Azapropazone Induced Bullous Drug Eruptions

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Received March 10, 1977

Abstract. Azapropazone is a new, powerful, anti-inflammatory analgesic. Initial trials have confirmed its efficacy as an antirheumatic agent, with a low incidence of adverse reactions. Recently the authors have seen two patients, each of whom developed a distinctive but clinically dissimilar, bizarre, bullous eruption after taking this drug. A brief account of these cases has been published elsewhere (1).

Key words: Azapropazone; Bulla; Drug eruption

CASE REPORTS

Case 1

A 62-year-old woman was prescribed azapropazone (Rheumox, Robins), 900 mg daily, for osteoarthritis. After 2 weeks of treatment she developed blisters, initially round her eyes. Within a few days the eruption spread to involve her face, neck and chest.

The patient had no previous history of skin disease. She took regular doses of chlordiazepoxide and at the time of her illness had just completed a course of trypsin with chymotrypsin for a painful bruise. Examination revealed a number of fragile blisters over the face, neck, chest and vulva. No mucous membrane lesions were present.

Histological examination of a skin biopsy revealed changes compatible with pemphigus foliaceus.

Immunohistological studies failed to demonstrate the presence of immunoglobulins or complement in the epidermis or along the basement membrane. There were no circulating antibodies to the basement membrane nor inter-epidermal cell spaces.

All the patient's drugs were withdrawn. The lesions regressed rapidly following treatment with topical corticosteroids and resolved totally within 2 weeks. The patient later resumed taking her azapropazone of her own volition and blisters returned within 48 hours.

Case 2

A 68-year-old woman with a 10-year history of osteoarthritis had regularly been taking hydrochlorothiazide with amiloride (Moduretic) and dextropropoxyphene with paracetamol (Distalgesic) for 2 years. In October 1976 she began a course of azapropazone, 1200 mg daily. In her fifth week of therapy she developed a dramatic eruption in which numerous bullae arose from sheets of erythema on the lower legs and backs of both hands (Fig. 1). The distribution of the eruption was more prominent in light-exposed areas but spared the face. However, there was no recent history of exposure in excess of ambient Leeds winter sunshine.

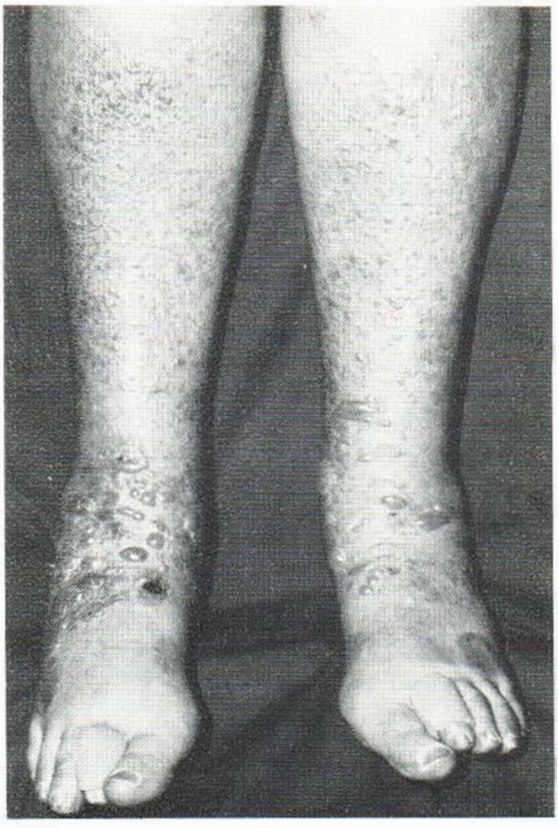

Fig. 1. Pemphigoid-like blisters on lower legs.

Histological examination revealed a sub-epidermal bulla. The superficial dermis contained a predominantly eosinophil polymorph infiltrate and the overall appearances were those of bullous pemphigoid. Immunohistology did not demonstrate any basement membrane zone or intercellular staining for immunoglobulins or complement. Deposits of IgM and C3 complement were found in the walls of dermal blood vessels. Neither A.N.F. nor circulating antibodies to skin constituents were present. The patient showed evidence of mild renal impairment (creatinine clearance 53 ml/min).

In view of the ferocity of the rash the azapropazone therapy was discontinued and the patient treated with a 2-week course of oral prednisolone. The eruption resolved rapidly and has not returned since cessation of steroid therapy. It was not felt justifiable to rechallenge this patient with azapropazone. A patch test to azapropazone (a highly insoluble substance) in soft paraffin proved negative.

DISCUSSION

Initial trials have confirmed that azapropazone is an effective, anti-inflammatory analgesic with a low

incidence of gastric and cutaneous side effects (4, 8). However, pharmacodynamic studies indicate that 60% of the drug is excreted unchanged by the kidneys; this may place patients with renal impairment in a more vulnerable position with regard to the development of side effects. The second patient reported above had a reduced creatinine clearance.

Bullous drug eruptions are well-recognised. Pemphigus has been described in association with penicillamine therapy (7) and a case of pemphigus induced by rifampicin has also been described (5). In these cases the classical immunological features of pemphigus were present.

A photosensitive bullous dermatosis has been reported after treatment with nalidixic acid (2) and seemingly may also occur with high dose frusemide therapy (3).

In our cases neither of the immunological features of pemphigus nor pemphigoid were present and the pathogenesis of each eruption must remain in doubt. The two eruptions were quite distinct clinically. Both patients were receiving other medication, and thus the possibility of a drug interaction exists. Azapropazone is related clinically to phenylbutazone (personal communication from manufacturers). Recently an eruption consisting of acral haemorrhagic blisters has been described in patients receiving treatment with phenylbutazone (6).

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Immunoelectron Microscopy of Linear Dermatitis Herpetiformis: Report of a Case

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Received March 21, 1977

Abstract. Linear deposits of both IgA and C_3 were found along the BMZ (by direct IF), and band-like IgA deposits directly below the basal lamina (by HRP–anti-HRP electron microscopy), in a case of clinically typical DH. No circulating antibodies could be detected.

Key words: Dermatitis herpetiformis; Immunofluorescence; Immunoelectron microscopy

Two different distribution patterns of IgA and C_3 deposits are demonstrated by direct IF in cases of clinically typical DH (4): (i) the more common papillary type with finely granular (speckled) precipitates dispersed over the tips of the dermal papillae and the upper strata of the dermis, and (ii) the rather rare, linear (continuous) type exhibiting a band-like array of deposits along the BMZ of skin.

Yaoita & Katz (10) and Stingl et al. (8) were the first to report on IEM of typical granular (speckled) DH, describing a chunky (granular) pattern of IgA deposition well below the basal lamina and sparing the lamina lucida.

The paper by Yaoita & Katz (10) also describes two different ultrastructural patterns of Ig-deposition in linear-type DH: a linear dermal and a linear lamina lucida pattern, the former exhibiting IgA just below the basal lamina in a band-like distribution; the latter characterized by localization of IgA deposits in a similar band-like fashion but within the lamina lucida.

The observation of a pertinent case prompts us to report our own results of IEM in linear DH.

List of abbreviations: Immunoglobulin(s): Ig; Complement (fraction): C; Basement membrane zone: BMZ; Dermatitis herpetiformis: DH; Bullous pemphigoid: BP; Immunoelectron microscopy: IEM; Immunofluorescence: IF; Horseradish peroxidase: HRP.