

Case Report

## Primary Hodgkin Lymphoma of RIB - A Rare Case Report

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### ABSTRACT

Hodgkin lymphoma is a well known lymphoproliferative disease which presents as a nodal lesion with secondary involvement of extranodal sites like skin, bone or any other organ system. This case report is regarding a 55 year old female presenting with osteolytic mass in the fifth rib. Imaging studies revealed no other associated findings like organomegaly or lymphadenopathy. Histological and immunohistochemical findings were in favour of Primary extra nodal Hodgkin lymphoma nodular sclerosis type.

**Keywords:** Lymphoma, Osteolytic, Nodular sclerosis.

### INTRODUCTION

Hodgkin lymphoma (HL) is characterized by a polymorphous population of cells which includes the neoplastic Hodgkin cells and Reed-Sternberg cells along with predominance of reactive non neoplastic cells. Hodgkin lymphoma accounts for about 1% of all cancers and 11.5% of all lymphomas. <sup>(1)</sup>

Hodgkin lymphoma has a bimodal age distribution with first peak in 15-34 years and the next peak after 54 years with slight male predilection except nodular sclerosis type of Hodgkin lymphoma. In contrast to malignant neoplasms in general and lymphomas in particular, which are characteristically composed of clonal monomorphic populations of cells, HL presents as a mixture of different cells assembled in a variety of histologic patterns. The dense accumulation of inflammatory cells is attributed to the chemokine released by Reed Sternberg cell (RS cell). <sup>(1)</sup>

Cervical nodes are the most often involved with rare involvement of inguinal and axillary nodes. Other rare sites which could be involved are Waldeyer's ring, mesenteric nodes and rarely popliteal nodes. Mediastinal involvement is exclusively seen in nodular sclerosis subtype of Hodgkin lymphoma. The extra nodal site for HLs is gastrointestinal tract, lungs, skin, central nervous system, bone and thyroid. <sup>(2)</sup> Hodgkin lymphoma presenting as extranodal disease is very rare. It is important to rule out secondary dissemination as the prognosis is poor. Imaging studies like magnetic resonance imaging and computed tomography are helpful to exclude lesions elsewhere. Most of the extranodal lymphomas are Non Hodgkin lymphoma, most commonly diffuse large B cell lymphomas. The incidence of extranodal Hodgkin lymphoma is less than 1%. <sup>(3)</sup> Among the subtypes of Hodgkin lymphoma, nodular sclerosis type is the most common and also

has a better prognosis followed by mixed cellularity. Immunohistochemistry is required to differentiate it from reactive lesions. These immunoprofiles are known to have an impact on the clinical behaviour and treatment response. Reed Sternberg cells of classical Hodgkin lymphoma show positivity for CD30, a tumor necrosis factor receptor glycoprotein and 85% will express CD15, the Lewis X carbohydrate adhesion molecule. In general CD 15 negative patients have a higher rate of relapses irrespective of other prognostic factors. Morphologically, the hallmark cells of HL are Reed Sternberg cell and its variants which includes lacunar cells, mononuclear cells, mummified cells and lymphohistiocytic cells (L&H). Reed Sternberg cells are binucleate cells measuring about 15 to 45 micrometers with abundant homogenous granular eosinophilic or amphophilic cytoplasm. Nuclei are vesicular with well defined nuclear membrane and prominent eosinophilic nucleoli. The two nuclear lobes may face each other resulting in owl eye appearance. <sup>(1)</sup>

The possibility that RS cells are clonal B cells that have lost their B cell phenotype due to destructive somatic mutation is yet to be elucidated. Although EBV (Epstein barr virus) has been detected more commonly in mixed cellularity and lymphocyte depleted type of Hodgkin lymphoma, its presence is not mandatory to substantiate the diagnosis. <sup>(4)</sup> The characteristic immunophenotype for Reed-Sternberg cells and Hodgkin (mononuclear cells) is CD15 positive, CD30 positive, CD45 negative. The predominant types of lymphocytes in HL are usually of the CD4 + (helper) T-cell phenotype; these lymphocytes form rosettes around the R-S cells. CD20 + B cells are in a minority. A second antibody highly effective in the identification of H cells and R-S cells is directed against the CD30 antigen. Cautious interpretation of CD 30 positivity is necessary as reactive

immunoblasts, histiocytes and plasma cells are also CD 30 positive. The antibodies for CD30 are Ki-1 in frozen tissues and Ber-H2 on paraffin-embedded tissues. CD30 is also expressed by neoplastic cells in anaplastic large-cell lymphoma. The loss of CD15 expression in Reed Sternberg cells in pediatric classical Hodgkin's lymphoma is said to be a poor prognostic factor. <sup>(1)</sup>

CD45, the leukocyte common antigen (LCA), is expressed in 7% of R-S cells only. Therefore, the combination of CD15+, CD30+, and CD45- is the diagnostic immunophenotype of R-S cells and their variants. CD45 expression does not exclude the presence of R-S cells when CD15 and CD30 are also expressed; however, CD45+ in association with CD15- and CD30- is not consistent with a diagnosis of classical HL. Flow cytometry has little role in the diagnosis of HL because the characteristic R-S cells constitute a minority. Albeit, flow cytometry helps to rule out cases of Non Hodgkin lymphoma. <sup>(1)</sup>

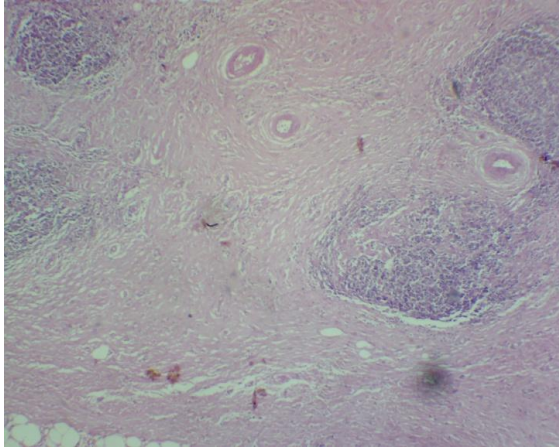
## CASE PRESENTATION

A fifty five year old female presented with a slow growing mass lesion over the fifth rib. She had paroxysmal pain but no systemic symptoms or generalised lymphadenopathy. General condition was good. Complete hemogram was normal. ESR was elevated to 120 mm/hour. X-ray chest and Computed tomography chest revealed an osteolytic lesion destroying the rib and extending into soft tissue. The lung fields were normal and no mediastinal or paratracheal lymph nodes were seen. CT abdomen revealed no specific pathology particularly no organomegaly or lymphadenopathy. The lesion was excised with adequate clearance and sent for histopathological examination.

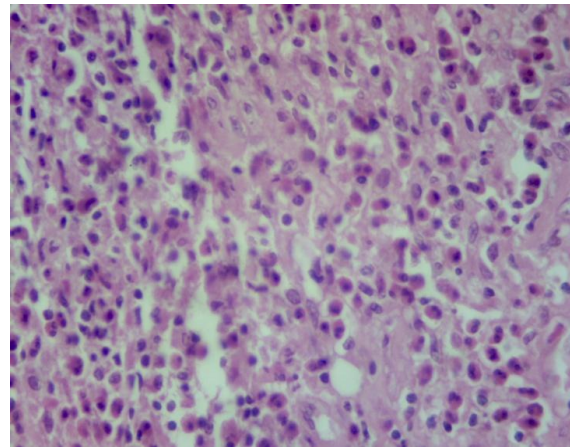
The specimen was routinely fixed in 10% neutral buffered formalin, subjected to routine tissue processing. Grossly cut surface revealed a firm well

defined pale white mass with speckled yellow areas. Histopathological examination revealed a polymorphous population of inflammatory cells separated by broad fibrous bands. Inflammatory cells were predominantly eosinophils and

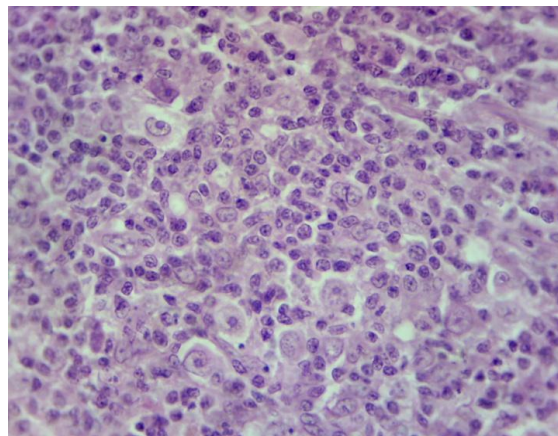
histiocytes with dense collections of neutrophils around the destroyed bone. Occasional large mononuclear Reed Sternberg like cells were seen. The possibility of Langerhans cell histiocytosis and Hodgkin lymphoma were considered.



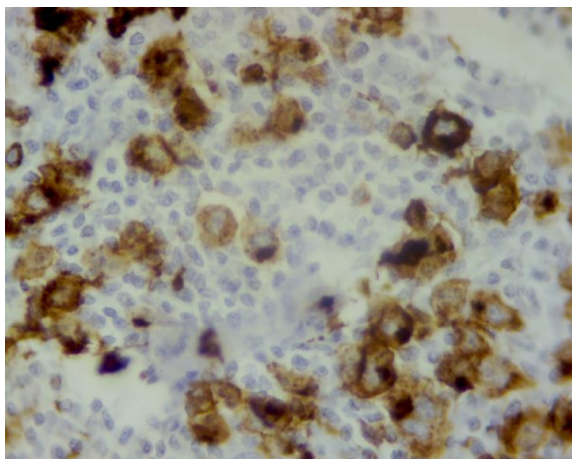
**Figure 1:** Scanner view – histological section shows broad bands of sclerosis ( Haematoxylin and Eosin stain H&E - 4X view)



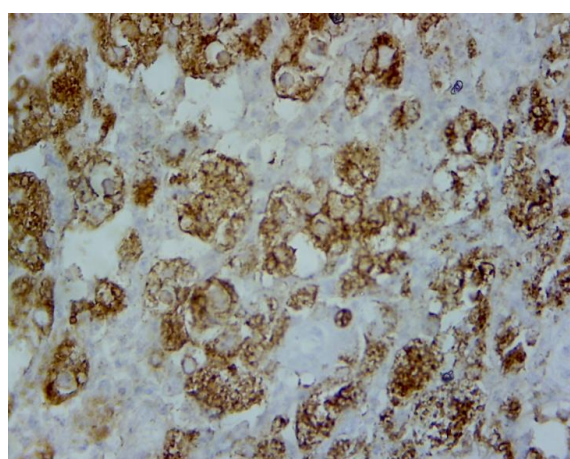
**Figure 2:** High power view shows scattered Reed Sternberg cells in a polymorphous population of inflammatory cells (H&E - 40X)



**Figure 3:** High power view shows many mononuclear Reed Sternberg cells in a polymorphous population of inflammatory cells (H&E - 40X)



**Figure 4:** Immunohistochemistry, high power view shows CD 30 positivity in Reed Sternberg cells. (40 X)



**Figure 5:** Immunohistochemistry, high power view shows CD 15 positivity in Reed Sternberg cells.(40 X)

A panel of antibodies against CD15, CD30, CD 20, CD45, CD3, S 100 and CD1a were used for immunohistochemical analysis. The mononuclear cells were positive for CD 15, CD30. These cells were negative for CD45 and CD3. Other markers were also negative. With these features a diagnosis of Primary extranodal Hodgkin lymphoma – Nodular sclerosis type was made.

## DISCUSSION

Hodgkin lymphomas of classical type are malignant lesions of the lymph nodes having bimodal age distribution. <sup>(4)</sup> The incidence of extranodal lymphoma is less than 1%. <sup>(3)</sup> The extra nodal site for HLs is gastrointestinal tract, lungs, skin, central nervous system and thyroid. Bone involvement is seen in the end stage of Hodgkin lymphoma and rarely Hodgkin lymphoma presents as primary lesion of the bone. <sup>(4)</sup> Primary bone HL involves mandible, scapula, ribs, vertebra, pelvis, femur and tibia. <sup>(2)</sup> Mixed cellularity and nodular sclerosis subtype of classical type of Hodgkin lymphoma are the more common histological types seen in bone. <sup>(4,5)</sup> Hodgkin lymphoma of bone manifests as four different types (1) primary solitary bone lesion; (2) primary multifocal bone lesion; (3) bone and other extra nodal site involvement; and (4) recurrent involvement of bone.

The primary Hodgkin lymphoma of bone is a diagnosis of exclusion. Thorough clinical examination and imaging study is mandatory to exclude secondary involvement. The WHO criteria for diagnosis of primary bone lymphoma are (1) a solitary bone tumor, with or without involvement of regional lymph nodes, and (2) multiple bony lesions without involvement of lymph nodes or viscera. <sup>(6)</sup>

Li et al have reported the first case of primary Hodgkin lymphoma of bone involving the rib occurring in Chinese. <sup>(4)</sup> As per the Ann Arbor staging system, it is

important to differentiate primary osseous Hodgkin lymphoma (stage I disease) from systemic bone involvement, as secondary involvement of bone is equivalent to stage IV disease. Radiological bone involvement of Hodgkin lymphoma can present as lytic or sclerotic lesion with or without periosteal reaction. <sup>(7)</sup> Sclerotic bone lesion is due to invasion from the adjoining lymph nodes. In our case it was lytic bone lesion involving right fifth rib. Studies done recently have suggested that <sup>2</sup>(18F)fluro-2 deoxy-D- glucose positron emission tomography(PET) / computed tomography(CT) helps to differentiate primary Hodgkin lymphoma of bone from systemic Hodgkin lymphoma with secondary invasion of bone. <sup>(8)</sup>

Osteomyelitis, eosinophilic granuloma and peripheral T cell lymphoma have to be differentiated from Primary Hodgkin lymphoma of bone by thorough histological examination. <sup>(5)</sup> Immunohistochemical expression for CD30 and CD15 is absent in eosinophilic granuloma. Eosinophilic granuloma of bone shows clonal neoplastic proliferation of Langerhans cells that express CD1a, S-100 and Langerin. <sup>(4)</sup> Immunohistochemically, most of Non Hodgkin lymphomas of bone are positive for CD45 and B cell or T cell lineage markers with or without CD30 expression. Co-expression of CD15 and CD30, but lacking CD45 expression of tumor cells may be helpful to confirm the diagnosis of Hodgkin lymphoma of bone. <sup>(4)</sup> Thus immunohistochemical studies are required to solve diagnostic confusion between primary Hodgkin lymphoma of bone from the other histopathological entities.

## CONCLUSION

To conclude we report a of primary Hodgkin lymphoma of bone- nodular sclerosis subtype which is a very rare presentation. Complete clinical examination, radiological evaluation, histopathological examination and

immunohistochemistry with broad panel of markers are required to confirm the diagnosis. An accurate and definitive diagnosis with appropriate treatment for these patients will have a great impact on prognosis and survival.

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