Rare disease

Primary bony Hodgkin's lymphoma

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Hodgkin's lymphoma most commonly presents with progressive painless enlargement of peripheral lymph nodes, especially around the cervical region. At the time of diagnosis osseous involvement is uncommon and even in the late stages only 9–35% of cases have any bony involvement. Rarely Hodgkin's lymphoma presents as an osseous lesion without involvement of lymph nodes, therefore the histological diagnosis of osseous Hodgkin's lymphoma can be problematic. Here, the authors present a rare case of primary osseous Hodgkin's lymphoma and a review of the literature.

BACKGROUND

Hodgkin's lymphoma is typically a systemic disease with involvement of cervical and mediastinal lymph nodes. In late stage Hodgkin's lymphoma, osseous localisations have been described in 10–20% of cases^{1–6} with less than 2% of cases showing skeletal lesions at the time of initial presentation. Few case reports of primary bone Hodgkin's lymphoma, involving either single or multiple bones have to our knowledge been described in the literature^{7–8}). The bones frequently involved are the pelvic bones, humerus, vertebra and femur. The clinical radiological and histological features of this disease can mimic other medical conditions, including osteomyelitis, making the diagnosis difficult and often leading to delay in treatment. Herein, we reviewed the clinical features, radiological findings, microscopic and ancillary studies and differential diagnosis of primary Hodgkin's lymphoma of the spine in a 63-year-old Iranian woman.

CASE PRESENTATION

A 63-year-old Iranian woman presented with low back pain from 1 year ago. She also had irregular low-grade fever. Her pain was dull in character and was moderately intense without any radiating character. The pain was exacerbated by movement. She gave a history of general weakness, anorexia, weight loss and night sweats. There was no history of bleeding manifestation, respiratory, urinary or gastrointestinal symptoms. Established medical problems included rheumatoid arthritis, osteoporosis and hyperthyroidism. She gave a history of partial thyroidectomy 2 years ago. She had received aspirin, propranolol, propyl thiouracil, methotrexate and prednisolon. On examination, the patient was found to be alert and had normal vital sign. There was no lymphadenopathy. There were no petechiae or ecchymoses. On abdominal examination, spleen and liver were not palpable. On local examination, lumbar area was tender on deep palpation, but there was no obvious swelling. Respiratory and cardiovascular system were normal.

INVESTIGATIONS

Investigations revealed a haemoglobin=10.6, total leucocyte count of 14700, platelet count of 461000, alkaline phosphatase of 400 (normal value of 64–306 U/l), lactate dehydrogenase of 750 (normal value of 250–500 U/l), erythrocyte sedimentation rate=108. Given the history of rheumatoid arthritis, concerns about an underlying vasculitic process had been raised. As a result, a series of immunologic studies were ordered to investigate other potential causes of the illness. These investigations revealed positive results for antineutrophil cytoplasmic antibody (ANCA) (PR3-ANCA=35 Eu/ml) (normal value <5 Eu/ml). XR revealed mixed osteolytic and osteosclerotic lesions in l2 and l4 with decreased height of l2 (figure 1A,B). MRI showed hypointense changes in multiple vertebrae, especially in l2 to l5 with pathologic fracture in l2 and l4 (figure 2). Posterior dislocation was seen in l2. The initial clinical impressions were malignancy or collagen vascular disease. We reviewed the glass slides related to previous thyroidectomy which was negative for malignancy. A needle biopsy specimen of the spine showed changes that were indistinguishable from those associated with low-grade chronic inflammation, which was not diagnostic. Inevitably open biopsy performed from lumbar vertebra and the patient underwent vertebroplasty. Histopathological examination of resected bone revealed polymorphic inflammatory cell infiltration separated by fibrous bands. Inflammatory infiltration was composed of reactive lymphocytes, eosinophils and plasma cells. In this reactive cellular background, scattered multilobated and mononuclear Reed–Stenberg cells and lacunar cells were detected (figures 3 and 4). The monoclonal antibodies against CD 15, CD30, CD45, CD20 and CD3 were used for IHC analysis. Reed–Stenberg cells showed positive staining for CD15 and CD30 and were negative for CD45 CD3 and CD20. Histopathological and immunohistochemical features of vertebral bone were concordant with Hodgkin's lymphoma, nodular sclerosis. Cellular bone marrow aspirate and biopsy showed no evidence of lymphomatous infiltration.

Figure 1 (A, B) X-ray revealed mixed osteolytic and osteosclerotic lesions in L2 and L4 with decreased height of L2.

Figure 2 MRI showed hyposignal changes in multiple vertebrae, especially in L2 to L5 with pathologic fracture in L2 and L4.

DIFFERENTIAL DIAGNOSIS

In general, differential diagnosis include osteomyelitis, non-Hodgkin's lymphoma, metastasis, leukaemia and primary bone sarcoma.

TREATMENT

Then ABVD was started and the symptoms resolved immediately. After six cycles of ABVD, the patient achieved complete remission and she refused local radiotherapy.

OUTCOME AND FOLLOW-UP

In the last physical examination (5 months after treatment), general condition of the patient was good and the patient was in remission.

DISCUSSION

In 1832, Thomas Hodgkin first published a small series of cases describing enlargement of lymph nodes or the spleen in which he described 'some morbid appearance of

Figure 3 Section showed inflammatory infiltration composed of reactive lymphocytes, eosinophils and plasma cells with scattered classic Reed–Stenberg cells (x10).

Figure 4 Section showed inflammatory infiltration composed of reactive lymphocytes, eosinophils and plasma cells with scattered classic Reed–Stenberg cells (x40).

the absorbent glands and spleen'.⁹ In the first half of the twentieth century, the identification and classification of this lymphoma was further refined, leading to the names used today for the major types of Hodgkin's lymphoma, nodular sclerosis, mixed cellularity, lymphocyte depletion and nodular lymphocyte predominant. A fifth type, lymphocyte rich was added in 1998.¹⁰ Hodgkin's lymphoma typically involves the lymphatic systems at one or more sites. Bony involvement in Hodgkin lymphoma is seen in the advanced stages. As a matter of fact widespread bony involvement in Hodgkin's lymphoma have been reported but it virtually always occurs in association with extensive lymph nodes.¹¹ Osseous involvement in Hodgkin's lymphoma occurs through hematogenous spread or direct spread from the contiguous involved lymph node. Primary extranodal presentation occurs in approximately 1% of Hodgkin's lymphoma.^{12–13} Primary bone involvement of Hodgkin's lymphoma is particularly rare, occurring in less than 1%. Usually pain is the presenting symptom in primary bone disease. Weight loss and malaise may be absent. Our patient had persistent pain, irregular fever, night sweats and weight loss. Few case reports of Hodgkin's lymphoma, involving either single or multiple bones have been described. The bones frequently involved are the pelvic bones, humerus, vertebra and femur. The presented case had multiple lumbar vertebral bone involvement. Our investigations showed positive cANCA result, although ANCA test, especially cANCA test results may serve clinician as adjunct evidence for the diagnosis of systemic vasculitis, especially Wegener's granulomatosis, several recent reports¹⁴ document false positive cANCA test results in patients with tuberculosis, Hodgkin's lymphoma, HIV infection, nasal septal perforation, monoclonal gammopathies and drug induced Wegener-like disease. Radiologic evaluation reveals osteosclerosis alone, osteolysis alone or a combination of the two. Osteolytic lesions are poorly defined and are associated with periostitis in approximately one-third of the cases.¹⁵ It must be said in parentheses that destruction of bone (osteolysis) or cartilage (chondrolysis) may be an associated feature of numerous neoplastic, infectious, metabolic, traumatic, vascular, congenital or

vascular disorders. A group of heterogeneous conditions remain in which the cause is not known. These conditions are termed primary idiopathic osteolysis syndromes. In our case XR revealed mixed osteolytic and osteosclerotic lesions in L2 and L4 with decreased height of L2 (figure 1A,B). MRI showed hypointense changes in multiple vertebrae, especially in L2 to L5 with pathologic fracture in L2 and L4 (figure 2). Posterior dislocation was seen in L2. Tc 99 bone scan may disclose other clinically unapparent sites of bone involvement. Histologically, mixed cellularity and nodular sclerosis are commonly observed subtypes of Hodgkin's lymphoma. Identification of Reed–Stenberg or their variants in the appropriate non-neoplastic background consisting of lymphocytes, granulocytes, histiocytes, plasma cells and fibroblasts is required for diagnosis. Immunohistochemistry of Reed–Stenberg cells for CD 15 and CD 30 confirms the diagnosis. Our case was nodular sclerosis subtype of primary osseous Hodgkin's lymphoma and was confirmed by IHC methods. The histologic picture is sometimes confusing and small biopsy specimens are often not diagnostic, it was true about our case. In a series of 17 cases¹⁶ the initial histological diagnosis was variously reported as paget disease, metastatic tumour, chronic osteomyelitis, primary sarcoma and Ewing sarcoma. In general differential diagnosis include osteomyelitis, non-Hodgkin's lymphoma, metastasis, leukaemia and primary bone sarcoma. Patients with one or multiple bone lesions usually respond well to combined modality treatment including chemotherapy and local radiotherapy. Our patient underwent vertebroplasty and received chemotherapy. The question remains as to whether primary osseous Hodgkin lymphoma has a better prognosis than Hodgkin lymphoma with bony involvement. We think that this patient must be considered as a stage IV B of disease because of B symptoms and multiple bones involvement. Although the patient responded very well to chemotherapy, we think her prognosis will be poor. Surgery should be considered for lesions that present a risk of pathological fracture. In conclusion since there have not yet been any characteristic symptoms, laboratory or radiologic findings identified, the diagnosis of osseous Hodgkin's lymphoma is difficult and may be delayed.

Learning points

- ▶ Primary bone involvement of Hodgkin's lymphoma is particularly rare, occurring in less than 1% of cases.
- ▶ The clinical, radiological and histological features of this disease can mimic other medical conditions, including osteomyelitis, making the diagnosis difficult and often leading to delay in treatment.
- ▶ Since there have not yet been any characteristic symptoms, laboratory or radiologic findings identified, the diagnosis of osseous Hodgkin's lymphoma is difficult.
- ▶ Patients with one or multiple bone lesions usually respond well to combined modality treatment including chemotherapy and local radiotherapy.

Competing interests None.

Patient consent Obtained.

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