Rare disease

Hodgkin's lymphoma with cutaneous involvement

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Summary

We report a case of a 22-year-old previously healthy woman with Hodgkin's lymphoma who presented initially with multiple lymphadenopathy and later, with a solitary cutaneous ulcer. Unlike Non-Hodgkin's lymphoma subtypes, skin involvement of Hodgkin's lymphoma is extremely rare. The prognosis of Hodgkin's lymphoma with skin infiltration is felt to be extremely poor. Contrary to other reports, this case demonstrates that a good response with standard therapy is possible.

BACKGROUND

Hodgkin's lymphoma (HL), previously known as Hodgkin's disease is a type of lymphoma, originating from white blood cells called lymphocytes. HL is characterised by the orderly spread of disease from one lymph node group to another and almost always begins in lymph nodes and accounts for 0.58% of all cancers diagnosed.¹ The incidence of HL has a bimodal peak as a function of age.¹ More than 80% of patients present with cervical lymph node involvement, and more than 50% have mediastinal disease. Isolated extralymphatic involvement in the absence of nodal disease is rare. Patients usually present with painless lymphadenopathy. One-third of the patients present with B symptoms such as unexplained fever, drenching night sweats and weight loss.² Visceral involvement by HL may be secondary to extension from adjacent lymph node regions or it may be haematogenous, such as nodular disease in the liver, spleen or multiple bony sites. HL only rarely involves the gut-associated lymphoid tissues such as Waldeyer's ring and Peyer's patches, upper aerodigestive tract, central nervous system and skin.² HL in the skin represents an incidence of 0.5%.³ We report a case of a 22-year-old previously healthy woman with HL who presented initially with multiple lymphadenopathy and later, with a solitary cutaneous ulcer over the mid-chest area.

CASE PRESENTATION

A 22-year woman presented with 2-year-old history of multiple swellings over bilateral neck and axilla and later a fungating mass over the mid-chest. The swellings were insidious in onset, gradually progressive in nature and were associated with pain which was severe in intensity and relieved only after medication. Patient also gave a history of fever, cough with expectoration, night sweats and uneasiness. General physical examination revealed multiple, enlarged, hard lymphadenopathy in bilateral cervical, axillary and inguinal region associated with hepatomegaly. Examination of the chest revealed a fungating mass 2.0×1.5 cm in size, over the mid region of chest (figure 1).

INVESTIGATIONS

Routine blood biochemistry parameters were within normal limits. Chest x-ray revealed radiodense non-homogenous opacity in bilateral parahilar region and lower lobe of right lung extending peripherally up to right lateral chest wall (figure 2). Contrast CT scan confirmed bilateral mediastinal and hilar lymphadenopathy with parenchymal lesions in the lung and involvement of right anterior chest wall, right parasternal region and skin and partly compressing the right bronchus (figures 3 and 4). Positron emission tomography (PET) scan revealed multiple lymphadenopathy with diffuse involvement of axial skeleton. 18F-fludeoxyglucose (FDG) whole body PET-CT scan revealed enlarged bilateral level II–V cervical and supraclavicular lymph nodes, bilateral axillary level I–III paratracheal, anterior mediastinal, prevascular, aortopulmonary window, subcarinal, right internal mammary, right intercostal and bilateral hilar lymph nodes. A pleural based opacity was noted in the anterior part right lung lower lobe (figure 5). FDG-avid supra-diaphragmatic lymph node was seen. Abdominal and pelvic examination

Figure 1 Pretreatment photograph showing fungating mass with ulceration over the mid-chest region.

Figure 2 Chest x-ray showing radio-dense non-homogenous opacity in bilateral parahilar region and right-lower lobe of lung extending peripherally up to right-lateral chest wall.

revealed FDG accumulation in peripancreatic, paraaortic and hepatogastric lymph nodes. Histopathological examination of the excision biopsy of cervical lymph node and punch biopsy from the ulcerative lesion revealed HL with nodular sclerosis type.

DIFFERENTIAL DIAGNOSIS

The diagnosis of classic HL requires pathological identification of characteristic binucleated tumour cells (Reed-Sternberg cells),³ or mononuclear cells (Hodgkin's cells) within an inflammatory milieu. These malignant cells represent 0.1–10% of all cells in a biopsy, are derived from germinal centre B cells in more than 98%, and are

distributed in a background of reactive cells.^{4 5} Typically, these cells stain positively for CD15 and CD30 but not CD20.¹ Other than HL, cells resembling Reed-Sternberg cells may be present in other B and T cell lymphomas, carcinomas, melanomas and sarcomas.⁵ In particular, HL must be distinguished from other conditions that present with cutaneous lesions such as mycosis fungoides, granulomatous slack skin disease (cutaneous T-cell lymphomas), eosinophilic granuloma, histiocytic lymphoma, lymphomatoid papulosis and anaplastic large cell lymphoma. The latter two may also have CD30 positive cells and require the more specific CD15 positive expression to be differentiated from HL.

TREATMENT

There is no specific treatment for HL with skin lesions. Standard treatment is chemotherapy with ABVD/BEACOPP/Stanford V with or without involved field radiation depending on the stage and bulk of the disease.⁵ Among these the most common chemotherapy protocol used as in our present case is ABVD, that is, doxorubicin 25 mg/m², bleomycin 10 mg/m², vinblastine 6 mg/m² and dacarbazine 375 mg/m² as days 1 and 15 schedules and to be repeated after every 28 days for 6–8 cycles.⁵ Skin lesions due to HL, as in our case, have been reported to respond to current standard treatment without further therapeutic modalities such as surgical excision, topical therapy or local cutaneous radiation (figure 6).

OUTCOME AND FOLLOW-UP

Overall HL has good prognosis with greater than 80% 5-year survival.⁵ However, cutaneous involvement is usually associated with diffuse lymphadenopathy, late stage disease and poor prognosis.³ Our case was an exception; the outcome was favourable with a good dermatological response. Rare cases of cutaneous HL with indolent clinical courses have previously been described showing slow progression to generalised lymphadenopathy over years. Thus, it is important to recognise this malignancy, complete the appropriate work-up for staging and initiate prompt treatment.

Figure 3 Transverse section of contrast enhanced computed tomography of thorax showing enhancing mass lesion in right parasternal region in right-anterior chest wall and right hilar region partly compressing the right bronchus.

Figure 4 Transverse section of contrast enhanced computed tomography of thorax showing enhancing mass lesion in right parasternal, parenchymal and in lower lobe of the right lung extending peripherally up to right lateral chest wall.

DISCUSSION

HL accounts for 0.58% of all cancers diagnosed. There is a slight male predominance (1.1:1). The incidence of HL has a bimodal peak as a function of age, early peak, from

ages 25–30 years and second peak, from ages 75 to 80 years.¹ Aetiology and pathogenesis of this disease remains unknown. A few risk factors such as familial predisposition, infections with Epstein-Barr virus or

Figure 5 18F-fludeoxyglucose positron emission tomography-CT whole body scan showing viable primary pathology involving the lymph node groups on both sides of the diaphragm and viable metastasis to right lung.

Figure 6 Post-treatment photograph showing mid-chest region with good remission.

HIV and immune suppression have been implicated.² This disease has been divided into two major groups according to the WHO: the rare nodular lymphocyte-predominant and classical HL. Classical HL contains four subtypes: nodular sclerosis, mixed cellularity, lymphocyte rich and lymphocyte depleted. Each subtype has its own clinical features, pathological characteristics and prognosis.⁴ Patients with HL usually present with painless lymphadenopathy. One-third of the patients present with B symptoms such as unexplained fever, drenching night sweats and weight loss and they have poor prognosis.⁴ Ninety per cent of patients present with contiguous sites of involvement. Visceral involvement by HL may be secondary to extension from adjacent lymph node regions or it may be haematogenous, such as nodular disease in the liver, spleen or multiple bony sites.^{4 5} HL only rarely involves the gut-associated lymphoid tissues such as Waldeyer's ring and Peyer's patches. It also very rarely involves the upper aerodigestive tract, central nervous system and skin.² It is extremely rare to have extranodal involvement of other organs, the central nervous system or the integument—as in our patient.²

Non-specific skin involvement such as pruritus, hyperpigmentation, urticaria, erythroderma or acquired ichthyosis occurs in 17–53%. However, these are thought to be paraneoplastic syndromes rather than direct tumour infiltration. Direct tumour involvement is extremely rare. In 1906, Grosz reported the first case of a patient with Hodgkin's disease and multiple brownish, lentil to walnut-sized, ulcerating nodules.⁵ Since then, the incidence has been reported to occur in 0.5–3.4% of HL patients. The number of cases had diminished over time

due to improved treatments and the utilisation of stem cell transplantation for relapsed disease. Most common form of presentation is single or multiple dermal or subcutaneous nodules that become ulcerated and involve the skin area over the chest.³ The mechanism for the skin involvement in HL is not known but postulated to be retrograde lymphatic spread from tumour-involved lymph nodes, direct extension into skin by tumour cells in underlying lymph nodes, or haematogenous spread of the tumour.^{1 2}

CT scan of chest helps to evaluate the extent of intrathoracic spread. An abdominal and pelvic CT scan should be obtained to evaluate enlarged nodes in the retroperitoneal area, hepatosplenomegaly or focal nodules in the spleen or liver.² FDG-PET is more sensitive than CT for initial staging and for follow-up study to evaluate residual disease. A needle biopsy of the posterior iliac crest bone marrow should be restricted to patients with B symptoms or clinical evidence of subdiaphragmatic disease, because the yield is exceedingly low in asymptomatic patients with limited clinical disease. The overall incidence of bone marrow involvement in HL is only 5%. According to Ann Arbor staging system, skin involvement in HL is stage IV disease.²

Learning points

- ▶ Although cutaneous involvement of Hodgkin's lymphoma (HL) is extremely rare, it merits consideration in the category of atypical causes of non-specific papules, plaques and ulcers; therefore, enlisting a haematopathologist may be required.
- ▶ 18F-fludeoxyglucose whole body positron emission tomography-CT scan is an important diagnostic tool in establishing the diagnosis and extension of the disease.
- ▶ Contrary to most reported cases of HL involving skin, our case demonstrates that a good response with adequate therapy is possible.

Competing interests None.

Patient consent Obtained.

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