The Sarcoidosis-Lymphoma Syndrome: Acceleration of the Cutaneous Sarcoidosis during Chemotherapy of the Lymphoma

Sir,

The sarcoidosis-lymphoma syndrome is characterised by a lymphoproliferative disorder that develops after the onset of sarcoidosis. We report here a patient with this syndrome who developed a low grade B cell non-Hodgkin's lymphoma (NHL) after sarcoidosis. During treatment of the lymphoma his cutaneous sarcoidosis became rapidly worse.

CASE HISTORY

A 36-year-old man presented an annular lesion over his presternal region (Fig. 1). Diascopy suggested a granuloma and histological examination of a skin biopsy confirmed the clinical diagnosis of sarcoidosis. At this stage all haematological and biochemical investigations, including an angiotensin converting enzyme level, were normal. However, a chest X-ray demonstrated bilateral hilar lymph-

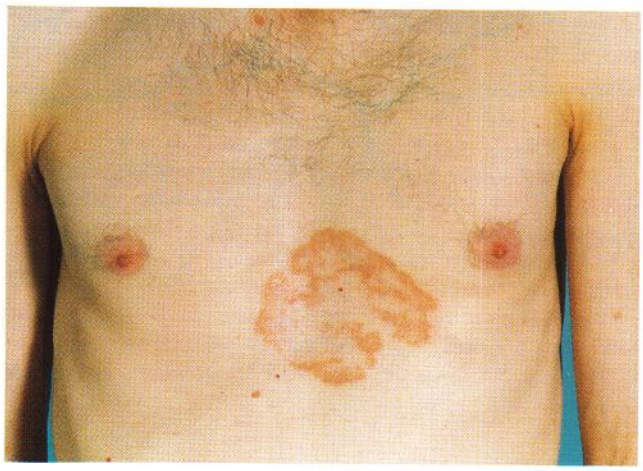

Fig. 1. Annular lesion over the presternal region.

adenopathy, and the histological findings of a trans-bronchial biopsy and an analysis of cell populations from a broncho-alveolar lavage were consistent with the diagnosis of sarcoidosis. The pulmonary changes regressed with oral prednisolone but the cutaneous lesions did not.

Six years later the patient returned with a widespread lymphadenopathy. Histological examination of samples of lymph node and bone marrow showed a diffuse centrocytic/centroblastic B-cell NHL (Kiel Classification).

Over the next 3 years he was treated with various chemotherapeutic regimens, including CHOP and MOP, all of which led to temporary remissions of the lymphoma. More recently, three courses of fludaribine were given. During the third course, several pigmented macules appeared on the forehead and below the left ala nasi (Fig. 2). A biopsy of one of these showed characteristic sarcoidal histology. During a fourth course of fludaribine further lesions appeared on the face. A remission of the lymphoma has now been induced.

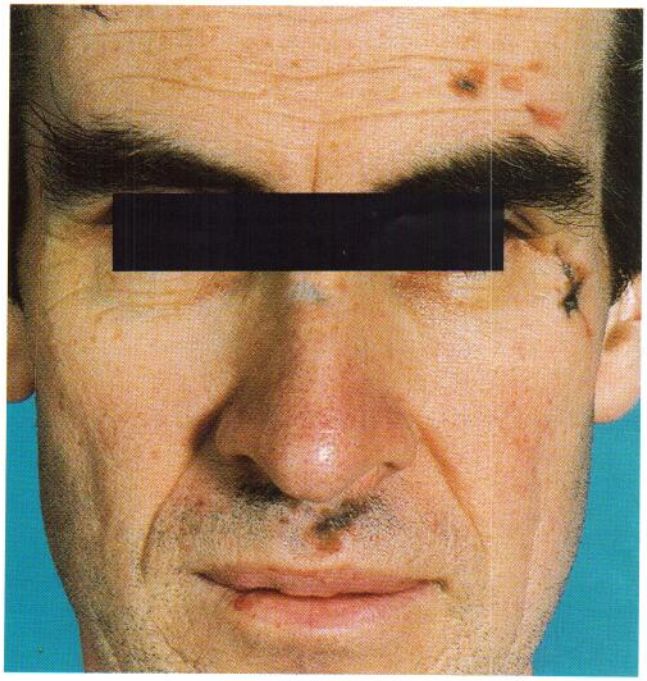

Fig. 2. Pigmented macules on the forehead and below the left ala nasi.

DISCUSSION

The sarcoidosis-lymphoma syndrome is a rare disorder, in which sarcoidosis predates the development of a lymphoma or other lymphoproliferative disorder by a median time of 95 months (1). Hodgkin's and non-Hodgkin's lymphomata (2) are the most frequent malignancies found in this syndrome, but the following NHLs have also been recorded: hairy cell leukaemia (3), angio-immunoblastic lymphadenopathy with dysproteinaemia (4) and myeloma (1). Chronic lymphatic lymphoma, acute myeloid leukaemia (5) and acute lymphoblastic leukaemia (6) have also been implicated. Two large Scandinavian studies have shown that the incidence of lymphoproliferative disorders in patients with sarcoidosis is at least 5.5 times greater than expected (1, 7).

The reason for this is unclear, but two hypotheses have been put forward. The first is that idiopathic sarcoidosis predisposes to generalised tumour susceptibility (7), but this has not been proven (8). The second is that sarcoidosis with non-regional haematological malignancies may be the generalised counterpart of the localised sarcoidal reactions sometimes seen in the presence of solid regional tumours (9), and perhaps due to tumour antigen release. However, such a relationship with a malignancy, extending over a long period of time, seems unlikely, though in several of the reports of associated acute myeloblastic leukaemia, the malignancy was of a surprisingly chronic type (5).

The sarcoidosis of patients who develop a lymphoid neoplasm is almost invariably of the chronic active type, typified by lymphopenia, persistent disease activity and the need for steroid therapy. One feature of this type is the large number of CD4+ lymphocytes in the granulomata, in contrast to decreased levels of these cells in the circulation. Hyperactivity of humoral immunity is also found (1).

Granulomatous skin lesions are well documented in association with haematological malignancies and their precursors, either at the time of presentation or as a complication of the neoplasm (11). Granuloma annulare and sarcoid-like granulomata have also been described in myelodysplastic syndromes in the absence of lymphomatous infiltration (12).

The time lapse between the diagnosis of sarcoidosis and the lymphoma, the age of our patient, and chronic activity of his sarcoidosis are all characteristic of the sarcoidosis-lymphoma syndrome. In support of this, tissue diagnosis of both facets of the condition was obtained at their respective presentations.

It is not clear why the cutaneous sarcoidosis of our patient should have accelerated during chemotherapy of his lymphoma. Induced changes in delayed-type hypersensitivity may have been responsible. Alternatively, tumour lysis may have increased tumour antigen release, and secondarily increased granulomata formation. However, this theory would not explain why activation occurred during treatment with one cytotoxic agent but not with others.

Clinicians and pathologists should be aware of this syndrome and of the possibility of an exacerbation of sarcoidosis during chemotherapy.

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