Primary Hodgkin's Lymphoma With Chest Wall Ulceration and Hypereosinophilia: A Rare Presentation and Diagnostic Dilemma

Wan Ahmad Syahril[1], Tumian Nur Rafeah

From [1]Department of Internal Medicine, Kulliyyah of Medicine, International Islamic University Malaysia, Kuantan, Pahang, [2]Department of Internal Medicine, Faculty of Medicine, Pusat Perubatan Universiti Kebangsaan Malaysia, Jalan Yaacob Latif, Kuala Lumpur, Malaysia

Correspondence to: Dr. Wan Ahmad Syahril Rozli, Kulliyyah of Medicine, International Islamic University Malaysia, Kuantan, Pahang, Malaysia. Phone: +6095574712/+60199538513. E-mail: wasrwa76@hotmail.com

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ABSTRACT

Hodgkin's lymphoma (HL) with cutaneous manifestation is a rare condition which usually occurred late in the course of the disease. Due to its rare presentation, misdiagnoses are common. We report a 26-year-old Chinese gentleman who presented with painless and large anterior chest wall ulceration. Computed tomography scan showed sternal mass and erosion, with skin and anterior mediastinal extension. The second histopathologic examination (with immunohistochemistry) of the skin biopsy showed HL with mixed cellularity pattern. However, there was a marked dominance of eosinophils in both the peripheral blood and the tissue samples. This was a very unusual presentation of extranodal HL with ulceration and pronounced hypereosinophilia. The diagnosis was only made after the second biopsy because of the rare occurrence.

Key words: *Hypereosinophilia, Primary Hodgkin's lymphoma, Sternal erosion*

Hodgkin's lymphoma (HL) usually presents as lymph nodes enlargement with a contiguous spread from one nodal group to the next along the lymphatic pathways. Chest wall area is a rare site of HL presentation, and not much has been reported in the literature, especially the isolated primary type [1]. Skin involvement in HL usually in the form of chronic ulceration, and occurs later in the course of the disease. It presents as a primary disease or as a result of cutaneous spread from a systemic disease. Commonly, the ulcers are necrotic, multiple, infected, and occur on the tumor itself [2]. Primary bone involvement in HL is extremely rare, in about 1% of the cases [3,4]. The dilemma in management usually arises in determining whether the lesion represents primary manifestation or dissemination of systemic disease, because dissemination has a poorer prognosis [4]. Despite sparse data available, it is known that HL patients who present with skin ulceration have poorer prognosis, albeit better than non-HL [4]. We report this rare case to point the importance of repeating the tests especially in cases that did not fit well with the clinical presentation.

CASE REPORT

A 26-year-old Chinese gentleman presented with painless and progressively enlarging anterior chest wall ulceration for 5 months, with no constitutional symptoms. He denied swelling in any other part of the body, night sweats, cough, or evening rise of temperature. There was also no significant past medical or surgical history. On examination, the blood pressure was 134/78 mmHg, and pulse was 74 beats per minute. General examination was not remarkable, and there was no palpable cervical or inguinal lymphadenopathy. Clinically, there was an ulceration measuring approximately about 8 cm×10 cm in diameter located at the upper midsternal area, and the surface was full of slough (Fig. 1). There was no discharge. Abdominal examination revealed no organomegaly and the rest of the systemic examination was unremarkable.

Blood tests revealed a hemoglobin level of 14.4 g/dL, with elevated erythrocyte sedimentation rate of 69 mm/h and lactate dehydrogenase (LDH) of 268 U/L. The full blood picture (FBP) test was also normal. It was worked out in the line of a chronic infected wound of an unknown cause with malignancy as one of the primary diagnosis. Computed tomography (CT) scan showed a soft tissue mass at the upper margin of the manubrium sternum to the midbody of the sternum, measuring 6 cm×10.3 cm (width) ×8.4cm (length). There was associated bony destruction of the manubrium sterni, with an enlarged right pretracheal node (2.4 cm×2.5 cm), and multiple subcentimeter supraclavicular, and axillary lymph nodes bilaterally (Fig. 2). Biopsy taken from the ulcer showed underlying vasculitis process with eosinophilia. Both the histology and the histochemical staining of the mononuclear cells for lymphoma were negative in the first biopsy. The patient defaulted his follow-up in the clinic and requested for at own risk discharge from the ward. He only later turned up to the clinic 1 month after that.

A repeat CT scan subsequently to check for suspected progression showed the destruction of the manubrium sterni as well as an extension of the mass into the anterior mediastinum (Fig. 3). There were also multiple enlarging axillary nodes

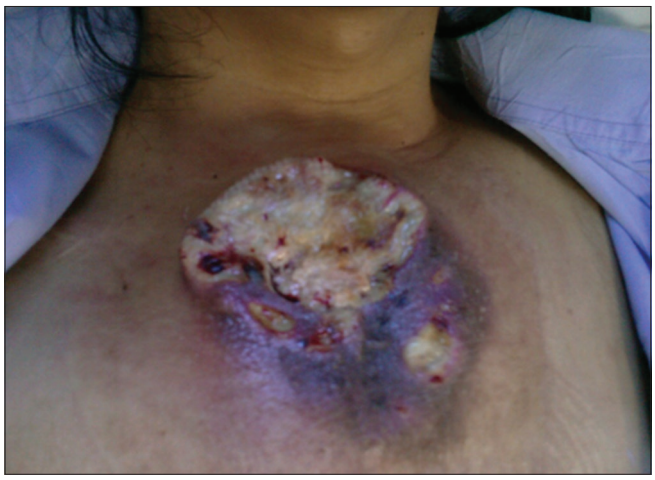

Figure 1: Photograph of the anterior chest wall depicting ulceration in the patient

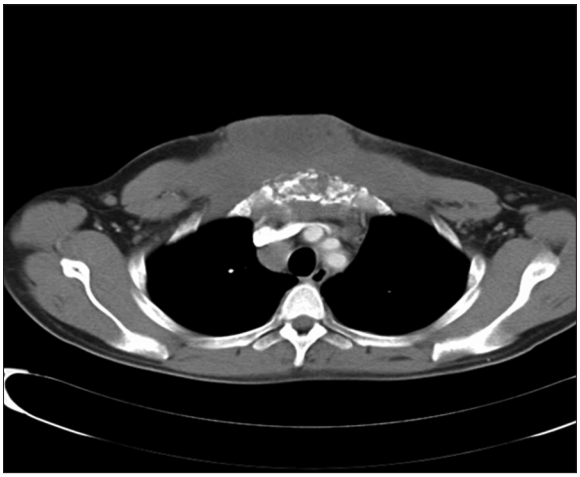

Figure 2: CT Thorax of the patient showing a large anterior chest wall mass with sternal erosion

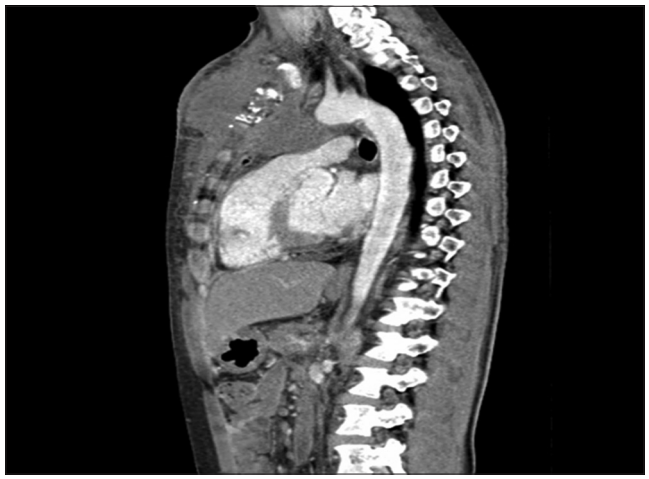

Figure 3: Sagittal section of the CT Thorax showing a large anterior chest wall mass extending into the anterior mediastinum, with associated sternal erosion

compared from before, largest measuring 1.3 cm on the left and 1.4 cm on the right. A second biopsy of the same lesion was taken after 1 month and was consistent with HL with mixed cellularity pattern; with the presence of Reed - Sternberg cells and multiple eosinophils. Immunohistochemistry study showed the malignant cells were positive for CD30, CD15, CD79a, and negative for CK, LCA, CD20, and CD45. Another histochemical staining was all negative.

The repeat FBP did not show any immature blast cells, but there was again a significant elevation of eosinophils of 27.3% of the total white blood cell differential count. The repeat LDH level was not elevated. Bone marrow and trephine biopsy examination showed reactive marrow without evidence of lymphoma infiltration. Connective tissue disease screening was negative. Serum Complement C3/C4 levels were also normal; with normal serum Beta-2 Macroglobulin of 2.15 µg/ml. Vasculitis screening of antineutrophil cytoplasmic antibodies and also serum cryoglobulins were also normal. Swab Culture grew *Pseudomonas* sp., which was most likely due to colonization. The calcium, phosphate, and alkaline phosphatase were all within normal levels even with the presence of sternal erosion. The patient was planned for chemotherapy but defaulted.

DISCUSSION

The incidence of HL peaks above the age of 70 years [1]. Chronic skin ulceration in lymphoma is rare and usually signifies poor prognosis. Bone involvement rarely presents as initial presentation; instead, it occurs later in about 10–20% cases in the course of the disease [3]. There have been many case reports of malignant Non-Hodgkin Lymphoma with a solitary chest wall mass, but chest wall ulceration itself is a rare presentation of HL and only occurs in about 6.4% of the total cases [5,6].

We were having difficulty to assess this patient initially, especially because he did not turn up for scheduled follow-ups, and also no other points to suggest underlying malignancy. Clinically, there was no other lymph nodes enlargement. The initial biopsy result showed evidence of vasculitis with wall infiltration and surrounding area of necrosis. The cellular infiltrate was polymorphous and not suggestive of a lymphomatous process. The findings of the first biopsy also open to a possibility of connective tissue disease, because of the presence of multiple eosinophils with vasculitis in the sample. However, all the vasculitis screenings were negative.

A repeat biopsy was done out of suspicion and showed mixed cellularity type of HL, less common than the nodular sclerosing type. The mixed cellularity type is the second most common type, with 15–30% incidence. However, the other organs involvement in mixed cellularity type is not common, with only 1–3% incidence [7]. The biopsy also showed the presence of Reed–Sternberg cells, with CD30, CD15, and CD79a positive. The positivity of CD 15 and CD 30 has excluded thymoma from the differential diagnosis [8]. The eosinophilic infiltration is another rare presentation in this patient. Connective tissue disease screening tests were negative, and complement levels were normal. The eosinophilia can be explained by the cellular type of Hodgkin's disease. The mixed cellularity histologic type of Hodgkin's

disease has a multiple, and diffuse pattern of cellular infiltration, with background infiltrates of eosinophils and Reed–Sternberg cells. Reed–Sternberg cells produce chemoattractant that recruits eosinophils and produce tissue eosinophilia. Interleukin 5 also increases marrow production of eosinophils through ProGrowth and survival effects on eosinophilic precursors. This may lead to the wrong interpretation of it as having eosinophil infiltrates; which may lead to a false interpretation [9].

The presence of sternal erosion in association with HL is confusing because bony erosions are also related to tuberculosis, small cell bone tumors or osteomyelitis [10]. However, there were no clinical signs or symptoms pointing toward tuberculosis. The biopsy also did not show any evidence of granulomatous changes, nor any evidence of other infections or small cell bone tumor. Radiographic bone involvement is seen in 20% of patients with Hodgkin's disease, and in 4% as initial presentation [7]. The sternum is commonly involved, and the lesion is usually lytic in nature, followed by skull, ribs, and scapula, with soft tissue involvement. The bony lesions may be lytic, sclerotic, or mixed, whereby 90% of the lesion is usually lytic and mixed type. In another survey, axial skeleton is more commonly involved (77%) than appendicular skeleton (23%) [8]. The surveys also showed that majority present between the ages of 20 and 30 years [11].

It is important to determine whether the cutaneous involvement is the primary manifestation or dissemination of systemic disease because of differing prognosis. This presentation was primary in view of negative bone marrow and Trephine biopsy results. The whole-body CT scan also showed no other suspicious mass, apart from multiple subcentimeter cervicals and para-aortic lymph nodes. Apart from the axillary lymph nodes measuring about 1.3 cm in diameter, other lymph nodes were not enlarging in size comparing with the two serial CT scans made for the patient within the 6 months period.

The effective treatment for primary sternal HL is unclear because of its rarity, but it was suggested that patients undergo chemoradiotherapy [11]. The overall 10-year survival rate is slightly <90 %, which is better than non-HL of similar presentation.

CONCLUSION

Primary sternal Hodgkin's disease with eosinophilia is rare, and misdiagnoses are common. This case illustrates the importance of having a high index of suspicion toward malignancy, even though there was no evidence showed in the first presentation. A repeat biopsy including clinical and radiologic assessment should always be considered in patients; especially, if it did not correlate well with the clinical presentation.

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