Primary lymphoma of bone in children- A case series.

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ABSTRACT

Lymphoma is a malignant disease primarily originating from the lymphoid cells. Lymphoma can be classified as Hodgkin (HL) and Non Hodgkin lymphoma (NHL). Most lymphoma in bones are non-Hodgkin lymphomas and 80% are Diffuse Large B cell subtype (DLBCL). All children with primary lymphoma of bone (PLB) that were diagnosed and treated at Agha Khan University Hospital from 25th October 2000 to 25th October 2020 were included in this case series. Three cases of Paediatric PLB were documented. All of them were DLBCL. Chemotherapy was started. None of them required surgery. One of them expired and the rest of the two are in remission. The disease is rare so we had very few patients. Our case series suggests that PLB in children can be managed successfully with a multidisciplinary approach and focusing on chemotherapy and radiotherapy.
Keywords: Chemotherapy, Diffuse Large B cell, Lymphoma, Non Hodgkin lymphoma, Primary lymphoma of bone

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INTRODUCTION

Lymphoma is a malignant disease primarily originating from the lymphoid cells. Lymphoma can be classified as Hodgkin (HL) and Non Hodgkin lymphoma (NHL). Most lymphoma in bones are non-Hodgkin lymphomas with 80% are Diffuse Large B cell subtype (DLBCL). Primary lymphoma of bone(PLB) is very rare and accounting for 3-7% of all primary bone malignancies with NHL less than 1 % and extra nodal lymphomas 5%.[1-4] Most common presentation of the disease is pain or swelling of the affected area. Such nonspecific symptoms can delay the diagnosis. On plain radiograph PLB has no specific features. Usually it is a lytic lesion with cortical involvement in advanced disease. MRI and Positron Emission Tomography(PET) CT can helps in diagnosis but biopsy is the gold standard. With all the expertise and advancement in technology we must rule out the other differentials like osteomyelitis, SAPHO (synovitis, acne, pustulosis, hyperostosis, and os-teitis) syndrome, mastocytosis, other small round blue cell tumors and metastatic cancer to the bone.

We have to address pediatric lymphoma separately from adult counterpart because pediatric lymphoma appears different from adult malignancies. The course of paediatric lymphoma is more indolent and curable than adult lymphoma. On the contrary pediatric patients presents late for diagnosis and may have extensive bone involved. Even in such cases 95% remission is possible. Surgery is not recommended unless there is a pathological fracture or an impending fracture.[1]

CASE SERIES

All children with primary lymphoma of bone(PLB) who were diagnosed and treated at Agha Khan University Hospital from 25th October 2000 to 25th October 2020 were included in this case series. Diagnosis was based on biopsy of the tumor. Children who had primary lesion in the bone were included. Children who received treatment for primary lymphoma in areas other than the bone, received treatment for secondary lymphoma of bone

or patients who otherwise did not fulfill the inclusion criteria were excluded from this case series.

We presented three cases of paediatric PLB. All the data obtained was reviewed and analyzed after permission from the Ethical Review Committee. Informed written consent was obtained from parents of the children for treatment and publication of results.

CASE 1

A 5 years old boy presented to the OPD clinic with complains of right knee swelling for the last 3 months. On examination firm swelling was noted in the left femur. His gait was normal and knee range of motion was 0-120 degrees. Distal neurovascular status was intact. X-ray showed a lucent lesion with surrounding sclerosis involving the meta-diaphysis of the right femur (Fig. I) There was associated periosteal reaction noted anteriorly as well as posteriorly. Soft tissue swelling was also appreciated. There was subtle irregularity appreciated in the epiphysis along its medial margin best seen on the frontal projection. PET scan was done which showed hyper metabolic lesions with destruction of the underlying bone seen over distal end of both femurs (intact bilateral epiphyseal plates). Metabolically non-active sclerosis was seen over the proximal one third of the right tibia with a focus of mild Fluorodeoxyglucose (FDG) uptake. Hyper metabolic soft tissue nodal disease was seen in right inguinal region, posterior compartment of the right thigh and right popliteal region. Hyper metabolic deposit was also seen over the inferior angle of left scapula without apparent bony destruction. (Stage IV disease). He was started on chemotherapy. He got admitted with febrile neutropenia and pneumonia. The child could not survived the therapy and expired after one month of diagnosis.

CASE 2

A 12 years old boy was presented to our OPD with complaints of left hip for the last 3 months. On examination firm swelling was noted in left hip area. His gait was normal and hip range of motion was normal. Distal neurovascular status was intact. Radiographs showed highly aggressive lesion in the right ileum with significant soft tissue swelling. The appearances were suggestive of malignant lesion such as Ewing's sarcoma, osteosarcoma or lymphoma. MRI showed large soft tissue density mass seen in the left side of the pelvis involving the left iliopsoas muscle, tenser fascia latae, the gluteus medius and minimus muscles and with extensive destruction of the right iliac bone. Posterior and lower half of the left side of the sacrum was also involved. Three phase skeletal scintigraphy revealed large areas of soft tissue abnormality involving the pelvis and the left hip region with evidence of abnormal tracer uptake over proximal part of left ileum, distal part of left acetabulum and adjacent part of left SI joint. All these findings were highly suggestive of hematoma/abscess with local involvement of right hemi pelvis. CT chest showed suspicious ill-defined nodules in both lungs causing a strong suspicion of sarcoma with metastatic deposits. Biopsy was done which showed DLBCL. He was started on Rituximab, Cyclophosphamide, Hydroxydaunorubicin Hydrochloride, Oncovin and Prednisone(R-CHOP) regime cycles followed by radiotherapy. Post therapy the scan showed remission. The child was clinically healthy at 3 years follow up.

CASE 3

A 10 years old girl presented to our OPD with complaints of lower back swelling. On examination the swelling was 3x3cm on right lower back at the level of L4-L5 vertebra and paraspinal region. X-ray pelvis showed lytic lesion in the right iliac blade (Figure: II). Bone scan and whole body skeletal imaging findings were consistent with metastatic involvement of right iliac bone and manubrium sterni. CT scan showed erosion and destruction of the right ilium with surrounding periosteal reaction. Diffuse metastatic deposits in both lung fields were detected on CT chest. Biopsy was done which showed DLBCL. She was started on R-CHOP regime cycles followed by radiotherapy. Post therapy the scan showed remission. The child was clinically healthy at 4 years follow up.

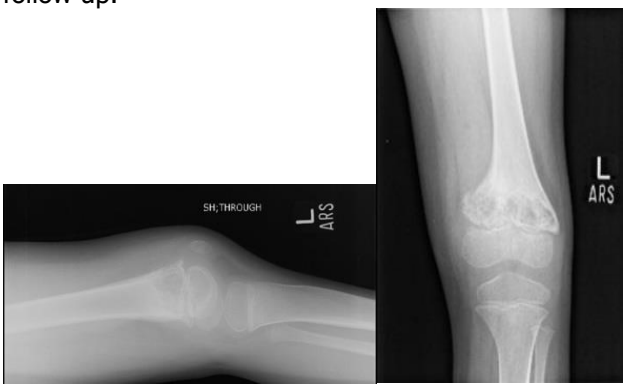

Figure I: X-ray showing a lucent lesion with surrounding sclerosis involving the meta-diaphysis of femur. There was associated periosteal reaction.

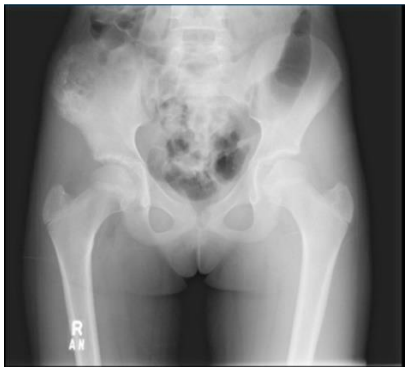

Figure II: X-ray pelvis showing lytic lesion in the right iliac wing.

DISCUSSION

Patients with primary bone lymphoma can be very difficult to diagnose and manage. Diagnosis is delayed due to nonspecific history and nonspecific radiologic findings and multiple biopsies have been required to diagnose PLB.[1] PLB can present as low grade (slow growing), intermediate grade and high grade. The most common sites of involvement are femur (27%), pelvis (15%), tibia (13%), humerus (12%), spine (9 %), mandible (2%), skull (1%), scapula (1%), radius (1%), and ulna (1%).[3] Median age of diagnosis of adult PBL is 45 to 60 years.[4] PLB has also been reported to arise around prosthetic devices,[4] necessitating the need for regular monitoring of children with mega prosthesis.

Management of PLB is different from sarcomas.[5] History is vague in case of PBL with only pain and swelling as the main presenting complaints. Plain x-ray has nonspecific findings and MRI needs to be done to see the local extent of the disease.[2] MRI shows marrow infiltration and extra osseous extension.[6] Biopsy is needed to know the type of tumor and metastatic workup is required to evaluate the extent of the disease in the body. PET CT is recommended so that anatomical and physiological characteristic of the lesion is identified.[2] Differential diagnosis of such lesions in pediatric population includes Ewings sarcoma and osteosarcoma.[3]

Chemotherapy is the standard treatment of PLB and the role of immunotherapy is not yet clear.[1,7] In pediatric population the disease pattern and prognosis is different from adult patients and pediatric population can go in remission even if the initial diagnosis is at advanced stage.[1] PLB cannot be managed by one specialty. A multi disciplinary team comprising of Orthopedic surgeons, histopathologist, medical oncologists, radiotherapist and psychologist must manage all cases of PLB. At our institute such patients are discussed in the Tumor Board which comprise of all the faculties from the relevant fields. In view of the disease stage and disabilities treatment options are decided and advised to the patients. These patients also need long term follow-up because post treatment 7 to 10% of local relapse is noted and 17 to 22% of distant metastasis is reported in the literature.[1]

Meticulous surgical technique must be adopted for biopsy of PLB so that adequate tumor tissue ensure correct histological diagnosis. Chisholm[8] had to take multiple biopsies in 30% cases of PLB in his series of 54 patients. Chisholm was of the opinion that PLB should be included in the differential diagnosis of any paediatric bone tumor which exhibits necrosis. The optimal treatment strategy of PLB should focus on the histological types and stage of the disease.[9] Doll and Wulff[10] treated 2 children of PLB of femur with chemotherapy as per NHL-BFM95 protocol and both the children were in remission at 24 and 18 months follow up.

CONCLUSION

Remission can be achieved in children with primary lymphoma of bone treated with chemotherapy and radiotherapy. Early diagnosis and multi disciplinary approach is however mandatory and can result in good prognosis. The Orthopaedic surgeons must increase the awareness of this disease and consider primary bone lymphoma in the differential diagnosis of all paediatic bone lesions.

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