

mechanism may also participate in the development of coma-induced bulla. Our patients showed many features that were similar to those in previously reported cases of drug-induced coma: comatose mentality, bullous skin lesions mainly at the pressure sites, hyperthermia, hypoxia and damaged epidermis with necrosis of the sweat glands and ducts. However, there was no obvious evidence of drug intoxication. These findings suggest that hyperthermia, coupled with hypoxia and local pressure, could cause sweat gland fatigue and degeneration. We believe that an additional factor may be a direct toxic effect of drugs. Further cases should therefore be studied for detection of the exact mechanisms of bullous skin lesions and extensive sweat unit necrosis in comatose patients with or without drug intoxication.

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Management of Generalized Pruritus in Dominant Dystrophic Epidermolysis Bullosa Using Low-dose Oral Cyclosporin

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Sir,
Dystrophic epidermolysis bullosa (DEB) comprises a group of inherited mechanobullous disorders characterized by blisters and erosions occurring after minor traumas frequently associated with milia formation, nail dystrophy and scarring. The blisters occur at sublamina densa level associated with quantitative or qualitative changes in anchoring fibrils due to a congenital abnormality of collagen VII (1–3). Several subgroups and phenotypical variants of DEB have been described (4).

Itching is a common symptom in many types of epidermolysis bullosa (EB), including junctional and dystrophic types (1). Here we present a patient diagnosed as DEB associated with intense pruritus without typical prurigo-like or lichenoid lesions of epidermolysis bullosa pruriginosa (EBP).

CASE REPORT

A 27-year-old female patient was referred with a complaint of severe itching. She had been suffering from skin blistering after minor trauma since the age of 3 months. Pruritus started 2 years ago. She had no atopic history. The father, two sisters, one brother had similar complaints, showing a probable otosomal dominant hereditary pattern. Dermatological examination revealed generalized erythematous plaques with crust formation, scattered excoriations, occasionally atrophic scars with milia formation, and some intact bullae localized on the trunk, back skin and extremities of the patient (Fig. 1a, c). Most of

the toenails were dystrophic. General health was not impaired. Histopathological examination showed dermal blistering at papillary dermis level. Direct and indirect immunofluorescence was performed without showing a co-existing acquired autoimmune bullous disorder. Electronmicroscopical investigation revealed that the blister was beneath the lamina densa of the dermal-epidermal junction. Serum iron levels, IgE, thyroid function, renal function and liver function tests were in the normal ranges.

The patient received 2.5 mg/kg/day of oral cyclosporin. During the therapy, the patient was carefully monitored by renal function tests and blood pressure. The majority of the lesions had responded to the therapy after 2 months (Fig. 1b, d).

DISCUSSION

Fine et al. (4) reported the revised classification system of inherited EB, which was a consensus paper of the second international consensus meeting on diagnosis and classification EB. According to this classification system, DEB has three major subtypes, including dominant DEB (DDEB), recessive DEB-Hallapeau Siemens (RDEB-HS) and recessive DEB-non Hallapeau Siemens (RDEB-nHS). However, EBP is classified in another table as one of the rare phenotypical variants of DEB. The term EBP was first used by McGrath et al. (1) to describe a group of patients with DEB characterized by lichenoid lesions, toenail dystrophy and hypertrophic violaceous scars associated with intense pruritus. It is



Fig. 1. Generalized erythematous plaques with crust formation, scattered excoriations, atrophic scars with milia formation and some intact bullae are to be seen on the back skin before (a) and after (b) treatment and on the extremities before (c) and after (d) treatment.

well known that pruritus may also occur in other EB subtypes, including junctional and dystrophic types and many cases associated with generalized pruritus cannot be included within any classical subgroup of DEB (1).

Our patient showed the clinical, histopathological and ultrastructural features of DEB, the probable dominant type. She also had intense pruritus. However, the lesions were not typical for EBP. It was recently reported that all types of DEB were due to alterations of the same gene (COL7A1) that encoded type VII collagen, the major component of the anchoring fibrils (4–7). DEB may be considered as a group of diseases presenting a wide range of phenotypic features in different patients based on the same genetic pathology.

The itchy lesions of our patient were more generalized than those of the other affected family members. The pruritus may be the consequence of an abnormal reactivity of some patients against their inherited bullous disorder. This reaction may also be considered as a late reaction in the blistering site, probably due to histamine liberation (2). Our patient did not show typical prurigo-like or lichenoid features of EBP, so we made the diagnosis of DDEB associated with generalized pruritus.

The treatment of DEB is generally based on the prevention of blister formation. Until today, oral and

topical agents, including pulse topical corticosteroid therapy, cyclosporin, minocyclin, phenytoin, tocopherol acetate and tacrolimus, have been reported to be successful in occasional cases of DDEB, RDEB and EBP (8–14). The lesions of our patient responded very well to oral cyclosporin after 2 months of therapy. On the other hand, the remission of blisters can be contributed to the relief of severe itching and scratching. According to the literature and our own observation, we suggest that low-dose oral cyclosporin is the best medical treatment for DEB associated with pruritus. However, we believe that this treatment must be used with care for short periods, since we know that neoplasia formation is one of the risks of long-term use of cyclosporin and DEB patients have an increased risk of developing squamous cell carcinoma.

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A Patient with Immunological Features of Paraneoplastic Pemphigus in the Absence of a Detectable Malignancy

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Sir,

The diagnostic criteria of paraneoplastic pemphigus (PNP) include a specific serology with circulating antibodies directed to an antigenic complex consisting of plectin (> 400 kDa), desmoplakin I (250 kDa), bullous pemphigoid antigen 1 (BP Ag 230 kDa), envoplakin-desmoplakin II (210 kDa) and periplakin (190 kDa). In addition, PNP antibodies may react with recombinant desmoglein 3 and with a 170 kDa protein, detected by immunoprecipitation and regarded initially as a degradation product (1). Antibodies to the 170 kDa molecule have been found more recently in almost all PNP sera (2), suggesting that they may play an important pathogenetic role (3) in the disease.

We describe here a patient with clinical, histological and direct immunofluorescence (DIF) features of PNP, but lacking a detectable neoplasm and with antibodies immunoprecipitating only the 170 and 210 kDa antigens.

CASE REPORT

A 70-year-old man with a history of alcohol abuse presented with mucosal erosions and a bullous eruption of the trunk of 1-month duration. Clinical examination revealed erosions in the oral cavity, partially covered by a creamy material. The glans penis appeared oedematous with multiple painful erosions. An acute purulent con-

junctivitis and some erythematous target-like bullae on the upper chest and legs were present. Erosions extended also to the pharynx and larynx.

Laboratory tests showed only an increased erythrocyte sedimentation rate (40 mm/h) and moderately high levels of cholesterol and triglycerides (230 mg/dl and 167 mg/dl, normal values <200 and <160 mg/dl, respectively). Other routine laboratory tests were within normal limits. Histopathology of 2 biopsies, one from the oral cavity and one from the right clavicular area, showed basal acantholysis and some necrotic keratinocytes. DIF disclosed IgG and C3 deposits in the intercellular substance of epidermis and granular deposits of C3 at the dermo/epidermal junction. Indirect immunofluorescence (IIF) with monkey oesophagus as substrate showed IgG directed to the cytoplasm of the basal cells. IIF with rat bladder as substrate showed IgG antibodies directed to the intercellular substance of the epithelium. Immunoblotting analysis using cultured keratinocytes as source of antigens was performed as described elsewhere (4) and showed 3 bands at 200, 170 and 120 kDa. Immunoenzymatic tests did not show serum antibodies directed to Desmoglein 1 and 3. Immunoprecipitation, done as reported elsewhere (5), showed antibodies to the molecules of 170 and 210 kDa (Fig. 1).

Because of the clinical, histological and immuno-