REFERENCES


Accepted December 12, 1995.

G. Filipou, 1 L. Bugatti, 1 K. Peris 2 and S. Chimenti, 2* Departments of Dermatology, 1USL 5, Jesi, Ancona, and 2University of L’Aquila, Via Vetello-Loc, Coppito 2, I-67010 L’Aquila, Italy.

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

Sir,

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

CASE HISTORY

A 36-year-old man presented an annular lesion over his presternal region (Fig. 1). Dacyscopy suggested a granuloma and histological examination of a skin biopsy confirmed the clinical diagnosis of sarcoïdosis. 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-
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 lymphoma (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 cryoglobulinaemia (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 solic 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 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 granuloma, 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 granuloma 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 granuloma 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.

REFERENCES

Paraneoplastic Pemphigus: Oral Involvement as the Sole Manifestation

Sir,

The concept of paraneoplastic pemphigus was first established by Anhalt et al. (1) in 1990, with the recognition of a distinct variant of the pemphigus spectrum associated with malignancy. The reports on paraneoplastic pemphigus have multiplied over the last 5 years, all exhibiting the features of a severe, usually fatal, mucocutaneous disease with unique histological and immunological characteristics. The common histological findings in these patients include dyskeratotic keratinocytes and basal vacuolization, in addition to the invariable suprabasilar acantholysis. The ability of antibodies in the patients' sera to bind to a variety of epithelia and to precipitate a unique complex of four antigens is the hallmark of diagnosis of this recently acknowledged entity (1-6).

We describe a case that shares the immunological and histological characteristics of the reported paraneoplastic pemphigus cases but is unique in its clinical behavior.

CASE REPORT

A 50-year-old Jewish man of Iranian descent was hospitalized in September 1993 for evaluation of painful oral erosions that interfered with his ability to eat. He had a 10-month history of high-grade non-Hodgkin's lymphoma, with remission believed to be induced by multiple-agent chemotherapy consisting of VP16, Adriamycin, cytoxan, Oncovin, prednisone, and bleomycin. The erosions appeared about 3 months after completion of this treatment. Cultures taken by the referring physician for fungal organisms and herpes simplex, and serological tests for herpes virus, were all negative. When treatment with acyclovir, antifungal agents, and antibiotics proved ineffective, the patient was hospitalized for further evaluation.

Physical examination at admission revealed severe ulcerations and pseudomembranes involving the tongue, palate, buccal mucosa and lips (Fig. 1). There was no skin eruption and no involvement of other mucous membranes. A solitary enlarged inguinal lymph node was palpated. Results of laboratory studies, including complete blood count and serum chemistry profile, were within normal limits.

A biopsy specimen obtained from the oral mucosa showed suprabasal acantholysis, interface vacuolization and dyskeratotic keratinocytes (Fig. 2). Direct immunofluorescent studies of a perilesional biopsy revealed intercellular IgG deposits, as well as linear deposits of C3 along the basement membrane zone. Indirect immunofluorescence of a sample of the patient's serum demonstrated IgG autoantibodies directed not only to the intercellular substance of stratified squamous epithelium, but also to the intercellular substance of rat bladder transitional cell epithelium. Further immunological and immunoprecipitation studies were not performed at that time and, in view of the patient's deteriorating status and the recurrence of the lymphoma disclosed by bone marrow biopsy, salvage chemotherapy was immediately commenced with cytoxan, Adriamycin, Oncovin and prednisone. A second remission was accompanied by a striking improvement in the oral lesions. A serum sample obtained at the time of the remission was unfortunately negative on indirect immunofluorescence for anti-intercellular antibodies, probably accounting for the subsequent failure to immunoprecipitate proteins synthesized by keratinocyte cultures.

Accepted December 5, 1995.

S. G. Koehane1, J. A. Sevin1, M. J. Tidman1, J. A. M. Anderson2 and F. A. Carey2. Departments of 1Dermatology, 2Haematology and 3Histopathology, University of Edinburgh, The Lauriston Building, The Royal Infirmary, Edinburgh, EH3 9YW, United Kingdom.