Skin Involvement in Hodgkin's Disease: A Case Report

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Skin involvement of Hodgkin's disease, which typically occurs in the advanced stage, is rare and is associated with a poor prognosis. We report a case of Hodgkin's disease which recurred solely in the skin and followed a favorable clinical course. A 44-year-old Japanese man was diagnosed as having a mediastinal Hodgkin's disease in January 1983. After a complete remission, recurrent skin tumors appeared in the left supraclavicular and anterior chest regions in March 1988. No evidence of lymph nodes or visceral organ involvement was detected. The tumors regressed after chemotherapy. There is no evidence of the disease 7 months after discharge.

Key words: Lymphoma, Extranodal, Mediastinum

Unlike non-Hodgkin's lymphomas, in which skin involvement is well recognized (1), skin infiltration of Hodgkin's disease is rare. In a review of 1810 patients with Hodgkin's disease, Smith and Butler could find only nine (0.5%) patients with histologically confirmed cutaneous involvement (2). In other studies, the incidence is reported to be 0.5–7.5% of the patients with Hodgkin's disease (2–4). Such involvement usually occurs in the later stages of the disease, and is associated with a poor prognosis (2, 4, 5). Skin involvement indicates that the patient has stage IV disease by the current staging system for Hodgkin's disease. However, a few cases with skin involvement which have an exceptional favorable prognosis have been reported (6, 7). We report herein a case of Hodgkin's disease which developed new skin lesions as the sole evidence of recurrence. The patient is well and with no evidence of disease 7 months after discharge.

CASE REPORT

A 44-year-old Japanese man with no contributory past medical history complained of cough, sputum, and low-grade fever. He was admitted to a hospital in January 1983. Chest X-ray revealed a mediastinal

tumor. In February 1983 a thoracotomy with histological study revealed mediastinal Hodgkin's disease of the nodular sclerosis type. Complete resection of the tumor was not possible. He received radiation (total 30 Gy) and chemotherapy (total Adriamycin 250 mg, Cisplatin 300 mg) with complete remission. In March 1988 the patient noticed two skin nodules in the left supraclavicular and left anterior chest region and in July 1988 biopsy of the skin lesions was performed in our outpatient clinic. Histological examination revealed recurrence of Hodgkin's disease. He was admitted to our hospital in September 1988. His general condition was good with no evidence of lymph node or visceral organ involvement by a thorough metastatic survey. The skin lesions disappeared after several courses of chemotherapy (Etoposide 300 mg, Cytarabine 240 mg, Vindesine 3 mg, Vincristine 1 mg, Prednisolone 300 mg/course). He was discharged without major problems in February 1989. The patient is well and free from evidence of the disease 7 months after discharge.

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PATHOLOGICAL FINDINGS

Gross appearance (Fig. 1)

The skin lesion on the left anterior chest and that on the left supraclavicular region measured 4×2 cm and 2×1 cm, respectively. The resected specimens were similar in gross appearance; the lesions were white and slightly firm nodules with well defined margins. They were located mainly in the dermis and subcutaneous tissue. The tumor on the anterior chest infiltrated into the underlying pectoralis major muscle. No hemorrhage nor necrosis was seen.

Microscopic appearance

The involved dermis and subcutaneous tissues showed a heavy infiltrate of large, atypical mononuclear and multinuclear cells with numerous small lymphocytes, plasma cells, eosinophils, and

Fig. 1. Cut section of the skin lesion situated on the left anterior chest. The white slightly firm tumor (4×2 cm) has a well demarcated margin.

Fig. 2. Histological findings of the skin lesion seen in Fig. 1. Thick collagen fiber separates the cellular infiltration into nodular lesions (H & E, $\times 71$).

neutrophils. Thick birefringent collagen fiber separated the cellular infiltration into nodular lesions (Fig. 2). The large atypical mononuclear and multinuclear cells had abundant eosinophilic cytoplasm and irregular nuclei with prominent nucleoli. Some of these cells had the diagnostic appearance of Reed-Sternberg cells (Fig. 3). Many mononuclear cells with small nucleoli and abundant water-clear cytoplasm were seen grouped in clusters. They appeared to be lacunar cells (Fig. 4). The histologic diagnosis was the nodular sclerosis type of Hodgkin's disease.

Immunohistochemical findings

Immunohistochemical study was performed using the avidin-biotin-peroxidase complex method (8).

Fig. 3. Higher magnification of Fig. 2 shows a heavy infiltrate of large, atypical mononucleated and multinucleated cells with numerous small lymphocytes, plasma cells, eosinophils, and neutrophils. Diagnostic Reed-Sternberg cells are seen in the center and the lower right (H & E, $\times 710$).

Fig. 4. A cluster of mononuclear cells with abundant water-clear cytoplasm appear to be lacunar cells (H & E, $\times 350$).

Fig. 5. a. Immunohistochemical staining with Dako M1 antibody. Reed-Sternberg cell (center) and neutrophils show positivity in the cytoplasm. b. The cytoplasm of Reed-Sternberg cell is positive with Ber-H2. (a and b. avidin-biotin-peroxidase complex method, counterstained with methylgreen, $\times 710$).

The cytoplasm of the Reed-Sternberg cells showed immunoreactivity with Dako M1 monoclonal antibody (Dakopatts, Denmark, identical with Leu M1 antibody) and Ber-H2 (Dakopatts) (Fig. 5). Staining for leukocyte common antigen was negative in the mononuclear and multinuclear cells.

DISCUSSION

Most of the reported cases of Hodgkin's disease with skin involvement are associated with advanced disease at the appearance of skin lesions and have a short survival time (2, 4, 5). White and Patterson reported that 11 of 16 Hodgkin's disease patients with skin involvement had stage III or IV disease on admission (4). The mean survival time after the development of skin lesions was 11.8 months in their series. Smith and Butler reported that only one of nine patients survived and six patients died within 5 months following the diagnosis of skin involvement (2). These data support the concept that cutaneous involvement is a grave prognostic sign in Hodgkin's disease.

Several authors believe that skin involvement of Hodgkin's disease is secondary to regional lymph flow obstruction by lymph nodes massively involved by the tumor cells (2, 4, 5, 9). On the contrary, a few cases of Hodgkin's disease, which developed

skin lesions without lymph node involvement and followed a benign clinical course, are reported (6, 7). Williams reported a case which showed disseminated skin lesions as the sole evidence of recurrence (7). The patient had been free of the disease for two and half years (7).

White and Patterson (4) analyzed 16 patients of skin involvement of Hodgkin's disease, and proposed three mechanisms for cutaneous involvement: 1) retrograde lymphatic spread, distal to involved lymph nodes (11 of 16 patients); 2) direct extension from an underlying nodal focus (3 patients); and 3) hematogenous dissemination (2 patients). An overwhelming number of reported cases of cutaneous involvement of Hodgkin's disease fall into the first category (2, 4, 5, 9). Although it is rare, a hematogenous mechanism is suggested in the present case due to the absence of lymphadenopathy and underlying lesions.

The present case showed small nodular lesions on the anterior chest and the supraclavicular region which are reported to be the most common sites for skin involvement of Hodgkin's disease (2, 4). White and Patterson reported that 11 of 16 patients developed lesions in the chest, and three in the lower cervical region (4). Other sites for skin involvement are reported to be the scalp, thigh, flank, and

abdominal wall (2, 4).

Bluefarb (10) categorized the specific skin lesions of cutaneous involvement of Hodgkin's disease as follows: 1) papules, 2) infiltrations or plaques, 3) nodules or tumors, 4) ulcerative lesions, 5) various combinations of these lesions, and 6) erythroderma. The most common clinical presentation is of single or multiple dermal or subcutaneous nodules; many of them grow progressively and some become ulcerated (2, 4, 6).

In the series of White and Patterson, the mean interval between the initial diagnosis of Hodgkin's disease and the onset of skin involvement was 32.1 months, and the longest was 13 years (4). In the present case, the development of skin lesions took 6 years.

An increasing occurrence of secondary malignancies is well recognized in treated Hodgkin's disease patients (11). The differential diagnosis of Hodgkin's disease in the skin includes lymphomatoid papulosis, mycosis fungoides, and non-Hodgkin's lymphomas (12). Even giant cells resembling Reed-Sternberg cells may be found (11-13). Therefore, the histological differential diagnosis is often difficult (11-13).

Recently, Ree et al reported that Reed-Sternberg cells stain positively with Leu M1 antibody (69.2% of their cases) and Ber-H2 (88.9%) (14). In the present case, the histological findings which are typical for the nodular sclerosis type of Hodgkin's disease and the combination of positive staining by Leu M1 and Ber-H2 and the absence of positivity for leukocyte common antigen confirm the diagnosis (15).

Since skin involvement was not an indicator of ominous prognosis in a few reported patients with Hodgkin's disease, the pattern of skin involvement should be taken into consideration in assessing the prognostic significance.

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