

polymerase (1). The method used involves damage to the cell membrane which allows ^3H -TTP and the unlabelled triphosphates to enter the cell body and to be incorporated into DNA after induction of DNA synthesis utilizing nuclear DNA-polymerase and preformed DNA as primer-template.

A cell population may be divided into 'proliferating' and 'non-proliferating' cells. ^3H -thymidine labelling indicates the fraction of cells in DNA synthesis (4), whereas the present method indicates the fraction of cells having the potential for replicative DNA synthesis. In experimental tumour systems this method has been shown to be a valid measure of the growth fraction (12). This ^3H -TTP single cell assay may provide a new parameter of human epidermal cell kinetics.

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Acute Generalized Pustular Bacterid and Immune Complexes

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Abstract. The case is described of a 39-year-old man with acute generalized pustular bacterid and high Clq -binding activity in the sera during the active stage. Histamine-induced vascular changes studied by immunofluorescence microscopy revealed a perivascular deposition of IgM and C3. These findings support the view that leukocytoclastic vasculitis underlying the subcorneal pustules is mediated by immune complex deposition.

Key words: Pustular bacterid; Leukocytoclastic vasculitis; Immune complex

Recently, Tan (5) reported the case of a 58-year-old woman, who suddenly developed widespread pustules and purpuric lesions after streptococcal upper respiratory infection. The acute clinical course and histopathological observations which revealed a leukocytoclastic vasculitis underlying the pustules, were quite different from those of pustulosis palmaris et plantaris (PPP). The author consequently considered this to be a true case of "acute generalized pustular bacterid".

We have investigated the immune complexes in both sera and tissues of a patient with acute generalized pustular bacterid and found a possible relationship between the immune complex deposition and leukocytoclastic vasculitis.

CASE REPORT

A 39-year-old Japanese man came to our clinic in October 1978, complaining of numerous asymptomatic pustules



Fig. 1. Numerous asymptomatic pustules on the palms resembled pustulosis palmaris et plantaris.

and necrotic papules of one week's duration. Three days before the appearance of the eruptions, he had had a common cold with sore throat and a mild fever. When first



Fig. 2. Various sized necrotic lesions with crusts and erythema on the lower legs.

seen by us, there were small crusty pustules scattered over the palms (Fig. 1), soles, tibial side of the lower legs and a few pustules on the dorsa of hands and feet and both forearms. On the lower legs, various-sized necrotic lesions with erythema (up to 3 cm in diameter) were also present (Fig. 2).

He was treated with oral administration (750 mg/day) of cephalexin (Keflex, Shionogi) and most of the pustules disappeared within a few days, but necrotic lesions on the lower extremities remained unaffected. Examinations after admission, led to a diagnosis of periodontitis, chronic tonsillitis and acute glomerulonephritis. He underwent tonsillectomy and extraction of decayed teeth. No fresh pustules appeared following this surgery. By the time of discharge in December 1978, the ulcerative lesions had resolved almost completely. To date there has been no recurrence.

Laboratory evaluation demonstrated a WBC count of 9400, elevated ESR of 18 mm/hour, positive C-reactive protein (+++) and massive proteinuria with macroscopic hematuria. ASO titre was 50 Todd units at first consultation, 625 units 2 weeks later and 333 units 5 weeks later, when the skin lesions had mostly subsided. Other results were all within normal limits.

Histological examination of a crusty pustule (Fig. 3) showed a subcorneal spongiform pustule with polymorphonuclear leukocyte (PMN) migration and a massive perivascular infiltration of PMN's in the middle to upper dermis. Vessel walls showed slight to mild hyalin degeneration. By fluorescent antibody techniques, no serum factor deposition was detected over the sections, except for slight perivascular deposits of fibrinogen.

To test for the presence of circulating immune complexes, 0.1 ml of 0.01% histamine hydrochloride was injected intradermally into areas of uninvolved skin. Four hours after injection, there was an apparent deposition of IgM and C3 around the vessel walls (Fig. 4). Furthermore,



Fig. 3. The intra-epidermal spongiform pustules consisted of accumulations of PMN's which were also present in a meshwork of residual cell walls of keratinocytes. In the dermis, endothelial swelling of vessel walls accompanied by perivascular infiltrations of PMN's and nuclear crusts (H&E stain, $\times 300$).

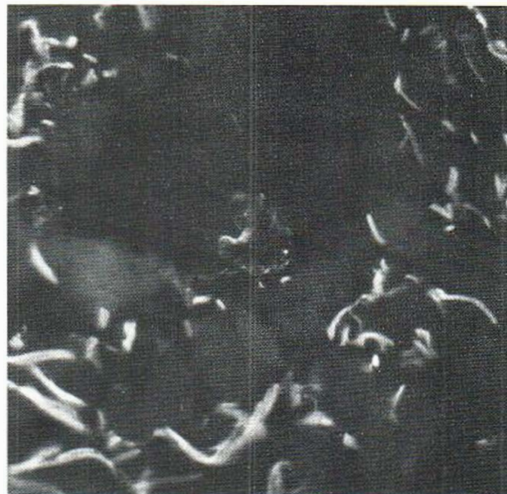


Fig. 4. In histamine-treated wheals, immunofluorescence microscopy studies revealed a deposition of IgM around the vessel walls, 4 hours after injection ($\times 700$).

C1q-binding activity (6) was 28.8% (normal range: less than 20%) at the first consultation and 16.4% when the skin lesions were in a state of regression.

At the time of remission of the disease, the patient was given intracutaneously 0.05 ml of a solution of bacterial antigens (Hollister-Stier Laboratories). No reactions had occurred by 15 min after injection, while only a *Strept. pyogenes* site showed erythema (21 mm $\times$ 19 mm) at 48 hours.

DISCUSSION

On the basis of clinical features and histological findings, we diagnosed this case to be one of acute generalized pustular bacterid. The presence of leukocytoclastic vasculitis was a most striking feature of the present case. Tan thought that this type of vasculitis would favour the Arthus-type hypersensitivity possibly elicited by streptococcal infection and suggested that pustular formation could result from a streptococcal production (5). We demonstrated high C1q-binding activity in the sera of the patient during the active stage of the skin lesions. Furthermore, histamine-treated skin showed perivascular deposition of IgM and C3, suggesting that these deposits may represent trapped circulating immune complexes (1). Although immunoreactions were not detected in the lesions, these findings seem to support the view that leukocytoclastic vasculitis is mediated by tissue-bound immune complexes. Lack of immune complex deposition in the lesions may be due to rapid

clearance of immune complexes by massive leukocytic infiltrations (2).

Parish (3) reported that bacterial antigens, immunoglobulins and complements were demonstrated in lesions of spontaneous cutaneous vasculitis preceded by streptococcal pharyngitis. Antibodies produced against bacterial polysaccharides proved to belong to the IgM class (4). The present findings, such as the deposition of IgM antibodies, the former streptococcal infection with high ASO titre, and positive skin reactions to streptococcal antigens, therefore, strongly suggest that streptococcal antigens may also play an important role in the pathogenesis of the vasculitis of this case. But mechanisms for the formation of sterile subcorneal pustules of acute generalized pustular bacterid still remain obscure.

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Cutaneous Eruptions and Intrauterine Contraceptive Copper Device

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Abstract. In the course of 6 months, 1888 intra-uterine contraceptive devices (IUCD) were inserted in a public clinic for contraception. In 10 of the women the IUCD subsequently had to be removed because of skin complaints. Four of these women as well as 3 out-patients of the Department of Dermatology, The Finsen Institute, who had been fitted with an IUCD were tested for metal allergy with closed patch tests and intracutaneous tests. None of the women was allergic to copper. One woman was allergic to nickel, which could be traced in minimal amounts in the copper wire of the IUCD, though causal connection between nickel in the IUCD and the skin symptoms is believed to be unlikely.

Key words: Intra-uterine contraceptive device; Copper; Nickel; Contact dermatitis; Internal provocation

Cutaneous allergic reactions to copper are extremely rare. However, in 1972 Barranco (1) reported a case of eczematous dermatitis caused by internal exposure to copper in an intra-uterine contraceptive copper device (IUCD) and in 1977 Forch, Kästner & Wagner (5) reported a second case. Both cases were verified by patch testing. In several cases of cutaneous eruptions in IUCD-using women, attention has been drawn to the IUCD as a possible cause of the dermatitis or of progression in a pre-existing skin disease, but final proof has constantly been lacking (2, 3, 6).

In order to estimate the practical significance of IUCD in skin diseases, we have conducted tests for metal allergy over a period of 6 months in IUCD-using women having skin complaints.

The IUCD

The copper in the IUCD's used in Denmark is quite pure and any contamination to the copper, for example in Gravigard® (Searle) which contains 115 mg copper with a surface area of 200 mm² does not exceed 0.01 % according to the registration specifications.

On request the manufacturer reported a nickel content of 0.00032–0.00038 % in the copper wire in the IUCD. Spectrographical analyses of nine copper wires from IUCD's as performed at NKT Metals, confirmed these figures, even though a certain fluctuation was found—as is