

spontaneous healing a few weeks after withdrawal of the drug (1, 2).

An essential issue to take into account in these patients is the high prevalence of cross-reactivity between the different aromatic anticonvulsants, which in some reports is up to 80% and makes the choice of an alternative drug for these patients difficult. Although valproic acid, lamotrigine and vigabatrine are considered the safest antiepileptic drugs for these patients, some cases of hypersensitivity anticonvulsant syndrome have been reported to be triggered by them (1, 2).

In conclusion, we present an extremely unusual case of AHS, since both pustular exanthem and severe tubulointerstitial nephropathy are exceptional in the context of this syndrome, especially if we consider their combined appearance.

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## A Four-Year History of Pruriginous Erythroderma Leading to the Diagnosis of Idiopathic Hypereosinophilic Syndrome

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Sir,

Idiopathic hypereosinophilic syndrome (IHS) is characterized by persistent eosinophilia (above  $1.5 \times 10^9/l$  for more than 6 months) of unknown origin in association with dysfunction of one or more organs due to tissue infiltration by eosinophils (1). Cutaneous, cardiac, neurologic and/or pulmonary manifestations are often observed. Among the skin lesions, erythroderma is a rare complication of IHS and has only been reported in a few cases (2–6).

### CASE REPORT

In December 1994, a 67-year-old man with no history of atopy or current medication was referred due to severely itching erythroderma of a few weeks' duration (Fig. 1), small bullae on the upper limbs (Fig. 2), a palmo-plantar keratoderma and slight edema of the skin. White cell count was  $12.2 \times 10^9/l$  with 9% eosinophils ( $1.1 \times 10^9/l$ , normal range 0–0.5). A skin biopsy showed non-specific, mild vasculitis with eosinophils. Topical treatment was not sufficiently effective but prednisone (1 mg/kg daily) relieved the skin lesions and pruritus, with normalization of blood eosinophilia. Between April 1996 and March 1997 the patient's symptoms relapsed, with blood eosinophilia ranging between  $1.5 \times 10^9/l$  and  $4.0 \times 10^9/l$ . Short courses of prednisone temporarily improved the skin lesions.

In June 1997 the patient was admitted to our



Fig. 1. Erythroderma with papulous and eczematous lesions. In 1942 the patient had a plate in his right femur following a fracture. Removal of the plate did not improve his skin condition.



Fig. 2. Bullous lesions on the external side of the right forearm.

department with a weight loss of 5 kg, a pruriginous erythroderma, and palmo-plantar keratoderma. He had developed severe dyspnea on exercise within 2 weeks. White cells count was  $13.6 \times 10^9/l$  and total blood eosinophilia  $2.7 \times 10^9/l$ . Serum IgE was 1958 KUI/l ( $N < 91$  KUI/l). Serum and immunoelectrophoresis, a search for ova and parasites in the stools and serodiagnosis for a parasitic infection all proved negative. Sézary cells in blood were negative. Multiple skin biopsies showed spongiosis, lesions of leukocytoclastic vasculitis and a marked infiltration by eosinophils in the superficial dermis (Fig. 3). There was no pleomorphism among the skin-homing lymphocytes. Leukocyte centrifugation on discontinuous metrizamide gradients showed a high proportion of "hypodense" eosinophils (43%), which is the hallmark of degranulated and activated cells, as seen in the IHS (7). There was a striking elevated serum level of soluble interleukin-2 receptor at 6195 U/ml ( $< 800$  U/ml), which is also observed in active IHS (8). Chest X-ray disclosed a bilateral pleuresis and a slight cardiomegaly. Echocardiography showed a septo-apical akinesia, an

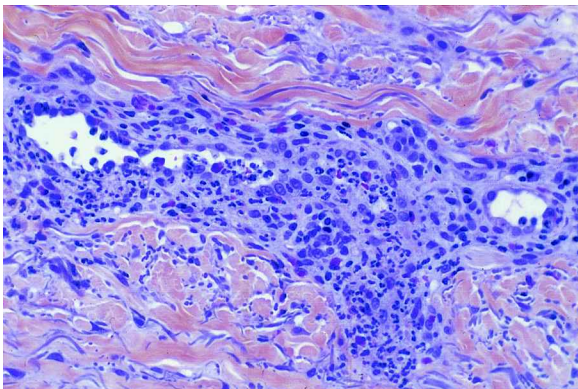


Fig. 3. Leukocytoclastic vasculitis with a marked perivascular infiltration by eosinophils in the superficial dermis (hematoxylin eosin  $\times 300$ ).

ejection fraction at 40% (normal 60–80%) and changes suggestive of an eosinophilic myocarditis. The patient had a dilated cardiomyopathy, fibrous changes of the mitral valve, and severe atherosclerosis.

The association of a eosinophilia greater than  $1.5 \times 10^9/l$  for more than 6 months, the lack of firm evidence for parasitic, allergic or other known causes of eosinophilia and signs of cutaneous and heart involvement led us to the final diagnosis of IHS. Prednisone (1 mg/kg daily) had a dramatic effect, but when tapered to 0.5 mg/kg daily, the eosinophil count began to rise, with recurrence of the pruritus. Therefore, hydroxyurea (1 g daily) in combination with 10 mg prednisone was started, which normalized the skin and cleared the pruritus. At present the patient takes a daily dose of 500 mg hydroxyurea, but prednisone was stopped 9 months ago. There has been no recurrence of the pruritus.

## DISCUSSION

We report on a patient with persistent blood eosinophilia, erythroderma and heart involvement indicative of eosinophilic myocarditis. The question is whether this patient had IHS with skin and heart involvement or an atopic erythroderma with heart involvement (9). Cutaneous manifestations of IHS are seen in 27% (1) to 64% (2) of patients, and exhibit polymorphic and/or non-specific symptoms (10, 11). The most frequent lesions are maculo-papulous, purpuric, ecchymotic or urticarial rashes sometimes with angioedema (12). Erythroderma is a rare manifestation of IHS (2–6). Differential diagnoses are atopic erythroderma or erythrodermic cutaneous T-cell lymphoma (the "Red Man syndrome"). However, our patient had severe cardiomyopathy with atherosclerosis, a high proportion of "hypodense" eosinophils similar to degranulated and activated cells (7), and an elevated serum level of soluble interleukin-2 receptor, as previously described in IHS (8), although persistent blood eosinophilia and heart involvement due to the toxicity of eosinophils is theoretically possible (9).

Histology and screening for Sézary cells in the blood were negative for erythrodermic cutaneous T-cell lymphoma (13). The third differential diagnosis is the "Red Man syndrome", where patients, usually males, develop exfoliative erythroderma of unknown etiology with keratoderma of palms and/or soles and increased IgE (14). Initial skin biopsies are non-specific, but biopsies taken later usually reveal pleomorphic infiltration. The cutaneous manifestations of our patient could have led to the diagnosis of the Red Man syndrome. However, the presence of severe heart involvement with signs of eosinophilic myocarditis and the absence of any pleomorphism among the skin-homing lymphocytes despite 8 years of follow-up are arguments for the diagnosis of IHS.

The principal cause of morbidity and mortality in

IHS is the cardiac involvement (15). A restrictive type of cardiomyopathy such as endomyocardial fibrosis is characteristic (16). Moreover, IHS can also present with a dilated cardiomyopathy and myocardial infarction, as in our patient (1, 15).

In our opinion, this case shows that clinicians should be aware of organ involvement in patients with protracted skin manifestations and blood eosinophilia. Early echocardiography is strongly recommended.

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## Two Cases of Coma-associated Bulla with Eccrine Gland Necrosis in Patients without Drug Intoxication

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Sir,

Bullous skin lesions with eccrine gland necrosis have been repeatedly described in drug-induced coma, while similar cutaneous changes in patients with non-drug-induced coma have only rarely been reported. We present two comatose patients with bullous skin lesion and eccrine gland necrosis on the dependent part of the body. There was no history of overdosage of drugs sufficient to evoke coma. Some different histopathologic findings were observed compared with drug-induced coma.

### CASE REPORT

#### Case 1

A 4-year-old boy in a deeply comatose condition was brought to the emergency room after a traffic accident.

Multiorgan failure with disseminated intravascular coagulation and multiple bone fractures were suspected. Two days later, blisters on erythematous bases presented on dependent parts of the body, such as the back, buttocks and right arm, which was the application site of cast for humerus fracture (Fig. 1). Histopathologic features showed subepidermal blistering and extensive epidermal eosinophilic necrosis without acantholytic cells or infiltrated inflammatory cells. Some thrombosed vessels were observed in the upper dermis (Fig. 2A). Extensive necrosis of the eccrine glands and ducts with partially preserved nuclei in the outer layer were also detected (Fig. 2B). No depositions of immunoglobulins or complements were seen using the direct immunofluorescent technique. The boy had not taken any drugs recently and revealed normal levels of administrated