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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-druginduced 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 complement were seen using the direct immunofluorescent technique. The boy had not taken any drugs recently and revealed normal levels of administered
with eccrine gland necrosis despite there being no evidence of drug intoxication. He was treated with frequent dressing and topical antibiotics and the skin lesions were much improved.

Case 2

A 53-year-old semicomatose man arrived in the emergency room after severe alcohol drinking. He had been a heavy alcohol drinker for 25 years and had alcoholic liver cirrhosis, diabetes mellitus, hypertension and chronic renal failure. He was diagnosed with hepatic coma with sepsis. Three days after admission, multiple blisters appeared on deep erythematous patches of dependent parts of the body, including the back, buttocks, posterior thigh and leg. Histopathologic examination revealed findings similar to those in case 1, but direct immunofluorescence was not performed. High fever (above 39°C) and very low O$_2$ saturation were also detected. He had had no drug intoxication history and showed normal levels of other therapeutic drugs. He died after 2 days from septic shock.

DISCUSSION

Most previously reported patients with these characteristic bullous skin lesions and sweat gland necrosis were comatose secondary to an overdosage of drugs or carbon monoxide (1–5). The implicated drugs included barbiturate, methadone, hydrocodone, diazepam, amitriptyline hydrochloride, clorazepate dipotassium, meprobamate, imipramine hydrochloride, acetyl-bromo-diethylacarbamide, and gluthethimide (2–5). In bullous lesions associated with drug-induced coma, histopathologic findings show intraepidermal or subepidermal vesicles with epidermal eosinophilic necrosis. The most striking and significant change is eccrine sweat gland and sweat duct necrosis.

Similar clinical and histopathologic features can also be observed in patients with non-drug-induced coma. Kato et al. (6) first reported bullous skin lesions in three comatose patients without a drug history and described the histopathologic differences in relation to drug-induced coma. They suggested that the most distinctive findings that can be observed in non-drug induced coma are: (1) inflammatory infiltrates are not found in the epidermis, (2) nuclei of the eccrine duct in the basal layer are partially preserved, and (3) thrombosis is evident in the dermal vessels. Although the precise mechanism of these characteristic skin changes is still unknown, Kato et al. (6) described immunoglobulin and complement deposition using the direct immunofluorescence technique, suggesting that immune mechanisms as well as local trauma should be considered in the pathoetiology. However, one of our cases (no. 1) showed negative findings in direct immunofluorescence, which indicates that Kato’s suggestion may not be relevant in all cases and that another patho-

\textbf{Fig. 1.} Intact or eroded bulla with erythematous base on the cast application site of upper arm in case 1.

\textbf{Fig. 2.} A. Subepidermal bulla with extensive epidermal necrosis. Some thrombosed vessels (arrowheads) were noted in the upper dermis (hematoxylin & eosin, × 40). B. Necrosis of sweat glands and ducts with partially preserved nuclei (arrowheads) in the outer layer (hematoxylin & eosin, × 200).

drugs, such as prophylactic antibiotics and antifungals. Body temperature was 38.7°C. Analysis of the peripheral blood gas showed an extremely low level of O$_2$ saturation. We diagnosed him as having coma-associated bulla...
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 mecanobullous 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 qualitative or quantitative 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 otsosomal 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 phenotypic 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