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An itchy vesiculobullous eruption in a patient with chronic lymphocytic leukaemia

B. COCUROCCIA, P. GISONDI, E. GUBINELLI, G. GIROLOMONI
Istituto Dermopatico dell'Immacolata, IRCCS, Rome, Italy

SUMMARY

Exaggerated reactions to insect bites are characteristic of patients with haemoproliferative disorders, particularly chronic lymphocytic leukaemia (CLL). Skin lesions usually appear after the diagnosis of leukaemia and seem unrelated to laboratory findings, disease course or therapy. Rarely, the eruption may precede the diagnosis of the haematologic malignancy. The patients usually do not recall of insect bites, and the diagnosis may require histological and laboratory investigations to exclude specific lesions or autoimmune bullous diseases. Lesions may run a chronic course and represent a therapeutic challenge. Here, we report an adult patient with CLL who developed itchy recurrent papulovesicular and bullous lesions. Differential diagnosis was made with cutaneous specific lesions of CLL, bullous pemphigoid and pemphigus vulgaris, but laboratory and histological investigations confirmed the diagnosis of an insect bite reaction. The patient was treated with oral H1 anti-histamines and topical corticosteroids under occlusion, with marked improvement after 10 days.

Keywords: Chronic lymphocytic leukaemia; CLL; skin; insect bites

INTRODUCTION

Chronic lymphocytic leukaemia (CLL) is a malignant lymphoproliferative disorder characterised by an accumulation of monoclonal lymphoid cells within the peripheral blood, bone marrow and other organs. Skin eruptions are common in patients with haematological malignancies. These can be due to either cutaneous seeding by neoplastic cells (specific lesions) or a non-metastatic (non-specific) phenomenon (1). Bullous eruptions, including autoimmune blistering diseases, are reported in a minority of patients affected by CLL (2–5). Exaggerated reactions to insect bites mainly to mosquito are rare, disturbing, non-specific phenomenon accompanying haemoproliferative disorders (6–10). The typical clinico-pathological findings include recurring papules, plaques and vesciculobullous lesions. These lesions may represent both a diagnostic and therapeutic challenges because in many patients there is lack of history of insect bites and because the eruption may be resistant to common therapies. We report a patient with CCL who developed recurrent itchy papulovesicular and bullous lesions clinically suggestive of an autoimmune bullous disease. The lesions turned out to be exaggerated insect bite reactions.

Correspondence to:
Dr Giampiero Girolomoni, Istituto Dermopatico dell'Immacolata, IRCCS Via Monti di Creta 104, 00167 Roma, Italy
Tel.: +39-06-66464736
Fax: +39-06-66464705
Email: giro@idi.it

CASE REPORT

A 65-year-old Caucasian man presented in May 2003 with a 4-month history of recurrent very itchy papular and bullous eruption. He was affected by a λ B-CLL on medication with chlorambucil until January 2002. The patient was taking irbesartan for essential hypertension since the age of 58 years. Examination revealed disseminated vesiculobullous lesions ranging from 0.5 to 7 cm in diameter on erythematous base, and rare necrotic elements particularly on the legs and forearms (Figure 1). Erythematous indurated papules as well as large plaques were also seen on the arms, thighs, legs and neck. Laboratory tests revealed a moderate peripheral eosinophilia (920 cells/μl). The total blood cell count, as well as liver and renal function tests, serum calcium and alkaline phosphatase, lactate dehydrogenase, protein electrophoresis and ESR were normal. Immunoglobulins (Ig) including IgE and β_2 microglobulin serum levels were within normal range. Antibodies against desmoglein 1 and 3, and the 180 kDa bullous pemphigoid antigen and anti-nuclear antibodies were absent. Chest X-ray and abdominal echo-scan did not reveal abnormalities. Histological examination of a skin sample showed epidermal spongiosis, marked oedema in the papillary dermis with a superficial and deep, perivascular and interstitial infiltrates composed of small lymphocytes and neutrophils and numerous eosinophils. Immunohistochemical staining disclosed that the lymphocytic infiltrate was composed predominantly of $CD3^+$ and $CD45RO^+$ T cells and very few $CD20^+$ B cells. Direct immunofluorescence performed on peribullous skin with antibodies against IgG, IgM, IgA and C3 did not reveal deposits. Indirect

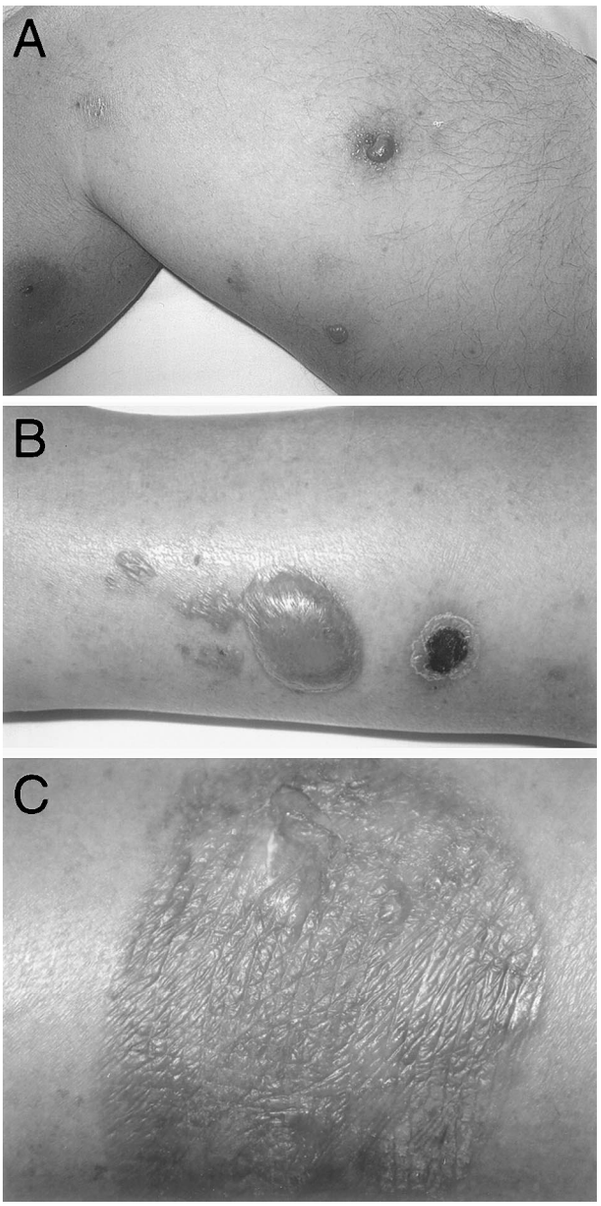

Figure 1 Large erythematous plaques, papulovesicular and necrotic lesions (A and B) and large bullae (B and C) in the lower legs

immunofluorescence test performed on salt split human skin was negative. The patient was treated with oral H1 antihistamines and topical corticosteroids of high potency under occlusion with marked improvement after 10 days. After a minor recurrence after 2 weeks and the use of an insect repellent for 2 months, no further lesions developed in a 6-month follow-up.

DISCUSSION

Exaggerated reactions to insect bites, mainly to mosquito, are infrequent disturbing disorders and sometimes difficult to treat non-specific phenomenon accompanying haemoproliferative disorders (2–6). These eruptions have been first described in 1965 by Weed (2). He defined an exaggerated reaction as a lesion more than 20 mm in diameter characterised by induration, oedema, erythema and intense pruritus at the site of a known mosquito bite or with evidence of a central punctum. The mosquito bite reactions reached their peak in 12–24 h, and in severe cases bullae up to 10 cm in diameter developed. These eruptions have been primarily described in patients with CLL, and occasionally in acute lymphoblastic leukaemia and mantle-cell and large-cell lymphoma (9). Hypersensitivity to insect bites with both intense skin response and general symptoms have been reported in Japanese children and also with a juvenile type of Epstein–Barr virus-associated natural killer cell leucaemia/lymphoma (11). Skin lesions usually appear months to years after the diagnosis of leukaemia and seem unrelated to laboratory findings, disease course or therapy (6,8–9). Rarely, but importantly the eruption may precede the diagnosis of the haematologic malignancy (9). Heightened insect bite reactions have been described in other diseases with altered immune reactivity such as HIV infection (12) and congenital agammaglobulinemia (13). The diagnosis is based on the clinical and pathological characteristics of the lesions. Clinical findings include recurring itchy papules, plaques and vesiculobullous lesions distributed on both exposed and non-exposed areas. Histologically, they are characterised by a superficial and deep-mixed inflammatory cell infiltrate containing eosinophils. The patients usually do not recall of insect bites. Here, we report a patient with recurrent papulovesicular and bullous lesions that histologically demonstrated the features of an insect bite. Differential diagnosis was made with cutaneous specific lesions of CLL, bullous pemphigoid and pemphigus vulgaris. The absence of circulating autoantibodies against 180 kDa bullous pemphigoid antigen and desmogleins, as well as the negative results of direct immunofluorescence study in the skin, excluded the diagnosis of autoimmune blistering disorders. Histologic examination and immunohistochemistry excluded specific lesions of CLL. In many instances, systemic corticosteroids in a dose equivalent to prednisone 40 mg/day are required to control symptoms, although the amelioration can be partial and transient. Dapsone, interferon alfa, intravenous Ig, phototherapy and chemotherapy have been used in refractory cases with variable results.

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