Case report

CUTANEOUS HODGKIN'S DISEASE

G. Torlone, K. Peris, G. Mazzocchetti, E. Caracciolo, I. Schmidt and S. Chimenti

ABSTRACT

A 40-year-old man presented with a one year history of erythematous papules and nodules on the trunk and in the right axilla. Three years earlier, a diagnosis of stage I Hodgkin's disease had been established. Complete remission was achieved following 4 cycles of ABVD (doxorubicin, bleomicin, vinblastine, dacarbazine) combination therapy. Histologic examination of a skin biopsy specimen showed the presence of a diffuse, dense infiltrate throughout the whole dermis to the subcutaneous tissue. The infiltrate was composed of small lymphocytes, eosinophils, plasmacells and Reed-Sternberg cells. Immunohistochemistry revealed the positivity of neoplastic cells for BerH2 (CD30) and LeuM1 (CD15) antibodies. Reactivity of small lymphocytes for UCHL1 (CD45RO) was also observed. Routine laboratory examinations were within normal limits. Bone marrow biopsy and instrumental investigations (chest X-ray, computed tomographic scans of abdomen and pelvis) showed no abnormalities. The presence of Epstein-Barr viral (EBV) genome was analysed by polymerase chain reaction (PCR) technique. EBV DNA, however, was not found. Based on histologic and immunohistochemical findings, a diagnosis of secondary cutaneous Hodgkin's disease was made.

KEY WORDS

Hodgkin's disease - specific skin lesions

INTRODUCTION

Hodgkin's disease (HD) is a malignant lymphoproliferative disorder histologically characterized by dense, mixed infiltrate of small T lymphocytes, histiocytes, plasmacells and eosinophils, and typical Reed-Sternberg cells (1). Cutaneous involvement in systemic HD may be either non-specific or specific. Non-specific skin manifestations include pruritus,

purpura, urticaria, exfoliative dermatitis, bullous lesions and herpes zoster. Specific skin lesions are far less common and may appear as plaques, papules, nodules, tumours or erythroderma, alone or in combination (2). We describe a case of cutaneous Hodgkin's disease in a 40-year-old man in whom nodal HD had been diagnosed and treated three years earlier.

CASE REPORT

A 40-year-old man presented with one-year history of persistent, erythematous papules and nodules, 0.5-3 cm in diameter, scattered on the trunk and in the right axilla (Fig. 1,2). Physical examination failed to reveal any lymph node

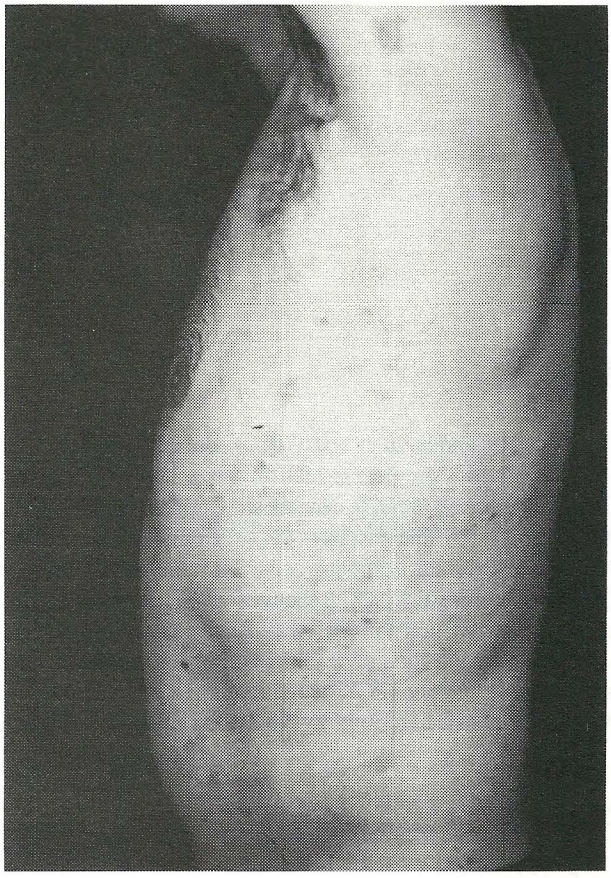

Fig. 1. A 40-year-old man with papules and nodules on the trunk.

involvement. Histologic examination of a skin biopsy specimen showed a diffuse, dense dermal infiltrate extending into the subcutaneous tissue (Fig. 3). The infiltrate was composed of small lymphocytes, histiocytes, eosinophils and multiple atypical large cells with prominent, basophilic nucleoli (Reed-Sternberg cells) (Fig. 4). Immunohistochemical investigations, performed with a standard 3-steps immunoperoxidase technique on routinely fixed, paraffin-embedded tissue sections, demonstrated the positivity of neoplastic cells for BerH2 (CD30) and LeuM1 (CD15)

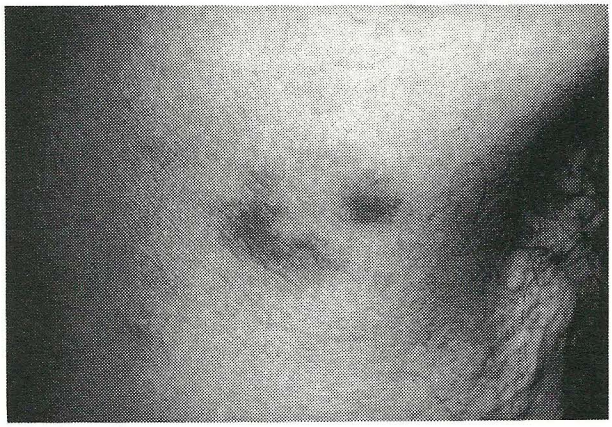

Fig. 2. A reddish plaque in the right axilla.

antibodies. Positivity for LN2 (CD74), KP1 (CD68) and UCHL1 (CD45RO) was also found. Negative reaction was observed with B lymphocytes associated marker such as L26 (CD20). The presence of Epstein Barr viral (EBV) genome has been evaluated by polymerase chain reaction (PCR) technique on formalin fixed, paraffin-embedded tissue sections employing oligonucleotide primers that bracket IR1 and IR3 regions. EVB-infected cell line P3T was used as positive control; normal kidney and placenta with no clinical, serologic or morphologic signs of EBV infection were used as negative controls. Samples containing all PCR reagents with the exception of target DNA were also used as negative controls. EBV DNA was not found in our specimen.

Three years earlier, stage I HD had been diagnosed on iliac lymph nodes. Histology showed features of nodular sclerosing subtype according to the Rye-classification. The patient had been successfully treated with 4 cycles of ABVD (doxorubicin, bleomicin, vinblastine, dacarbazine) combination therapy. The staging work-up of the patient, during our observation, revealed either normal or negative results for the following: routine laboratory examinations, bone marrow biopsy, chest X-ray, CT scans of the abdomen and pelvis. Based on patient's clinical history and histologic and immunohistochemical findings, a diagnosis of secondary cutaneous Hodgkin's disease was established. The patient has been treated with PROMACE/CytaBOM combination therapy.

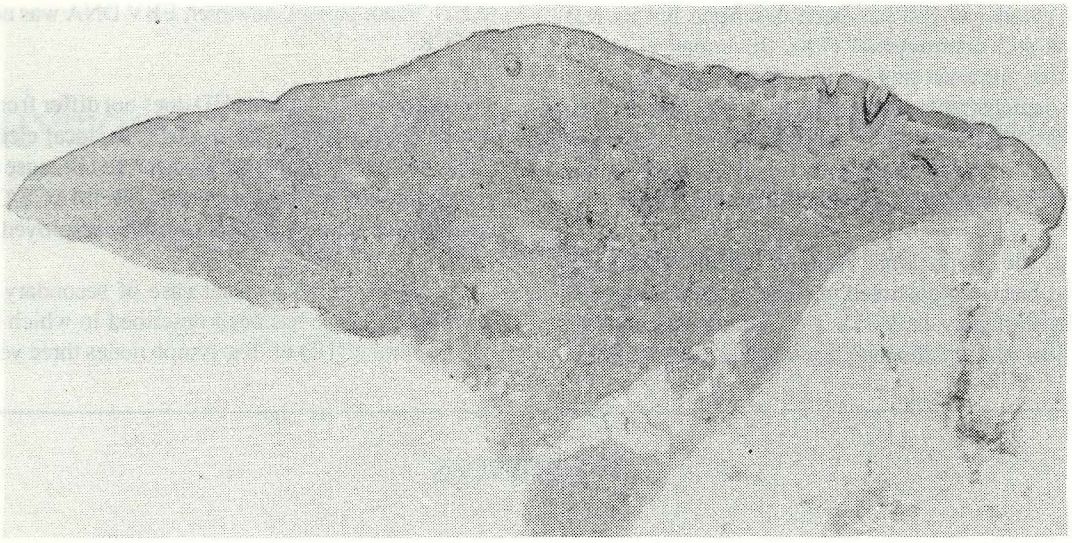

Fig. 3. Scanning magnification shows a dense, diffuse infiltrate through the whole dermis to the subcutaneous tissue (H/E, 25x)

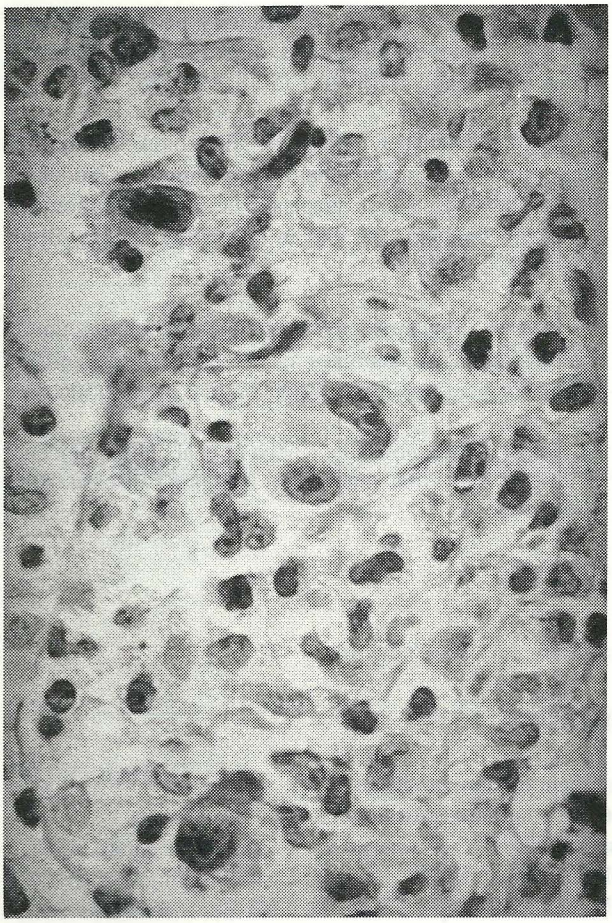

Fig. 4. Higher magnification reveals typical Reed-Sternberg cells (H/E, 400x)

Complete remission was achieved after 6 cycles. After a follow-up period of one year, no recurrence has been observed.

DISCUSSION

The first case of specific cutaneous lesions of HD has been already described in 1906 by Grosz (3). The patient was a 21-year-old man with lymphoadenopathy and skin nodules, some of which were ulcerated. Histology revealed "lymphogranulomatoid tissue and Reed-Sternberg cells" in both specimens. Since that time, several other cases of specific cutaneous involvement in HD have been reported. The incidence varies from 0.5 % to 7.5 % (4). Reddish papules and nodules located on the trunk are the most common clinical aspect. They usually occur in advanced stage of the disease and are associated with a poor prognosis (5). Our patient, however, had a history of limited disease and no evidence of systemic involvement at the time of our observation. The histology of skin lesions in HD can be classified according to the Rye classification (6). In our case, the nodular sclerosing subtype had been previously demonstrated on the iliac lymph nodes.

The immunophenotipic pattern can be useful in the diagnosis of cutaneous HD (6). Particularly, BerH2 (CD30) and LeuM1 (CD15) recognize Reed-Sternberg cells whereas KP1 (CD68) and LN2 (CD74) react with monocytes, macrophages and histiocytes respectively. Small lymphocytes can be CD4 or rarely CD8 positive. In this contest it should be mentioned that most reported cases had been misdiagnosed such as mycosis fungoides and lymphomatoid papulosis (1).

Primary cutaneous HD has been described but its real existence is still controversial (7,8). Silverman et al. (7) suggested that one must find a skin infiltrate consistent with HD and no demonstrable nodal involvement for at least three months after development of the skin lesions. However, following the literature, most of the reported cases, as our patient, represented secondary cutaneous HD (2,4-6).

Recently, the monoclonal form of Epstein-Barr viral genome has been demonstrated in some cases of nodal HD using molecular analysis (9-11). This finding suggests that EBV may play an etiopathogenetic role at least in a proportion of HD. In our patient, however, EBV DNA was not detected by PCR.

Treatment of cutaneous HD does not differ from that used for the nodal counterpart. In our case, local electron beam radiation therapy could not be performed because of the deep cutaneous involvement whereas PROMACE/Cyta BOM combination therapy was successfully employed.

In conclusion, an unusual case of secondary cutaneous Hodgkin's disease has been described in which the patient had had limited HD of iliac lymph nodes three years before.

REFERENCES

1. Chimenti S and Lombardo M (eds). Malattie linfoproliferative cutanee e sistemiche. Genova, Scuola Internazionale di Oncologia e Medicina Sperimentale, 1992, 245-246, 259-261.

2. Hayes TG, Rabin VR, Rosen T et al.: Hodgkin's disease presenting in the skin: case report and review of the literature. J Am Acad Dermatol 1990; 22: 944-947.

3. Grosz S.: Ueber eine bisher nicht Beschriebene Hauterkrankung (Lymphogranulomatosis cutis). Beitr Pathol Anat Allg Pathol 1906; 39: 405-430.

4. White MW and Petterson JW. Cutaneous involvement in Hodgkin's disease. Cancer 1985; 55: 1136-1145.

5. Derrick EK, Deutsch GP and Price LM. Cutaneous extension of Hodgkin–s disease. J R Soc Med 1981; 84(1): 684-685.

6. Cerroni L, Rieger E and Kerl H. Histologic and immunophenotipic analysis of cutaneous Hodgkin's disease. J Cut Pathol 1990; 17:289.

7. Silverman CL, Strayer DS and Wasserman TH. Cutaneous Hodgkin's disease. Arch Dermatol 1982; 118: 918-921.

8. Brehmer-Andersson E. The validity of the concept of primary cutaneous Hodgkin's disease. Acta Dermatol Venereol 1976/1977; (Suppl.) 75-78; 124-125.

9. Anagnostopoulos J, Herbst H, Niedobitek G, Stein H: Demonstration of monoclonal EBV genomes in Hodgkin's disease and Ki-1 positive anaplastic large cell lymphoma by combined Southern blot and in situ hybridization. Blood 1989; 74(2): 810-816.

10. Weiss L, Movahed L, Warnke R, Sklar J: Detection of Epstein-Barr viral genomes in Reed-Sternberg cells of Hodgkin's disease. N Engl J Med 1989; 320: 502-506.

11. Herbst H, Niedobitek G, Kneba M et al.: High incidence of Epstein-Barr virus genomes in Hodgkin's disease. Am J Pathol 1990; 137: 13-18.

AUTHORS' ADDRESSES

Giancarlo Torlone M.D., Department of Dermatology,
University of L'Aquila, Via Vetoio, 67010 Coppito, L'Aquila, Italy
Kety Peris M.D., same address
Giampiero Mazzocchetti M.D., same address
Ernesto Caracciolo M.D., same address
Iris Schmidt M.D., same address
Sergio Chimenti, M.D., professor and chairman, same address