

tor T cells has been suggested as a possible basic mechanism (9). On the basis of animal experiments these authors suggest that the ordinary balance between the B cells producing immunoglobulins and the T cells suppressing this production is disturbed in this type of allergy. This model could be applied to our patient too. The functional defect of the T cells when exposed to autologous serum could render them incapable of regulating the immunoglobulin production and it also could make their immunological surveillance function less efficient.

The interpretations suggested in this report are obviously hypothetical. Nevertheless, it is an attempt to reveal possible links between an unusual clinical picture in a patient and certain disturbances in his immune system.

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A Haemorrhagic Bullous Eruption of the Hands Caused by Phenylbutazone: A Report of 3 Cases

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Abstract. Three patients developed a haemorrhagic eruption on the hands after taking phenylbutazone. The reaction appeared within two weeks of taking the drug and is probably an allergic capillaritis. All patients showed generalised capillary fragility with a positive Hess test which became negative within a week of stopping the drug. A mechanism is suggested for the development and distribution of the blisters.

Key words: Bullous eruption; Phenylbutazone; Purpura

Skin manifestations of drug reactions caused by phenylbutazone and its analogues are not uncommon. They may present as a general exfoliative dermatitis, erythema multiforme, or toxic epidermal necrolysis (1) and may even prove fatal (2). More commonly they present as morbilliform, maculopapular, or urticarial eruptions (4, 12). Purpuric and haemorrhagic eruptions have also been reported. These may be secondary to thrombocytopaenia (7) or non-thrombocytopaenia secondary to angiitis (6, 13).

This present communication describes three cases of phenylbutazone sensitivity presenting as non-thrombocytopaenic purpura with distinctive bullous haemorrhagic lesions on the hands.

Case 1

A 60-year-old engineer reported to the Casualty Department with a three-day history of large haemorrhagic blisters on the hands. He had not suffered from skin trouble previously and was otherwise well. However, one week previously, whilst at work, he had suffered a minor sprain of the right wrist. He was given phenylbutazone 200 mg t.d.s. by his general practitioner, to be taken for one week. He was taking no other medication.

On examination, the eruption was found remarkably symmetrical on both hands. There were tense blood blisters between all the fingers, over the palmar surface of the proximal phalanges, and some extension to the dorsum of the terminal phalanges. The largest blisters were seen particularly between the thumb and first finger



Fig. 1. Bullous haemorrhagic eruption on the hands, as seen in Case 1.

of both hands (Fig. 1). The palms were spared, as was the dorsum of the hand. There was a small haemorrhagic blister on the dorsum of the right large toe. There was no other rash. Liver and spleen were not palpable. There were no blisters on the mucous membrane. Hess test was so positive that the test area was nearly a confluent area of purpura after 5 min.

Investigations:

Haemoglobin, 14.8 g.
WBC, 7×10^9 /litre, normal differential.
Platelets, 275×10^9 /litre.
ESR, 19 mm/hr.
Bleeding time, 2 min.
Prothrombin time, 13 sec (control, 13 sec).
Kaolin cephalin clotting time, 30 sec (control, 33 sec).
Thrombin time, normal.
Euglobin clot lysis time, 106 min (normal).
MSU, urea and electrolytes, plasma proteins, immunoglobulins, alkaline phosphatase and transaminases were all normal.
Antinuclear factor, negative.

The patient was treated with potassium permanganate (1/8 000) soaks twice daily and unguentum Merck applied under stockinette dressings. The blisters dried up within a week of stopping the medication. Hess test became negative and he suffered no recurrence of bullae.

Case 2

A 50-year-old housewife presented with an 8-day history of blistering hands. Initially she had noticed dry itching skin between the fingers and on the palm. Three days later she developed tense haemorrhagic blisters on the sides of the fingers, the interdigital clefts, the thumb and the thenar eminences. The centre of the palm and the back of the hand were spared. There was a fine purpura on the lower

legs and trunk. The liver was just palpable but not tender. The spleen was not palpable, nor was there any lymphadenopathy. Again, as in Case 1, Hess test was strikingly positive.

Two weeks previously she had been given phenylbutazone 100 mg b.d. for osteoarthritis of the right knee. She was taking no other medication at the time, although she occasionally took phenobarbitone for 'nerves'.

Investigations:

Haemoglobin 14.1 g.
WBC, 8×10^9 /litre.
Platelets, 345×10^9 /litre.
ESR, 30 mm/hr.
Bleeding time, 2 min.
Prothrombin time, 13 sec (control, 12 sec).
Kaolin cephalin clotting time, 33 sec (control, 36 sec).
Thrombin time, 14 sec (control, 14 sec).
Euglobin clot lysis time, 128 min (normal).
MSU, urea and electrolytes, liver function tests, plasma proteins, immunoglobulins were all normal.
Antinuclear factor, negative.

Case 3.

A 38-year-old right-handed nurse developed itchy haemorrhagic blisters on the hands 4 days after taking phenylbutazone 200 mg t.d.s. for backache. These blisters were on the palmar surface of the fingers, between the fingers and on the flexor aspect of the forearm. The dorsum of the hands were spared. The right hand was more severely involved than the left. Hess test was positive. She had had no previous skin disease and no 'allergies'.

Investigations:

Haemoglobin, 13.6 g.

WBC, 5.7×10^9 /litre.
 Platelets, 190×10^9 /litre.
 ESR, 24 mm/hr.
 Clotting profile, normal.
 Antinuclear factor, negative.

She was treated with a reducing dose of systemic prednisolone, starting at 30 mg daily and finishing after one week. Locally the blisters healed with potassium permanganate soaks (1/8 000) and emollient cream. The blisters healed within a week and Hess test became negative.

DISCUSSION

These cases are remarkable for the consistency of the clinical presentation. All the patients developed the eruption within 2 weeks of beginning the medication. They had never previously had phenylbutazone, or any similar drug. The pattern of the eruption was similar in all patients and unlike any previously described.

The haemorrhagic eruption caused by phenylbutazone may be the result of thrombocytopaenia (7), secondary to bone marrow depression, or the production of platelet antibodies (3). Allergic angitis is the other cause of the purpura. Capillaritis, as shown by a macular purpura, or arteritis, as shown by more nodular or ulcerative lesions, tend to come on within 2 months of taking phenylbutazone (6). Similarly, other allergic phenomena such as drug-induced Sjögren's (8), or generalized lymphadenopathy (10) also tend to occur early in the treatment with this drug.

In these 3 patients, the eruption appeared within the first 2 weeks of therapy. This tendency for the allergic reaction to appear early is supported by the observations of Sperling (12) who did not find any allergic phenomena occurring as a late side effect in a long-term follow up of 502 patients taking phenylbutazone for 2–10 years.

The skin biopsy in the second case showed a moderate degree of perivascular infiltrate with lymphoid cells. There were collections of these cells with a few polymorphs at the base of the epidermis and migrating into it. Van Joost et al. (5) showed that the skin lesions in a case of phenylbutazone sensitivity were produced by different immunological mediators in both blood vessels and in the basal cell layer. They concluded that the lesions in their case were produced both by the deposition of antigen–antibody complexes as an Arthus reaction, and also as a result of aggregated circulating antibodies. These latter may be reactive

with both epidermal basal cells and with basement membrane.

The distribution and nature of the eruption may be explained in part by a combination of trauma and capillary fragility. All cases showed marked positive Hess tests as a reflection of capillary fragility. Case 1, who was an engineer, used tools in his trade which required not only a gripping action, but also a twisting and rotating motion. Whereas direct gripping pressure may not produce bruising or bleeding, the effect of the shearing strain set up between the skin and the instrument, e.g. a screw-driver, during rotational movements, is more likely to damage the fragile capillaries and smaller arterioles. Shuster & Scarborough (11) showed that this differentiation between the effect of direct pressure and shearing strain was true, particularly in the production of senile purpura. It is therefore particularly interesting that the largest blister tended to occur between the first finger and thumb, i.e. at a point where a greater proportion of the shearing strain is applied. The second case was a housewife and the reason for the distribution of her eruption is less clear. However, performing everyday procedures, which require the same twisting action, such as wringing out a cloth, would subject her skin to a similar shearing trauma. The third case had a more marked eruption on the dominant right hand and this favours trauma as a precipitating factor in the production of the blisters.

There remains the possibility that this could be a fixed drug eruption. Although phenylbutazone is a common cause of fixed drug eruption (9) the presence of purpura elsewhere in Case 2, and positive Hess tests in all three cases, tended to make this unlikely. All patients recovered satisfactorily. They were not challenged with a test dose of phenylbutazone, as in previous cases (6) challenge has produced a more severe attack than the original lesion, even with a small dose.

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Norwegian Scabies Developing during Treatment with Fluorinated Steroid Therapy

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Abstract. A fit, normally intelligent young man developed Norwegian scabies after prolonged treatment with large quantities of clobetasol propionate ointment. The development of this overwhelming infestation from the normal eruption of scabies may be related to the local immunosuppressive effect of this potent topical steroid.

Key words: Norwegian scabies; Fluorinated steroid ointment therapy; Immunosuppression

Many factors have been implicated in the development of overwhelming infestation with the scabies

mite, so-called Norwegian scabies. Of these factors, mental defect, gross debility and loss of cutaneous sensibility are well documented (6).

More recently, cases have been described in patients who have demonstrable immune suppression or deficiency, due either to disease states (4) or as a result of immunosuppressive therapy (7). This report describes a case of Norwegian scabies precipitated by the prolonged use of excessive quantities of the powerful topical fluorinated steroid clobetasol propionate (Dermovate, Glaxo).

CASE REPORT

A 35-year-old bricklayer presented to his general practitioner with an itchy rash between the fingers and around the wrists. There was no previous history of skin disease, nor was there a family history of either eczema or psoriasis. This eruption was diagnosed as a cement dermatitis and treated with clobetasol propionate ointment. In the succeeding weeks the rash spread to involve the feet, legs and trunk. It was still very itchy and prevented him from sleeping. Within 3 months he had a widespread maculopapular erythema with some scaling and vesicopustules on the fingers and toes. He was using 100 g of ointment per week. The patient's wife and children also began to itch. The patient was referred 6 months after the eruption originally appeared, as the character of the rash had then changed.

Examination showed a fit man of average intelligence. There were widespread areas of excoriated erythema on the trunk and limbs. A remarkable feature was the symmetrical, well-demarcated, hyperkeratotic erythematous areas, seen particularly on the backs of the hands, fingers, over the elbows (Figs. 1 and 2) and on the feet.

Live acari were isolated from the many burrows on the hands and feet. There were no lesions on the face.

Treatment with benzyl benzoate for 3 days cleared the scaly lesions and, within 2 weeks, the erythema had subsided and he was no longer itching.

COMMENT

When he was seen at the clinic this man had typical hyperkeratotic Norwegian scabies. Originally, however, the eruption was consistent with more classical scabies. It was not until 4 months after the itching started that the hyperkeratosis and crusting became evident. The itching persisted throughout the whole of the illness and was not suppressed by medication. By this time the patient had applied over 7500 g of clobetasol propionate ointment, reaching a maximum of 100 g per week. Clobetasol propionate is a very potent topical steroid and has a considerable local immunosuppressive effect (8).