

GENERALIZED PUSTULAR TOXIC ERYTHEMA: PATHOGENETIC RELATIONSHIP BETWEEN PUSTULE AND EPIDERMAL APPENDAGE (HAIR FOLLICLE OR SWEAT DUCT)

Atsuhiko Ogino, Hachiro Tagami, Chie Takahashi and Takako Higuchi

Department of Dermatology, Faculty of Medicine, Kyoto University, Kyoto, Japan

Abstract. Seven patients are described, who had generalized toxic erythema with sterile pustules. Study of serial sections of the pustules confirmed a specific localization to hair follicle or epidermal sweat duct. Five patients had a past history of medications, exposure to an organic solvent, or infections.

Key words: Toxic erythema; Pustule; Drug eruption; Infection; Hair follicle; Epidermal sweat duct

The term toxic erythema is commonly applied to a generalized exanthematic eruption produced by drugs, chemical substances, foods, or infections, on the basis of allergic or toxic responses. The clinical features of toxic erythema are variable and include macular erythema, urticaria, petechiae and pustules (2). Toxic erythema with generalized pustulation is known as the reaction to phenylbutazone (4), but it has rarely been reported with other drugs (6, 11). The diagnosis of generalized pustular drug rash reported by Macmillan (6) depended only upon circumstantial evidence or exclusion of alternative diagnosis. No causative agents could be confirmed by a provocation test in most cases, since this type of the reaction is severe and involves internal organs such as the liver or kidney.

The relationship between a sterile pustule and epidermal appendages has been thoroughly debated as regards psoriasis (7, 9), eosinophilic pustular folliculitis (8) and erythema neonatorum toxicum (3, 5), but little is known about any such relationship in toxic erythema including drug eruptions (2, 11).

In this paper, we report on 7 patients with toxic erythema associated with generalized pustules and the interesting histological findings regarding these pustules.

REPORT OF CASES

Two typical cases are described in detail as follows and 7 cases are summarized in Table I.

Case 1. A 22-year-old housewife complained of pruritic disseminated macular or diffuse erythema on the trunk, of 3 days' duration. The eruption spread over the extremities and superficial small pustules then appeared on the erythematous base (Fig. 1). She had an elevated temperature of 37.7°C, a sore throat and swelling of the tonsils. She had taken no medicine and had not suffered from any infection before the onset of the illness. Laboratory findings disclosed a white blood cell (WBC) count of 19000/mm³ with 82% neutrophils, positive C-reactive protein and positive albuminuria. Bacterial culture of the pustules did not disclose any growth. Histologic examination revealed a dense cellular infiltration involving the upper layer of the dermis, composed of eosinophils, neutrophils, histiocytes and lymphocytes. Some of those cells were invading the epidermis, especially along the edematous portions bordering the epidermal sweat ducts (Fig. 2). Most of the subcorneal eosinophilic pustules were localized to the terminal portion of the sweat duct, produc-

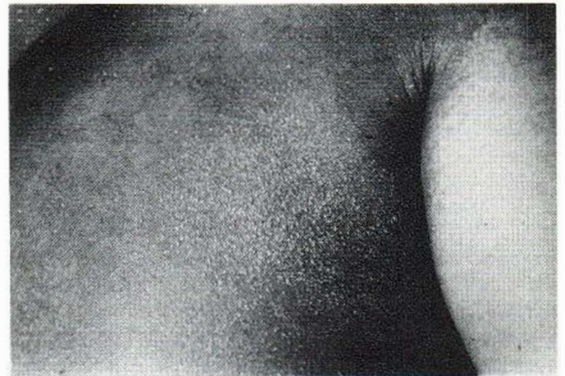


Fig. 1. Case 1. Densely developed pustules over erythematous base.

Table I. Generalized pustular toxic erythema

Case	Age/Sex Occupation	Pustule		Temperature	Throat	Swelling of lymph nodes (LN)	Leuko- cytes/mm ³ Neutro- phils, %	CRP
		Site	Histological localization					
1	22/F Housewife	Back, abdomen	Sweat duct	37.7°C	Redness		19 000 82%	+1
2	30/M Tax accountant	Nape, chest, axillae	Hair follicle	37.9°C		Cervical LN	10 100 89%	+2
3	38/M	Face, back	Hair follicle	Normal			7 300 70%	±
4	24/F Clerk	Neck, flank, arms	Possibly, sweat duct	38.5°C	Soreness		15 600 91%	+3
5	26/M Cook	Back	Hair follicle	High	Soreness	Axillary LN	20 000 76%	±
6	21/F Factory worker	Face, dorsa of hands	Hair follicle	41°C	Redness Soreness	Cervical LN	13 100 57%	+2
7	14/F Student	Groins, neck, trunk	Sweat duct	37.7°C		Cervical, axillar, inguinal LN	8 200 53%	-



Fig. 2. Case 1. Exocytosis of neutrophils, eosinophils and lymphocytes into the edematous areas surrounding an epidermal sweat duct. Hematoxylin-eosin, $\times 90$.

ing a funnel shape (Fig. 3). The lesions responded to systemic steroids (betamethasone 1.5 mg per day) and resolved one week later, followed by generalized exfoliation. Transient attacks of urticaria appeared during the treatment.

Case 2. A 30-year-old man developed generalized erythema with an elevated temperature of 37.9°C, 3 days after lancing of a gingival abscess and administration of ampicillin. Numerous small, superficial pustules soon appeared over the erythema on the nape (Fig. 4), chest and in the axillae. The cervical lymph nodes were swollen and tender. Laboratory findings exhibited a WBC count of 10 000/mm³ with 89% neutrophils, positive C-reactive protein and moderately positive albuminuria. There was a minimal growth of *Staphylococcus epidermitis* from the aerobic culture of the pustules. Histologic study showed a cellular infiltration consisting of leukocytes, eosinophils and histiocytes and scattered erythrocytes in the upper part of the dermis as well as aggregation of neutrophils in the follicular infundibulum and in the surrounding epidermis (Fig. 5). The affection responded well to a combination of oral steroid (betamethasone 2 mg per day) and antibiotics (cefalexin 1 000 mg per day). After one week, the lesions had regressed considerably, followed by a severe generalized exfoliation.

DISCUSSION

We have summarized the 7 cases under the heading generalized pustular toxic erythema, possibly caused by drugs, foods or infections (Table I).

Other laboratory findings	Possible etiologic factors (drugs, infections)
Albuminuria ++	
Albuminuria ±	Gingival abscess, intake of ampicillin
S-GOT 72U, total bilirubin: 1.2 mg %	
Albuminuria ±	Common cold, intake of aspirin and creosote
RA ++	Intake of herb medicine (licorice)
Albuminuria ++, S-GOT 54U, S-GPT 49U, eosinophils: 11%	Exposure to tetrachloroethylene (dry cleaning agent)
Albuminuria ±	Two weeks prior, rubella

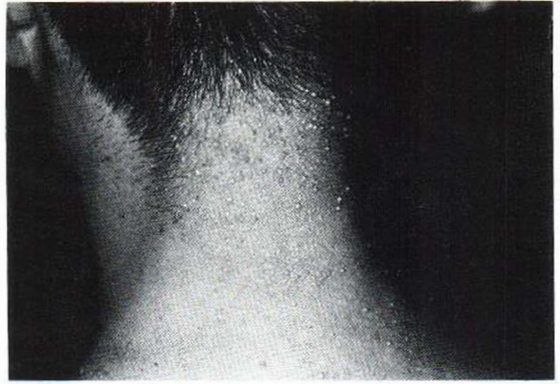


Fig. 4. Case 2. Numerous, small, superficial pustules over erythema on the nape.

These cases were clearly distinct from pustular psoriasis of the Zumbusch type but they showed a resemblance to the exanthematic type of Baker (1) or a benign variant of pustular psoriasis of Stevanovic (10), which usually have the following clinical characteristic features: 1) no concomitant typical psoriatic lesions, 2) development after infections

or after the administration of drugs, 3) short duration, 4) no recurrence, 5) frequent initial occurrence on the palms and soles. Baker himself doubted if this variant was true psoriasis. Our cases are diagnostically distinct from impetigo herpetiformis, subcorneal pustular dermatosis, scalded skin syndrome or scarlet fever, because of the clinical, histological and laboratory findings.

We studied serial sections of skin biopsy material from the pustules. Connection with a hair follicle was noted in 4 patients (cases 2, 3, 5, 6) and with an epidermal sweat duct in 2 patients (cases 1, 7). In the remaining patient (case 4) the possibility of such an association with an epidermal sweat duct was suspected.

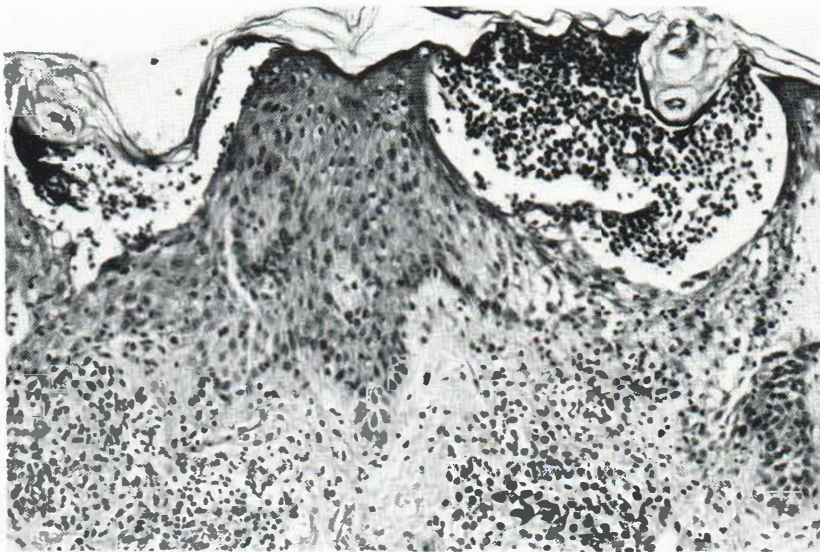


Fig. 3. Case 1. Eosinophilic pustules localized to sweat pores, producing a funnel shape. Hematoxylin-eosin, $\times 90$.



Fig. 5. Case 2. Collection of neutrophils in follicular infundibulum and in surrounding epidermis. Hematoxylin-eosin, $\times 90$.

Neumann (7) reported that in sections from psoriasis vulgaris or pustular psoriasis, all the spongiform pustules were seen to be situated around the acrosyringium. According to Shelley (9), pustules of pustular psoriasis and those induced by intra-dermal injection of killed Streptococcal organism in the patient with this disorder showed a distinct localization to the acrosyringium. He considered that some antigen, secreted by the sweat glands, and which escaped into the periductal epidermis as a result of sweat retention, is involved in the pathogenesis of the pustulation.

In 1970, Ofuji et al. (8) reported a new entity which showed crops of sterile pustules filled mostly with eosinophils, histologically located in the outer root sheath and accompanied by blood eosinophilia. Although the pathogenesis is still not known, they suggested that certain substances secreted by the sebaceous glands might have some relationship with the development of the skin lesions.

Erythema toxicum neonatorum represents a characteristic cutaneous eruption in the neonatal period, consisting of large erythematous areas, macules, papules or pustules, which are related to the hair follicles and contain many eosinophils (5). Furthermore, in some sections, these appeared to be related to sweat ducts (3).

In drug-induced pustular eruption, an eosinophilic abscess was reported to be present within an enlarged hair follicle (11). In our 7 cases, the correlation between pustulation on the toxic erythema

and epidermal appendages seems clear. However, the nature of the chemotactic factors remains obscure.

ACKNOWLEDGEMENTS

The authors are most grateful to Professor S. Ofuji and Dr S. Imamura for their help and encouragement.

PHARMACEUTICAL PREPARATION

Betamethasone—Rinderon
Cefalexin—Keflex
Ampicillin—Viccillin

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Received July 4, 1977

A. Ogino, M.D.
Department of Dermatology
Faculty of Medicine
Kyoto University
Shogoin, Sakyo-ku
Kyoto, 606
Japan