Scrofuloderma-Like Lesions in a Patient with Hodgkin's Disease

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Abstract

A 15-year-old boy presented with several months history of bilateral axillary lymph adenopathies which were ulcerated subsequently. He had received anti-tuberculosis therapy for more than six months based on suspicious diagnosis of scrofuloderma. Histopathologic examination confirmed the diagnosis of specific lesions of Hodgkin's disease. These lesions were probably metastatic due to retrograde lymphatic spread from his axillary lymph nodes, as this way is the most common mode of Hodgkin's disease spreading to the skin. The patient received chemotherapy regimen for Hodgkin's disease and ulcers resolved remarkably.

Keywords: Hodgkin's disease, cutaneous Hodgkin's disease, scrofuloderma

Introduction

Hodgkin's disease (HD) is a malignant condition of lymphoid origin, characterized by painless swelling of superficial lymph nodes or as an asymptomatic mass on chest X ray. The diagnosis is made based on the finding of Hodgkin / Reed-Stenberg cells on an appropriate cellular background of reactive lymphocytes. It rarely involves the skin primarily and usually presents only in the setting of advanced (stage IV) nodal or visceral disease[1,2]. Skin involvement has been reported in 17% to 53% of patients with HD. Paraneoplastic, non specific findings are more common than specific cutaneous finding of HD[3-5].

Case Report

In September 2006, a 15-year-old boy referred to our dermatology clinic for further evaluation of his suspicious scrofuloderma lesions being refractory to treatment. He presented with multiple axillary lymph adenopathies which were subsequently ulcerated and had a discharge for one year. He received anti-tuberculosis therapy for six months based on suspicious diagnosis of scrofuloderma, in spite of a negative smear and culture for *Mycobacterium tuberculosis* and a suspicious PPD test result (7 mm induration).

In clinical examination, multiple, bilateral, axillary and unilateral inguinal lymph adenopathies

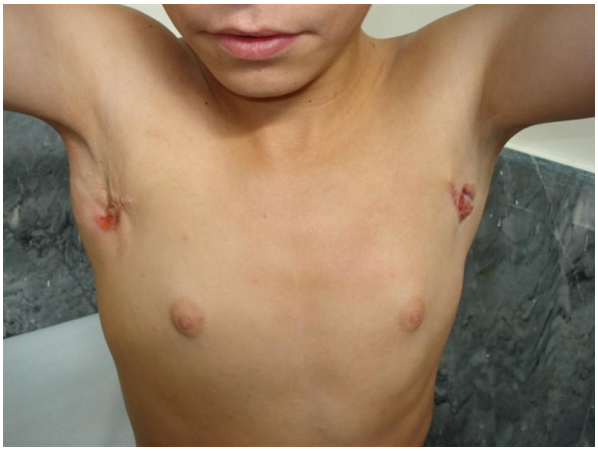


Figure 1. *Axillary ulcers with undermined edge and bloody discharge as well as multiple lymph adenopathies*

were found, which were non tender and immobile, with stony consistency and variable size. In the axillary region, there were ulcers measuring 3 x 4 cm and 3 x 3 cm in diameter with sharp undermined edges and granulation tissue at the base. Multiple fibrosing scars around the ulcers and a bloody stained discharge were also noted (figure 1).

Further systemic examination revealed no remarkable findings but a just palpable spleen. No constitutional symptoms such as fever, night rigors, weight loss, chronic cough, bloody sputum, diarrhea, recurrent infections and generalized pruritus were present. There was no history of tuberculosis in his family.

Except for hypochromic microcytic anemia, other laboratory findings such as white blood cells, platelets, erythrocyte sedimentation rate and CRP were normal. Tuberculin test was negative. Chest X-ray was normal. Computed tumography scan confirmed enlargement of palpable lymph nodes but showed no lymph adenopathies in the thorax, abdomen or pelvis. Abdominal ultrasonography revealed splenomegaly. The histopathological examination of an ulcerated lesion biopsy specimen showed dense and diffuse monomorphic infiltration of small lymphocytes in a background of numerous dilated vessels in the dermis, with invasion of these lymphocytes to the epidermis. Although there were a few indefinite mononuclear cells with mild atypia, Reed-Sternberg cells were not found. Ziehl-Neelsen and Periodic Acid-Schiff stainings were negative. These clinical findings were consistent with a malignant tumor with mesenchymal origin or an infectious disease such as scrofuloderma, actinomycosis, fungal infection or Crohn's disease. Cultures of the biopsy specimen for bacteria, mycobacteria and fungi were all negative. Soon after the first biopsy, total excisional biopsy from the inguinal lymph nodes was performed. The specimen exhibited a dense infiltrate of monomorphic lymphocytes, some histiocytes and neutrophils and scattered eosinophils. There were multiple neoplastic mononuclear cells resembling Reed-Stenberg cells in a nodular background with fibrosis (figure 2).

In immunohistochemical (IHC) studies, the atypical cells expressed CD20, CD45 (LCA), and also Ki67 (table 1) (figure 3). Thus the diagnosis of HD (lymphocyte predominant type) was considered on the ground of skin and lymph node biopsies and IHC study. A bone marrow biopsy showed good cellularity with no evidence of invasion by HD cells. The patient was referred to an oncology center and after six cycles of COPP (cyclophosphamide, vincristine, procarbazine and prednisolone) therapy, the ulcers were remarkably resolved.

Discussion

The cutaneous manifestations of HD include skin lesions with histological features of HD and other non-specific, paraneoplastic skin lesions. Non-specific lesions are more common than primary HD of the skin and are estimated to develop in 10–50% of patients with HD[6]. The most well-recognized paraneoplastic finding is severe pruritis, but other nonspecific findings such as urticaria, erythroderma, erythema nodosum, erythema multiforme, pigmentation, herpes zoster and acquired icthyosis have also been described in association with HD[4,7].

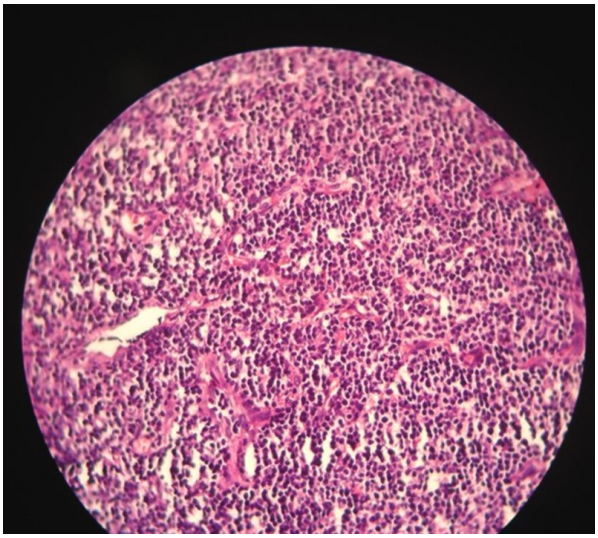
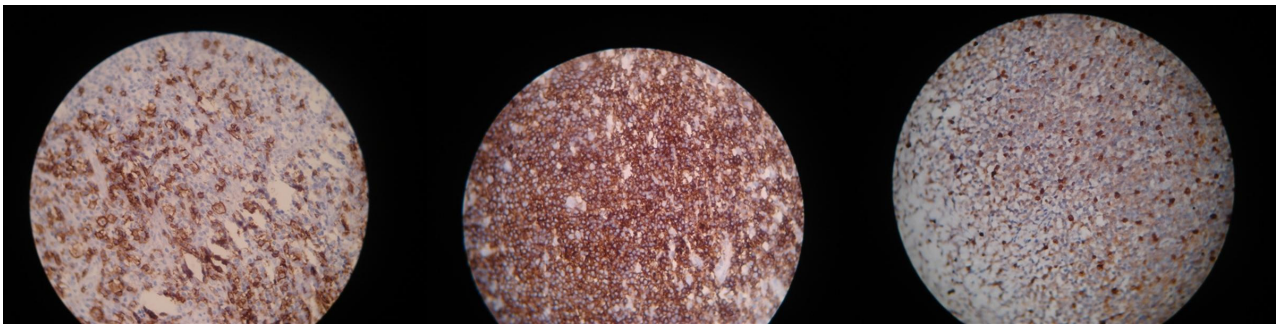


Figure 2. *Dense infiltrate of monomorphic lymphocytes and a few Reed-Stenberg cells in a nodular background with fibrosis in lymph node (H&E staining, magnification 40 x)*



A B C

Figure 3. *Positive IHC results for CD20 (A), CD45 (LCA) (B) and Ki67(C)*

The first report of specific cutaneous lesions of HD was that of Grosz in 1906[2]. The frequency of these lesions ranges from 0.5% to 7.5%[1,2,8,9] and they usually represent stage 4 of the disease which carries a poor prognosis[1,2,9-11]. In a retrospective chart review of 1049 HD patients, only three patients presented with cutaneous HD and two of them had progressive HD with ulcerated nodules on their chest.[12]

HD of the skin may present as papules, nodules, plaques or diffuse infiltration, and the larger lesions tend to ulcerate, as in our patient. The most common presentations are popular and/or nodular lesions[13]. There are few reports of ulceration, sinus formation or fistulization of skin lesions in HD[14-19]. Also there is a report of HD mimicking scrofuloderma from Japan in 1999, similar to our patient[20].

Ulcerative lesions can be divided into three types: (i) Grosz-Hirschfield type where nodules ulcerate; (ii) Coleman Anderson type where ulceration develops in the skin directly infiltrated from underlying lymph node or other tissue; and (iii) Dossekker-Kren-Saalfeld type ,which occurs when a primary cutaneous Hodgkin s lesions ulcerates .

Table 1: *Results of IHC evaluation with various markers of Reed-Stenberg cells in the lymph node specimen*

Marker	Result
CD20	+
CD45 (LCA)	+
CD8	-
CD30	-
CD15	-
Ki67	+
S100	-
CD1a	-
CD68	-

Three mechanisms for cutaneous involvement in HD are thought to occur: retrograde lymphatic spread to involved lymph nodes; direct extension from an underlying nodal focus; haematogenous dissemination, of which retrograde lymphatic spread is considered to be the most common route[1,2].

Because of the proximity of the ulcerated lesions to axillary lymph nodes, it is thought that skin involvement in our patient was due to retrograde lymphatic spread from involved lymph nodes. In most reported cases nodal involvement preceded the appearance of the skin lesions by 5 months to 9 years[1,8]. In this patient, lymph adenopathies appeared several months before the development of skin lesions. However, Smithers reported one case in which skin involvement preceded nodal disease[21], and in two other cases the disease presented with simultaneous skin and nodal involvement[1,8]. Primary cutaneous HD or skin involvement without disease at any other site is far less common, with only sporadic cases reported[6,22].

Although skin invasion by HD has a poor prognosis in almost all documented cases, in a 9-month follow-up of this patient, cytostatic therapy resulted in favorable responses in both skin and lymph nodes. Smith and Butler[6] reported 3 of 9 patients who survived 13 to 24 months after the diagnosis of skin invasion, and one with no evidence of recurrence after 6 years[1]. Two case reports indicate that long-term survival is possible on maintenance chemotherapy. These cases survived 3 years and 5 years, respectively, although neither one had a disease-free remission[10,23]. As our patient, the case of scrofuloderma-like lesions in 1996 remained in complete remission for more than 9 months[13].

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