

naevus lipomatosus. Takashima *et al.*³ reported a case with perifollicular fibrosis without any hair follicle changes, and suggested that naevus lipomatosus may be a form of connective tissue naevus with unique characteristics, including excess dermal fat and perifollicular fibrosis. Our case was characterized by umbilicated follicular papules on the surface, and histopathologically showed dilated follicular infundibulum containing keratin debris, and a surrounding well-circumscribed proliferation of basophilic loose connective tissue including mucin around hair follicles which formed epithelial strands anastomosed to each other, suggestive of fibrofolliculoma. Fibrofolliculoma is derived from both mesenchymal and epithelial components, whereas perifollicular fibroma is from only the epithelial component. Ackerman *et al.*¹⁰ suggested that fibrofolliculoma and trichodiscoma are different stages in the development of a single entity. These entities present as asymptomatic skin-coloured papules 1–3 mm in diameter, usually on the face, as solitary or multiple lesions. Histopathologically, fibrofolliculoma consists of strands of epithelial cells radiating from a follicular structure with infundibular features, and these strands may anastomose the infundibulum at several points. Around epithelial cords, there is a well-circumscribed proliferation of loose connective tissue composed of fine fibres with some intervening mucin. As far as we know, this case is the first report of naevus lipomatosus associated with fibrofolliculoma.

In conclusion, naevus lipomatosus may be accompanied by variable pilosebaceous abnormalities such as hypertrophic pilosebaceous units, perifollicular fibrosis and fibrofolliculoma, which suggests that naevus lipomatosus is part of the disease spectrum of connective tissue naevi.

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Nodal marginal zone lymphoma in association with hydroa vacciniforme-like papulovesicular eruption, hypersensitivity to mosquito bites and insect bite-like reaction

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SIR, Various skin lesions occur in association with malignant haematological neoplasms. Recently, unusual papular, vesiculobullous and ulcerative eruptions, including hydroa vacciniforme (HV)-like papulovesicular eruption (HVPVE), hypersensitivity to mosquito bites (HMB) and insect bite-like reaction (IBR), have been noted as new types of skin lesions occurring in association with neoplasms including chronic lymphocytic leukaemia, haemophagocytic syndrome, natural killer cell leukaemia/lymphoma, non-Hodgkin lymphoma, acute lymphoblastic leukaemia and mantle-cell lymphoma.

A 46-year-old Korean man presented with a 6-year history of intense skin reactions at mosquito bite sites and associated general symptoms. The skin reactions usually began with erythema and swelling after the mosquito bite, developed to haemorrhagic bullae, necrosis and ulcers, and healed with residual scarring within several weeks. For 4 years prior to presentation he had exhibited these papulovesicular eruptions not only in areas of known arthropod bites but also in the absence of known bites. Moreover, he developed necrotic vesicles and papules on the face and ears that resembled severe HV. This eruption was exaggerated by mosquito bites, but not by sun exposure. At presentation, he had ulcerated papules, bullae and depressed scars on the trunk and extremities. The clinical features suggested arthropod bites, but he recalled bites only at the right ankle and foot, and denied bites at other sites. In addition, he showed vesicles and varioliform scars on the face, which resembled HV (Fig. 1). He had high fever, multiple lymph node enlargement and hepatomegaly. Laboratory findings were normal except for an elevated eosinophil count (23%). No atypical lymphocytes were found in peripheral blood examination and bone marrow biopsy. Skin biopsies from the face, back and right ankle showed a

Fig 1. Clinical features at presentation. Multiple papulovesicles and crusts are seen on (a) the face (b) the trunk and (c) the right ankle.

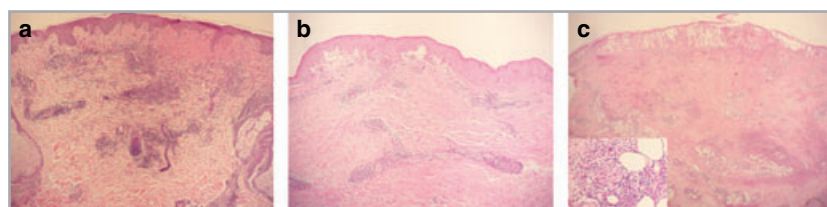
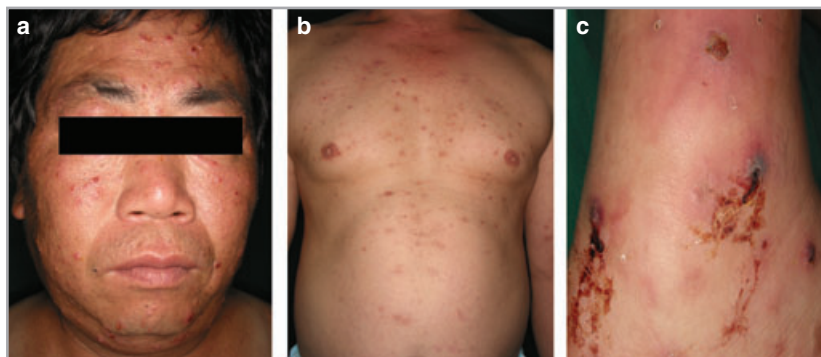


Fig 2. Biopsy specimens from (a) the face (b) the back and (c) the right ankle show epidermal spongiosis, and a moderate to dense dermal mixed inflammatory cell infiltrate with angiocentricity. A dense eosinophilic infiltrate is seen (c, inset) (haematoxylin and eosin; original magnification: a, b $\times 40$; c $\times 10$; inset $\times 100$).

basically similar pattern: epidermal spongiosis with focal necrosis, oedema of the papillary dermis, and a perivascular, periadnexal and interstitial inflammatory infiltrate composed of lymphocytes, eosinophils and neutrophils. The only difference was that the specimen from the right ankle, which was a site bitten by mosquitos, showed more oedematous changes and a more prominent eosinophilic infiltrate (Fig. 2). In situ hybridization staining for Epstein–Barr virus (EBV)-encoded small nonpolyadenylated RNA-1 was negative. Clonal rearrangement of the T-cell receptor was not observed. Biopsy of the enlarged lymph node in the neck revealed nodal marginal zone lymphoma. The patient was treated with six courses of CHOP (cyclophosphamide, hydroxydaunomycin, vincristine, prednisone) and the skin lesions showed much improvement, with residual scarring.

HMB is a disorder characterized by exaggerated skin reactions to mosquito bites and associated general symptoms.^{1–3} In cases of HMB, the diagnosis of mosquito bites has been based on the morphological and histological characteristics of the lesions, as many patients did not recall being bitten.^{4,5} In 1999, Barzilai *et al.* described eight patients with haematological disorders who were instructed to avoid outdoor activities and to use repellents and insecticides, but who developed bullous and ulcerative skin lesions.⁶ These authors suggested that the insect bites might not be necessary to initiate this eruption and they proposed the term 'IBR'. HVPVE was recently reported as a new subset of HV. Unlike in classic HV, the eruption is not necessarily induced or exacerbated by sun exposure and is associated with general symptoms.

Furthermore, some patients developed haematological malignancy.^{7–9}

It is of interest that HMB, HVPVE and IBR have several common features. First, they occur in association with haematological malignancies. Second, they show similar clinical features with papules, vesicles, necroses, ulcerations, crusts and pitted scars. Third, in association with local skin reactions, patients exhibit general manifestations including fever, lymphadenopathy and hepatosplenomegaly. Fourth, their histological features are also similar, showing a spongiotic epidermis and a polymorphous cellular infiltrate throughout the dermis with angiocentricity. Fifth, HVPVE has been reported mainly from Japan, Korea and Mexico, the same counties in which HMB is prevalent.^{7–10} Additional evidence indicating a close association among the three types of eruption is as follows: (i) some patients with HMB developed HVPVE several years before death;^{1,2,8–10} (ii) including our case, HVPVE was sometimes induced and exaggerated by insect bites;^{1,9,10} and (iii) there was a patient who presented HMB and IBR simultaneously.⁵

We describe a Korean man with nodal marginal zone lymphoma manifesting as HMB with concomitant occurrence of HVPVE and IBR, in whom HVPVE was exaggerated by mosquito bites. Although the pathomechanisms of these conditions are unknown, some cases have occurred in association with chronic EBV infection. Our case does not support a role for EBV in the evolution of the eruption. The pathogenic role of latent viral infection in these eruptions remains to be established.

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Successful infliximab therapy of psoriasis vulgaris and psoriatic arthritis in a patient with cirrhosis

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SIR, Psoriasis and psoriatic arthritis are thought to be autoimmune disorders in which tumour necrosis factor (TNF)- α plays a critical pathophysiological role. Infliximab is a chimeric monoclonal antibody that binds and inactivates TNF- α . To date, it is

licensed for use only in the treatment of Crohn disease and rheumatoid arthritis. However, numerous recent reports on the use of infliximab in the therapy of various types of psoriasis and psoriatic arthritis have shown promising results.¹⁻⁴

We report about a 52-year-old man with psoriasis vulgaris and psoriatic arthritis, noninsulin-dependent diabetes mellitus and hereditary α_1 -antitrypsin deficiency resulting in emphysema and in histologically diagnosed micronodular cirrhosis. Laboratory results were negative for hepatitis A, B and C viruses. The patient had a 30-year history of psoriasis and a 15-year history of painful swollen joints. Psoriatic arthritis, affecting mainly the distal interphalangeal joints of the index and middle fingers of the left hand and the ring and little fingers of the right hand, was diagnosed 6 years previously by means of scintigraphy and X-ray. Systemic treatment with methotrexate was initiated at that time, while the psoriatic plaques of the skin were treated topically with corticoids and vitamin D derivatives. Due to a considerable elevation of liver enzymes, treatment with methotrexate was discontinued after 3 months. On admission to our clinic, examination showed disseminated, sharply demarcated erythematous scaling plaques of 5-25 cm diameter, covering almost the whole body surface and predominating on the elbows, knees and back. Given the increasing pain and the deformation and functional impairment of the affected joints we initiated therapy with the monoclonal anti-TNF- α antibody infliximab 5 mg kg⁻¹, infused at weeks 0, 2, 6, 12 and 20. The infliximab therapy was complemented by topical treatment with dithranol until week 2 and skincare ointments containing urea during weeks 2-20. The patient received no systemic medication other than infliximab. Because of a positive skin reactivity to tuberculin testing and the absence of a preceding bacille Calmette-Guérin vaccination, therapy with infliximab was combined with prophylactic tuberculostatic medication in accordance with the recommendations of the Paul-Ehrlich Institute. This consisted of isoniazid 100 mg daily for 9 months. After this treatment the skin showed a significant improvement, paralleled by a decline in the Psoriasis Area and Severity Index score from 61.4 at week 0 to 11.8 at week 20, after the fifth cycle of infliximab therapy. At week 12 the patient reached the American College of Rheumatology preliminary criteria for improvement (ACR 20), which were originally designed for the clinical evaluation of rheumatoid arthritis. The criteria are met when a reduction of 20% in tender and swollen joint counts is achieved and at least three of five defined criteria concerning disablement, global assessment by the patient and physician, and diminution of pain and of C-reactive protein (CRP) are fulfilled.^{1,2} At week 12 the initially slightly increased CRP decreased towards the normal range. Aspartate aminotransferase, alanine aminotransferase, thromboplastin time and serum albumin remained within normal ranges throughout the five treatment cycles (Table 1). In our patient, infliximab was administered without incidence of any adverse reaction. Three months after the last infusion of infliximab the patient relapsed, with an increase in number of painful swollen joints and psoriatic plaques.