in children are relatively rare as they represent less than five percent of NHL. In our case, the child presented with bone involvement in the form of bone pains not relieved by rest, a palpable soft tissue mass, and systemic B symptoms but no lymphadenopathy. He was diagnosed as Primary lymphoma of bone (PLB). We are reporting a unique case for its rarity (Primary NHL of bone -diffuse large B cell lymphoma). In the paediatric population, it represents approximately three to nine percent of NHL cases [10].

## CASE REPORT

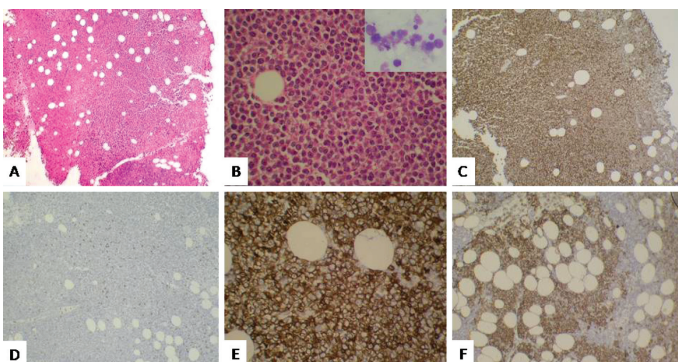
A six year old male child was admitted in our hospital with complaints of difficulty in walking since two months, low back pain for 15 days along with fever. At admission, patient was febrile with a temperature of 38°C, heart rate of 120 per minute, BP 90/66 mmHg and weighed 15 Kg. Scoliosis was noted at T12-L4 level and diffuse tenderness was present at thoraco-lumbar spine. There was no organomegaly or any significant lymphadenopathy. Bladder and bowel control was intact. Other systems were normal including fundus examination. X ray and MRI Spine was done on day 2 of admission which showed lesions suspicious of infective pathology in second lumbar vertebral region. Skull X ray revealed multiple osteolytic punched out lesions [Table/Fig 1]. Over the course of next ten days, the patient gradually developed hyperreflexia.

In view of spinal tenderness and lytic lesions in the skull, a bone marrow aspiration and biopsy was done. Bone marrow aspirate and biopsy was reactive in nature. The CT scan report showed multiple lytic lesions in vertebral bodies, bilateral pelvic bones, and upper part of femur with an impression of a leukaemic or metastatic disease. CT guided vertebral transpedicle biopsy was done at L2-L3 region. The biopsy specimen was subjected to a panel of immunohistochemical markers – CD3, CD20, CD45, CD10 and BCL 6. The tumor cells were diffusely positive for CD45, CD20 and CD10 with scattered CD3 positive T cells. Bcl6 was negative [Table/Fig 2 (A to F)].

Based on the morphology and immunochemical features a diagnosis of DLBCL immunoblastic variant arising from follicular



**[Table/Fig-1]:** Anteroposterior and lateral views of skull showing multiple osteolytic lesions



**[Table/Fig-2 (A to F)]:** Bone Marrow Biopsy – A. Diffuse sheets of lymphoid cells in hypercellular marrow (H&E stain, scanner view); B. Low power H&E stain view shows large lymphoid cells with atypical appearance; Similar cells in marrow aspirate smear (Inset, Leishman stain); Immunohistochemistry – C. Diffusely positive CD45 marrow (scanner view); D. Occasional CD3 positive T reactive cells (scanner view); E. Diffuse membranous CD20 positivity of the tumor cells (High power view); F. Diffuse CD10 positivity (scanner view).

centre cells was offered. Patient was sent to Tata memorial centre for further management.

## DISCUSSION

NHL only rarely present as a primary osseous lesions. PLB is defined as a lymphoma that is confined to the bone or bone marrow. It comprises approximately three to seven percent of all extra-nodal NHL and seven percent of Primary bone tumour [2-10]. As primary lymphoma of bone is a highly curable disease, differentiation from other causes of lytic bone lesions such as secondaries from carcinomas and other tumours is important. The child was admitted in the ward with the complaints pertaining to bone involvement. He had difficulty in walking since last two months, low back pain along with fever and diffuse tenderness over the back. All these changes indicate the presence of the disease which was indolent [11]. PLB can present in both adult as well as paediatric population but, with different prognosis, thus both are a separate entities. The majority of cases of DLBCL are primary but, it can also arise by transformation of B-CLL /SLL, lymphoplasmacytic lymphoma, follicular lymphoma, MALT lymphoma and lymphomatoid granulomatosis [14]. The diagnosis can be made by Fine needle

aspiration cytology (FNAC) or biopsy or by examination of bone marrow. Immunohistochemistry helps to make accurate diagnosis. Macroscopically, DLBCL usually forms a distinct tumour mass at extra nodal site. Microscopically, the commonest subtypes of PLB are B cell lymphomas with diffuse mixed cell or diffuse large cell histology. Sheets of large monomorphic lymphoid cells with one or more prominent nucleoli and a distinct rim of cytoplasm are usually noticed in DLBCL. CD 19, CD20, CD22 and surface immunoglobulins as seen in immunophenotyping are present in DLBCL [7]. The International prognostic index (IPI) has been shown to be useful a prognostic tool for predicting the behavior of the disease in NHL [13]. Elevated serum LDH or higher modified stages are associated with a trend toward poorer overall survival among children with CNS disease as seen by Sandlund et al [14]. Molecular profiling of DLBCL by various methods and to varying degrees may help separate DLBCL cases into different prognostic relevant groups and allow them to be treated accordingly [15].

## CONCLUSION

A greater tumour burden at diagnosis adversely influences the treatment outcome of children with NHL and CNS disease at diagnosis, suggesting a need for ongoing improvement in both systemic and CNS-directed therapy. DLBCL should be differentiated from other lymphomas and other malignancies morphologically in most cases. Immunohistochemical stains are of great help with the subtyping of NHL after morphological diagnosis. We also conclude that Transpedicular biopsy is an excellent tool to diagnose Primary lymphoma of bone in difficult cases.

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