

Exaggerated Insect Bite-like Reaction in Patients Affected by Oncohaematological Diseases

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Sir,

Patients affected by chronic B-cell lymphatic leukaemia (CBLL) and, more rarely, other oncohaematological diseases may present with papules, plaques, nodules and vesico-bullous lesions on exposed areas (1–3). These lesions are usually considered an exaggerated reaction to insect bites, although the patients not always had a history (except for the seasonal presentation of cutaneous findings), the clinical picture, and response to treatment suggestive of insect bite (3, 4). This phenomenon has been described in about 40 patients affected by lymphoproliferative disorders, 95% of whom had CBLL (1–7). Weed (1) first gave the definition of 'exaggerated delayed hypersensitivity to mosquito bites' and reported this condition only in patients affected with CBLL. Later, Houston & Keene (2) described a case of exaggerated insect bite-like reaction also in a patient with lymphocytic lymphoma. In 1986, Rosen et al. (3) studied 10 patients and suggested that the cutaneous lesions could be linked, in some way, to the oncohaematological conditions, without explaining the exact pathway.

Five patients affected by different B lymphoproliferative disorders, who presented with pruritic papules, nodules and vesico-bullous lesions on exposed areas during spring and summer time, are reported. We discuss an immuno-allergic mechanism, involving both allergic reaction to insect bite and the impairment of the immune response in oncohaematological patients.

CASE REPORTS

From 1995 to 2001, three patients affected by CBLL and two by non-Hodgkin B-cell lymphomas attended our department with polymorphous, erythematous cutaneous papules and plaques, some of them evolving into bullous lesions. During spring-summer all the patients developed very itchy lesions, plaques (Fig. 1) and sometimes bullae, mainly localized on upper and/or lower limbs and on the face. Three patients referred to have been bitten by mosquitoes, the other two denied this occurrence. At the time of the clinical examination, all the patients were living in or close to the area of Pavia, Italy, where seasonal infestations of mosquitoes (*Aedes*) are particularly widespread. All the patients underwent a 4-mm punch biopsy, necessary for a

histopathologic evaluation; a direct immunofluorescence test was carried out for four patients, to exclude autoimmune bullous diseases.

At the time of the eruption, one patient was on treatment with VACOP-B protocol (adriblastina, cyclophosphamide, etoposide, vincristine, bleomycin, prednisone), two patients with chlorambucil and one with cyclophosphamide. An 87-year-old patient was not under treatment. Blood analysis revealed peripheral eosinophilia in three patients out of five. Stool analysis searching for parasites was carried out in those three patients and proved negative. IgE was in the normal range in all the patients. Serum protein electrophoresis revealed that total immunoglobulins were in the normal range or little lower in all the patients, while all of them presented a different degree of decrease of IgG, IgM and/or IgA in sera. The other clinical and serological findings were unremarkable or consistent with their haematological condition.

The histopathology was characterized by a variety of findings, all of which were consistent with an arthropod bite reaction. In particular, a wedge-shaped, superficial or superficial-deep perivascular and often also interstitial infiltrate was present. It was mainly composed of eosinophils in association with lymphocytes and rarely neutrophils. The density or the depth of the infiltrate varied from case to case, also according to the age of the lesion. An oedema of the subpapillary dermis was always evident. One patient presented a subepidermal vesicle. In another patient spongiosis could be seen and



Fig. 1. The intense oedema due to insect bite caused ptosis on the upper eyelid of this old man.

a subsequent biopsy showed an intra-epidermal vesicle due to marked spongiosis. No flame figures were found.

On the basis of clinical and histopathological findings, as well as immunofluorescence studies, a diagnosis of exaggerated insect bite-like reaction in patients affected by oncohaematological diseases was made.

DISCUSSION

The occurrence of unusual hypersensitivity phenomena has been described in patients affected by lymphoproliferative disorders, especially CBLL (1–7). In 1965, Weed (1) termed these reactions an ‘exaggerated delayed hypersensitivity to mosquito bites in chronic lymphocytic leukaemia’, considering the cutaneous manifestations consistent with a peculiar response to insect bites, particularly mosquitoes. This assessment was supported not only by the evaluation of clinical features and the history of patients, but also by histopathological findings and intradermal tests made with mosquito antigen. Not only did three patients in our group report insect bites, but also their clinical presentation and histological findings were suggestive of a true, exaggerated insect bite. Systemic steroid together with oral antihistamine was a successful therapy for all our patients, although it could not prevent new eruptions.

In conclusion, exaggerated insect bite-like reaction has been reported not only in patients affected by CBLL, but also in those affected by non-Hodgkin B-cell

lymphoma. The hypothesis of an immuno-allergic pathway, related to the onset of the cutaneous eruption has been proposed.

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