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Erythema elevatum diutinum and Pre-AIDS

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da Cunha Bang F, Weismann K, Ralfkiær E, Pallesen G, Lange Wantzin G. Erythema elevatum diutinum and pre-AIDS. Acta Derm Venereol (Stockh) 1986; 66: 272–274.

Erythema elevatum diutinum (EED) is a chronic disease with symmetrical persistent erythematous nodules and plaques primarily in an acral distribution. EED is often associated with infections, especially of streptococcals. An immunological reaction has been proposed as pathogenetic mechanism. We describe a patient, who developed EED secondary to a LAV/HTLV III positive lymphadenopathy syndrome. Immunological investigation of a skin lesion and a lymph node biopsy is described. *Key words: Monoclonal antibodies; Immunological investigation; Skin biopsy; Lymph node biopsy.* (Received December 12, 1985.)

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Erythema elevatum diutinum (EED) is a rare chronic inflammatory dermatosis. Clinically it is characterized by symmetrically localized erythematous or purple nodules and plaques typically present on the extremities across the shins and buttocks. The nodules are often painful or burn, but frequently nonpruritic. The etiology is unknown. Histologically, the lesions are characterized by vasculitis with endothelial swelling, eosinophilic fibrinoid deposits, and a perivascular predominantly inflammatory infiltrate.

CASE REPORT

A 35-year-old homosexual man was admitted to the Department of Dermatology because of skin lesions of some months' duration. Clinical examination showed itching, hyperkeratotic infiltrated nodules on ankles, knees and elbows, and a slightly infiltrated plaque was observed on the abdomen. During the previous year the patient had suffered from generalized lymphadenopathy and within the last two months he had lost in weight and had felt tired. Biopsy from the skin lesions and a lymph node were investigated microscopically. Subsequently the patient was found to suffer from a latent syphilis indicated by a WR of 17. Previous tests had been negative. He was treated with benzathine penicillin i.m. 2.4 MU three times at weekly intervals. No improvement of the skin lesions after completion of the penicillin therapy was observed. Furthermore the patient developed B-hepatitis confirmed by positive HBsAg. The s-GOT was slightly raised and the hepatitis passed almost subclinically. Treatment of the skin lesions (EED) with dapsone was considered, but not carried out since the patient left the country shortly after having been treated for his syphilis.

Laboratory investigations showed positive LAV/HTLV-III antibodies in the blood. Immunoglobulin levels of IgG and IgA were above normal (17.7 g/l and 8.0 g/l respectively). The T helper/T suppressor ratio was 0.4. Wr dropped from 17 to 8, s-GOT rose to 49 U/l.

The following investigations were normal: Hgb, leukocytes, lymphocytes, thrombocytes, bilirubin, alkaline phosphatase, p-creatinine, IgM, cytomegalo-virus antibodies, and chest X-ray.

Immunological analysis

Biopsies from skin lesions and lymph node were frozen and stored in liquid nitrogen. 6–7 μm cryostat sections were dried overnight either at room temperatures or at 37°C, fixed in acetone and then stained by a three-stage immunoperoxidase method (1) using panels of monoclonal antibodies against lymphoid cells and their subsets described previously (2, 3).

RESULTS

Skin biopsy

The HE staining showed leukocytoclastic vasculitis with endothelial swelling, marked perivascular infiltrate of neutrophil leukocytes and nuclear dust admixed with lymphocytes, histiocytes, and some eosinophils. In a PAS staining a deposition of fibrinoid material was seen in and around blood vessels. Immunological investigation revealed a mixed lymphoid infiltrate composed of activated (interleukin-2 receptor positive) periferal T-cells of helper/inducer type in association with Langerhans' cells and macrophages. Many of the T-cells also expressed the transferrin receptor associated with cell proliferation. Neither B-lymphocytes nor follicular dendritic cells were identified.

Lymph node biopsy

Routine staining of formalin-fixed and paraffin-embedded lymph node revealed hyperplasia but also signs of involution in the B-zone. Changes diagnostic of LAV/HTLV-III lymphadenitis occurred in the B-zone and included follicular hyperplasia in association with follicular fragmentation/discruption and a partial depletion of the follicular mantle zone. Changes indicative of involution were also seen, i.e. loss of germinal centre cells and deposition of eosinophilic material or hyaline sclerosis in the germinal centres. Moreover, in other areas of the lymph node the architecture was changing into a diffuse angioimmunoblastic lymphadenopathy-like pattern with loss of germinal centres.

By the immunohistological staining of frozen lymph node sections an immense infiltration of CD 8-positive lymphocytes was disclosed in the remaining germinal centres.

The morphological and immunohistological findings were consistent with LAV/HTLV-III lymphadenitis stage II in the classification of Pallesen et al. (3).

DISCUSSION

The etiology of EED is unknown. Earlier findings (4, 5) have suggested an immune complex etiology and various bacterial antigens, especially streptococcal, are likely agents

in the initiation of this reaction (6, 7). Also non-bacterial diseases have been described with EED as paraproteinemias, diabetes mellitus and dermatitis herpetiformis (7).

In this case the patient was suffering from no less than three infectious diseases, i.e. lymphadenopathy syndrome (LAV/HTLV-III pos.), latent syphilis, and B hepatitis. The patient had persistent generalized lymphadenopathy as well as EED long time before the syphilis and B hepatitis infections were diagnosed. Until then the syphilis serology and HBsAg had been negative. Thus it is not likely, that the two latter were related with the EED. We suppose, that the LAV/HTLV-III infection in our patient was the initiator of the EED. The lymph node biopsy revealed changes characteristic of the LAV/HTLV-III in a progressed stage in accordance with the long duration of the skin symptoms. The finding of elevated levels of the immunoglobulins IgG and IgA has been described previously (4, 8). The histology of EED is not pathogenomic but nevertheless it is characteristic. We found lesions of early stages with a predominance of polymorphonuclear leukocytes in the perivascular infiltrate as well as vasculitis with endothelial swelling. In earlier lesions fibrosis occurred as the end stage of the inflammatory state. The characterization of the skin infiltrate by immunoenzymatic labelling of frozen sections with a panel of monoclonal antibodies showed a predominance of activated/proliferating T helper/inducer cells in association with Langerhans' cells and macrophages. A pattern similar to this is found in a range of other dermatoses containing lymphoid cell infiltrates (2) and consist with a concept of T-cell activation by the cutaneous antigen presenting cell for T lymphocytes, i.e. the Langerhans' cell (9).

EED is a chronic disorder. As in other neutrophil-mediated diseases, for example dermatitis herpetiformis and Sweet's syndrome (10), treatment of EED with dapsone has been successful (4, 6, 7, 11). Corticosteroid therapy, which may prevent the activation of the immunological pathway, has been effective only in high dosage (4). Dapsone therapy appears to be of suppressive but not curative effect since discontinuation of therapy results in relapse.

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