Case Report

Osseous Hodgkin's lymphoma with sternal involvement at presentation: Diagnostic challenges

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ABSTRACT

Hodgkin's lymphoma with sternal involvement at presentation is quite unusual. Owing to its rarity, it often poses vexing diagnostic challenges. We herein bring into focus a case of advanced stage Hodgkin's lymphoma, presenting with a sternal mass, initially misdiagnosed and treated as Langerhans cell histiocytosis. On subsequent follow-up, the patient developed recurrence and repeat biopsy and imaging suggested Hodgkin's lymphoma. The case report highlights the importance of clinical suspicion of unusual presentation of lymphohematopoietic tumors of the bone.

Key words: Hodgkin's lymphoma, Langerhans cell histiocytosis, sternal involvement

INTRODUCTION

Nodular sclerosis represents the most common subtype of Hodgkin's lymphoma and usually presents with mediastinal or cervical lymph node enlargement in young adults. Skeletal involvement in Hodgkin's disease is uncommon and seldom encountered at presentation.[1,2] Sternal location of the osseous lesions is even rarer.[3] Langerhans cell histiocytosis (LCH) is a clonal proliferation of specialized myeloid-derived dendritic cells called Langerhans cells, and may be localized, systemic or restricted to an organ system such as bone. In contrast to monoclonal proliferation in lymphoproliferative disorders such as Hodgkin's lymphomas, the cellular proliferation in LCH is polyclonal, and suggests a reactive process, related to immunologic dysregulation. There have been reports of the two entities developing in succession or coexisting in the same specimen, suggesting that a subset of these cases may represent biologic evolution or transdifferentiation of a common neoplastic clone.[4-6] Distinguishing one from the other is important since appropriate management may be delayed for want of timely identification and diagnosis.

We have highlighted the diagnostic dilemma in a case of advanced stage Hodgkin's lymphoma presenting with a sternal mass.

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CASE REPORT

A 25-year-old lady presented to our department with complaints of anterior chest wall swelling, fever and night sweats for one year. Clinical examination showed left parasternal swelling (5 cm × 5 cm) and left supraclavicular lymphadenopathy (2 cm × 1 cm). Two consecutive biopsies from the sternal lesion showed sheets of eosinophils, strongly suggestive of eosinophilic granuloma in spite of immunohistochemistry for S-100 being noncontributory [Figure 1]. Left cervical lymph node biopsy showed similar morphology and was confirmatory for LCH [Figure 2]. Contrast enhanced computed tomography (CECT) chest revealed a destructive lesion involving the sternum with a large soft tissue component and intrathoracic extension, and multiple large prevascular lymph nodes [Figure 3a and b]. Bone marrow examination was normal. The final impression was LCH and the patient was treated with low dose radiation therapy (20 gray in 10

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fractions over 2 weeks) to sternal lesion followed by three cycles of single agent chemotherapy with vinblastine (10 mg intravenous [IV] D1 every 4 weeks).

On follow-up, the sternal lesion showed near-total resolution but the patient developed multiple bilateral cervical and axillary lymph nodes. Repeat CECT chest and abdomen showed thickening of the sternal body and an ill-defined lytic lesion in manubrium sterni with multiple bulky lymph nodes in both axillae, left supraclavicular region, prevascular space, and anterior diaphragmatic region. There were also ill-defined focal splenic lesions with few splenic hilar lymph nodes [Figure 3c and d]. Axillary lymph node biopsy showed Hodgkin's lymphoma, nodular sclerosis, BNLI type II [Figure 4]. The case was discussed with the pathologist and the opinion of Hodgkin's lymphoma, nodular sclerosis, masquerading as LCH was made. The relative abundance of eosinophils and histiocytes had apparently led to the diagnosis of LCH at the outset. However, a closer look in retrospective showed atypical cells in all three biopsy specimens. Immunohistochemistry was positive for both CD30 and CD15 in the biopsy specimen from cervical node and CD30 alone in the specimen from axillary lymph node [Figures 2 and 4].

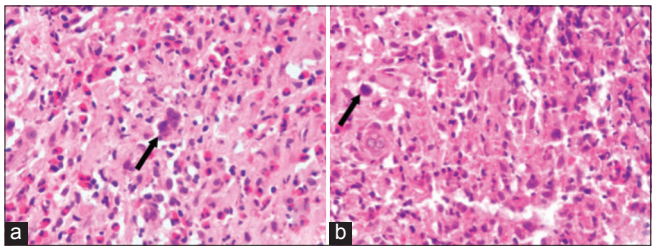

Figure 1: Photomicrograph from the sternal biopsy showing infiltrate rich in eosinophils and histiocytes. (a) Few interspersed atypical cells are seen among the infiltrate (arrow, H and E, ×40). (b) Focus of necrosis is also noted (arrow, H and E, ×40)

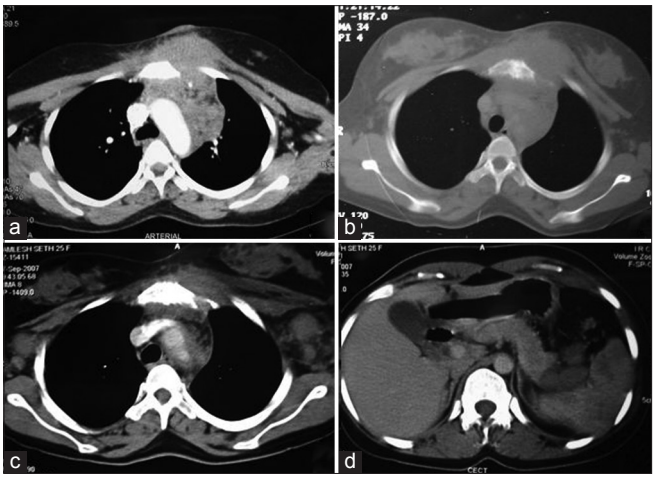

Figure 3: (a and b) Destructive lesion of sternum with large presternal and retrosternal soft tissue mass with mediastinal lymphadenopathy. (c) Postradiation and vinblastine chemotherapy, thickening and irregularity of sternal cortex, significant resolution of presternal and retrosternal soft tissue mass, bilateral axillary lymphadenopathy. (d) Ill-defined focal splenic lesions with few splenic hilar lymph nodes

Repeat bone marrow examination was normal. The diagnosis was revised as Hodgkin's lymphoma, nodular sclerosis, stage IIIBS. The patient received eight cycles of combination chemotherapy with ABVD regimen (adriamycin 25 mg/m^2, bleomycin 10 mg/m^2, vinblastine 6 mg/m^2, dacarbazine 375 mg/m^2 IV D1 and D15 q4 weeks). On the follow-up at 1.5 years, she is in complete clinical and radiological remission.

DISCUSSION

Osseous Hodgkin's lymphoma is a rare disease and thus its diagnosis may pose a challenge to the pathologist as well as the clinician.[2,7] A review of 21 cases of Hodgkin's lymphoma presenting with bone symptoms by Sekine *et al*. showed that most of them had been reported initially as metastatic bone tumor, osteomyelitis, bone sarcoma, and eosinophilic granuloma.[8]

Overlapping clinical and radiologic features make osteomyelitis the most common differential diagnostic entity.[2,9] Two of 25 cases with osseous Hodgkin's lymphoma reported by Ostrowski *et al*. were initially misdiagnosed as osteomyelitis.[2] We have previously described a similar case of skeletal Hodgkin's lymphoma, presenting as a large ulcerofungating sternal mass mimicking the chronic tubercular osteomyelitis in a 21-year-old man.[10] A long-standing discharging sinus, seldom found

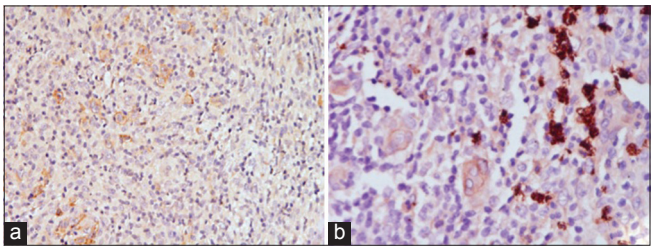

Figure 2: Cervical lymph node biopsy shows similar eosinophil-rich infiltrate admixed with numerous histiocytes along with atypical mononuclear and binucleate cells. Immunohistochemistry is positive for (a) CD30 (×20) and (b) CD15 (×40) in the large cells

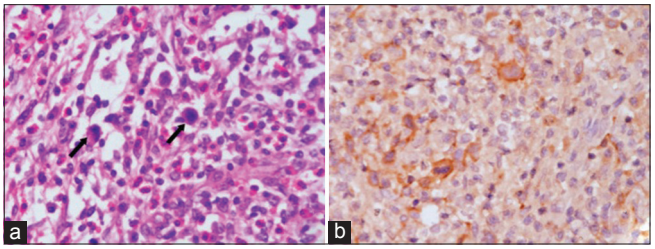

Figure 4: Axillary lymph node biopsy shows thick collagen bundles separating the nodules. (a) High power shows an infiltrate with numerous eosinophils along with atypical mononuclear and multinucleate cells (arrows, H and E, ×40). (b) Immunostaining for CD30 is positive in the large atypical cells (×40).

in lymphoma, is the hallmark of chronic osteomyelitis. There may even be history of extrusion of small bone fragments from the sinus. Acute exacerbations manifesting as pain, fever, increased erythrocyte sedimentation rate, or leukocytosis may mimic B symptoms of lymphoma.[11-13]

Osseous Hodkin's lymphoma has also been misdiagnosed as eosinophilic granuloma or LCH in some occasions, including two of 25 cases in Ostrowski's report.[2,14-16] Manoli *et al*. reported a case of osseous Hodgkin's lymphoma, where initial misdiagnosis as eosinophilic granuloma led to a diagnostic delay of 15 months and eventual death.[16] The abundance of eosinophils in lesions of both eosinophilic granuloma and Hodgkin's lymphoma is the cardinal cause of the diagnostic dilemma.[14,17,18] Immunopositivity for S-100, CD45, CD1a, MHC Class II antigen, and presence of Birbeck granules on ultrastructure favor a diagnosis of LCH.[17]

Langerhans cell histiocytosis may also coexist simultaneously with lymphoma, a rare association that has been described previously.[19-21] Egeler *et al*. have described a series of 91 patients of LCH with second malignancies. Of these, 39 had lymphomas (25 Hodgkin's lymphoma, 14 non-Hodgkin's lymphoma). Among these 39 cases, LCH was diagnosed after lymphoma in 11, the probable pathogenesis postulated as reactive proliferation due to lympholytic chemoradiotherapy. In 24 cases, the diagnosis was made concurrently. In the remaining four, the diagnosis of LCH preceded that of lymphoma, the proposed etiology being malignant evolution of the hyperplastic process.[19] Kjeldsberg and Kim reported 6 cases of lymphoma (3 Hodgkin's lymphoma and 3 non-Hodgkin's lymphoma) having incidental lesions of eosinophilic granuloma in the same lymph node biopsy specimen.[20] Imaging may be unable to distinguish between the two entities. Naumann *et al*. have described two cases of simultaneous Hodgkin's lymphoma and LCH, where 18F-fluorodeoxyglucose positron emission tomography could not distinguish between the two lesion types known pathologically.[21]

The rarity of this disease and the possibility of coexistence or sequential development of lymphoma and LCH, need to be emphasized both for the pathologist, as well as clinician. Both entities have a variable clinical course, treatment and prognosis. Further studies may help distinguish the possible etiopathogenesis mechanisms, and guide appropriate management.

CONCLUSION

Skeletal Hodgkin's lymphoma with sternal involvement at presentation is a distinct rarity and can pose multiple diagnostic challenges. The practicing clinician must be well aware of this entity to circumvent unnecessary delay in institution of treatment and subsequent disease progression.

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