

## Subcorneal Pustular Dermatitis—An Unusual Course

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In a patient with subcorneal pustular dermatosis (SPD) the appearance of new pustular lesions characteristic of the disease was triggered by two episodes of drug eruption (induced by dapsone and quinidine sulphate respectively) and by the intra-dermal injection of the recall antigens *Candida* and streptokinase-streptodornase, performed for evaluation of delayed hypersensitivity. Both episodes of drug eruption were probably the result of an immediate-type hypersensitivity reaction towards the offending drugs, as indicated by positive mast cell degranulation tests. *Key words: Drug eruption; Dapsone; Quinidine sulphate; Mast cell degranulation test; Delayed hypersensitivity skin tests.* (Received February 1, 1982.)

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The cause of subcorneal pustular dermatosis (SPD), first described by Sneddon & Wilkinson (12), is not known. Trigger mechanisms, including preceding or concomitant infection

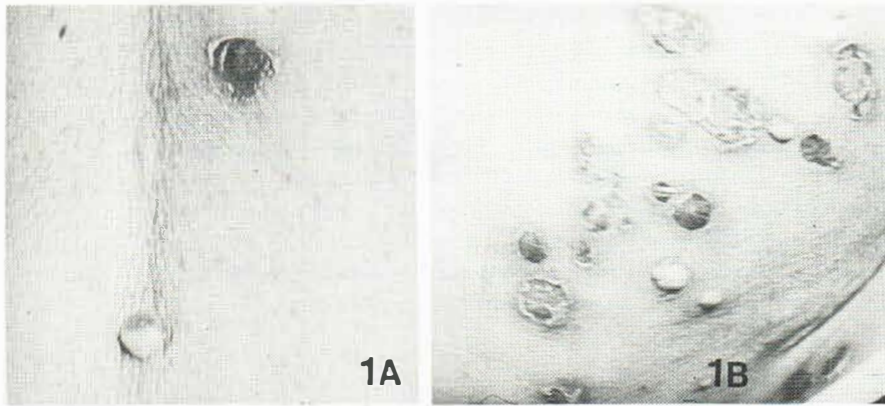


Fig. 1A. Flaccid pustule showing pus in the lower part and clear fluid in the upper part.

Fig. 1B. Flaccid pustules forming circinate or serpiginous patterns, with scaly and crusted edges.

and associated immunological abnormalities such as paraproteinemia and cryoglobulinemia, have been implicated in the pathogenesis (1, 5, 13). In the case of SPD presented here an unusual course of the disease was observed, during which the appearance of new pustular lesions characteristic of SPD was triggered by different types of stimuli.

#### CASE REPORT

The patient was a 68-year-old woman being treated with propranolol<sup>1</sup> HCl (80 mg × 2 daily) because of hypertension. This woman suddenly developed a pustular rash on the legs, axillae, groins, thighs and trunk, for which she initially received erythromycin (1.0 g daily). Close examination revealed flaccid pustules 1–3 mm in diameter surrounded by an erythematous halo. Some of these were isolated, showing pus in the lower part and a clear fluid in the upper part (Fig. 1A). In most areas, however, the pustules showed a tendency to coalesce, forming circinate or serpiginous patterns, with scaly and crusted edges, as well as "lakes of pus" (Fig. 1B). Nikolsky's sign was negative and mucous membranes were not involved.

Histological examination of a pustule revealed a subcorneal bulla filled with neutrophils, fibrin and a few acantholytic cells. The epidermis beneath the bulla also contained a few neutrophils. In the underlying dermis there was an extravasation of erythrocytes and an inflammatory infiltrate which was both diffuse and perivascular and consisted of neutrophils, lymphocytes, histiocytes and a few eosinophils (Fig. 2). Indirect and direct immunofluorescence tests proved negative and repeated cultures of material obtained from fresh pustules failed to reveal pathogenic organisms. The clinical, histological, immunofluorescent and bacteriological findings all supported the diagnosis of subcorneal pustular dermatosis (SPD) of Sneddon–Wilkinson. There was no evidence of an occult focus of infection, paraproteinemia, or cryoglobulinemia in this patient. Tests for delayed hypersensitivity performed by the intra-dermal injection of four recall antigens were positive with PPD, *Candida* and streptokinase/streptodornase (SK/SD) and negative with *Trichophyton*. One noteworthy finding was the appearance of new pustules characteristic of SPD in the areas injected with *Candida* and SK/SD, 96 hours after the injection.

<sup>1</sup> Generic equivalents of drugs appearing in the text:

Generic name	Trade name	Generic name	Trade name
Dapsone	Avlosulfone	Quinidine sulphate	Quinidine
Erythromycin	Erythrocin	Quinidine bisulphate	Quiniduran
Propranolol HCl	Deralin	Prednisone	Meticorten



Fig. 2. Sub-corneal bulla filled mainly with neutrophils. The epidermis beneath the bulla also contains a few neutrophils (H & E  $\times 40$ ).

Fig. 3. Exfoliation of the skin, with formation of large shallow erosions.

Following the diagnosis of SPD, treatment was instituted with dapsone at a dose of 100 mg daily. Three days later the patient developed a maculo-papular rash on the trunk accompanied by intense pruritus. Since this was suspected to be a drug eruption, both the dapsone and the erythromycin still being taken were discontinued but within a few days the rash assumed the form of exfoliative dermatitis, with the appearance of large shallow erosions, especially on the thighs (Fig. 3). A new wave of SPD pustules then appeared in the affected regions, accompanied by fever and a progressive worsening of the patient's condition. Two *in vitro* tests served to evaluate still further the clinical diagnosis of drug eruption: the macrophage migration inhibitory factor (MIF) test, performed as a modification of the Rajapakse technique (6, 9), and the mast cell degranulation (MCD) test, performed as a modification of the Schwartz technique (11). Whereas the MIF test was negative towards dapsone, erythromycin and propranolol HCl, the MCD test was positive towards dapsone. Administration of prednisone 80 mg daily led to a dramatic improvement and within several days all skin lesions disappeared.

Shortly before the patient's discharge, treatment had been instituted with quinidine sulphate (0.2 mg  $\times 3$  daily) and quinidine bisulphate (once daily) because of cardiac bigeminy. When prednisone was reduced to 35 mg daily 3 weeks later, a second erythematous rash appeared on the trunk. As before, a new wave of pustules occurred at the same site of the erythematous eruption. Prednisone was again increased to 80 mg daily and both quinidine sulphate and quinidine bisulphate were withdrawn, with the result that all skin lesions disappeared within a few days. An MIF test towards quinidine sulphate proved negative but an MCD test towards this drug was positive.

## DISCUSSION

The main significance of this case of SPD would appear to be the unusual appearance of new pustular lesions characteristic of SPD, triggered by different types of stimuli. These stimuli included two episodes of drug eruption induced by different agents (dapsone and quinidine sulphate) and presenting different morphological features (exfoliative dermatitis and erythematous rash). Laboratory evaluation of the clinical diagnosis of drug eruption was based on two in-vitro tests: the MIF test, which is a function of cellular immunity and which can detect a delayed hypersensitivity reaction towards a drug (3, 4, 10), and the MCD test, which detects the presence of specific IgE antibodies and can reveal immediate hypersensitivity towards a drug (7, 8, 11). Accordingly, both episodes of drug eruption were probably the result of an immediate-type hypersensitivity reaction towards the offending drugs.

Of particular interest in this patient was the fact that the intra-dermal injection of the recall antigens *Candida* and SK-SD also triggered the appearance of new pustules characteristic of SPD in the injected areas, as has been reported previously (2).

We can only speculate as to the mechanism responsible for the phenomenon of the evocation of new pustules characteristic of SPD by different types of stimuli. It is possible that trauma to the skin occurring during drug eruption and the process of intra-dermal skin tests induced a Koebner-like phenomenon. However, it is also quite likely that the immunological system, which was involved in both episodes of drug eruption as well as in the intra-dermal skin tests, was responsible for this phenomenon.

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