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Acute Generalized Exanthematous Pustulosis Associated with Paracetamol

Sir,

Acute generalized exanthematous pustulosis (AGEP) was named by Beylot et al. in 1980 (1) and its diagnostic criteria were established by Roujeau et al. (2). Drugs have been the causative agents of AGEP in most cases reported in the literature, particularly antibiotics.

Cutaneous reactions with paracetamol are rare. The most common cutaneous side-effects are acute hypersensitivity or fixed drug eruptions, and occasionally eczema or vasculitis. Three cases of AGEP associated with paracetamol have recently been described (2–4). We here report 2 new cases of AGEP induced by paracetamol (acetaminophen).

CASE REPORTS

Case 1

A 33-year-old man was admitted in March 1994 with a generalized pustular eruption. He described a history of three acute episodes of pustulosis, which had resolved spontaneously within 3 weeks. The eruption began 2 days before admission, with erythema on the face and the trunk, and became disseminated in 24 h with a temperature of 39°C. He was first unsuccessfully treated at home with terfenadine and triamcinolone. On the third day, he presented with several hundred small pustules arising on widespread erythema on the flank, axillae and groin (Fig. 1). There was no evidence of mucous membrane involvement, lymphadenopathy or hepatosplenomegaly.

Laboratory examination showed hyperleukocytosis, with 28.8 g/l white blood cells with 26 g/l neutrophils and no eosinophilia. C-reactive protein was elevated (266 mg/l) and the erythrocyte sedimentation rate was 40 mm in the first hour. Mycology, bacteriology and virology cultures from pustules were negative and blood cultures were sterile. Cutaneous biopsy showed a subcorneal pustule. PAS staining did not reveal any pathogens.

The eruption had begun 48 h after oral ingestion of 3 tablets of paracetamol (500 mg each) in one day for sinusitis. He had not ingested any other drug in the previous month. Paracetamol was stopped and there was spontaneous resolution of fever and pustules in 6 days, with superficial desquamation.

Patch tests were performed with paracetamol (diluted 5% and 20% in saline and petrolatum) 3 weeks after subsidence of skin lesion. They were negative after 48 h.

Case 2

An 83-year-old man was admitted in May 1996 with a disseminated erythematous rash, which had occurred 2 days after hip replacement. Within 48 h the erythematous skin was covered by hundreds of small non-follicular pustules. The confluence of pustules led to superficial desquamation. No mucous membrane lesion was present and there was no fever or lymphadenopathy.

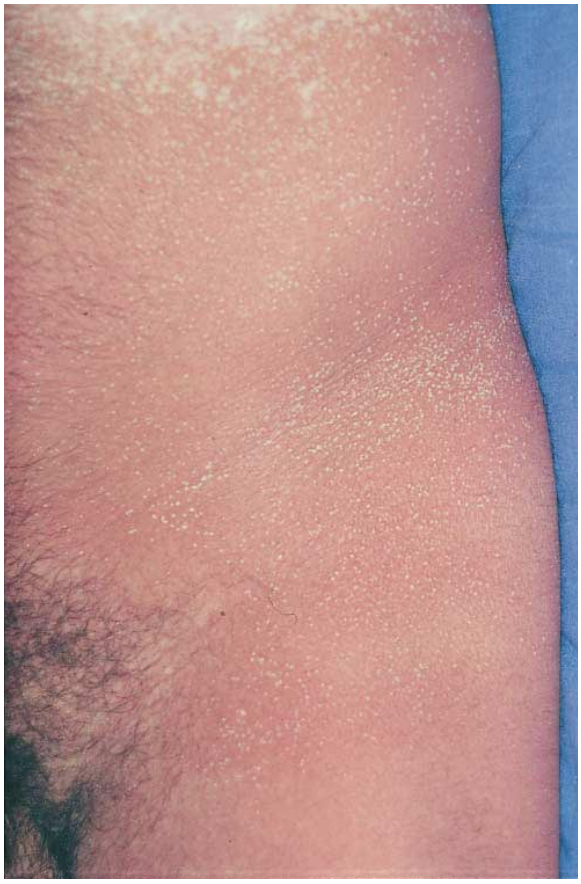

Fig. 1. Case 1 on the third day with small pustules and erythema.

Skin biopsy demonstrated subcorneal pustules; there were slight spongiosis, papillary oedema and a perivascular infiltrate. Staining with PAS did not reveal any pathogens.

Laboratory examination showed hyperleukocytosis, with 12.1 g/l

white blood cells, 10.7 g/l neutrophils and no eosinophilia. The erythrocyte sedimentation rate was 100 mm in the first hour; C-reactive protein was elevated at 271 mg/l. Liver function tests showed anicteric cholestasia (total bilirubinemia 59 μmol/l, conjugated bilirubinemia 13 μmol/l, glutamyl transpeptidase 303 IU/l, alkaline phosphatase 224 IU/l), and abdominal echography was normal. He had acute renal failure (creatinemia 134 μmol/l, uremia 12.9 mmol/l). The drugs introduced within 2 days before the rash began were fentanyl, vecuronium bromide, cloxacillin, gentamicin, a drug combination containing paracetamol, belladonna, opium and anhydrous caffeine (Lamaline®) and a drug combination containing paracetamol and codeine phosphate (Efferalgan codeine®). No other drug had been ingested for 1 month before. All these drugs were stopped and the eruption resolved within 5 days, with widespread desquamation. Abnormal laboratory findings also disappeared in 5 days.

Fifteen days after subsidence of skin lesion all the patch tests with paracetamol (diluted 5% and 20% in saline and petrolatum) and medication containing paracetamol were positive. They produced a pustular eruption on an erythematous base. The histologic features of the test with paracetamol crushed in petrolatum were subcorneal pustules similar to the original lesion. Patch tests with other drugs were negative. Patch testing with paracetamol was negative in 10 controls.

Involuntary rechallenge with intravenous proparacetamol as single drug used was responsible for recurrence of AGEP 1 year later.

DISCUSSION

The 2 patients presented AGEP induced by paracetamol. In fact, these 2 cases fulfilled the criteria of AGEP except for the fever in the second case. The other criteria, i.e. acute diffuse erythema covered by amicrobial pustules, subcorneal pustule on histopathological examination and hyperleukocytosis, were present. Resolution was rapid, in less than 7 days, as is usually observed.

Patch testing allows confirmation of the responsibility of a suspected drug. Vaillant et al. (5) considered positive patch testing as a rechallenge test when dissemination of an eruption similar to the original eruption occurred. When patch testing is positive without dissemination of pustules around the area tested we consider this as an argument in favour of the causative role of the suspected drug.

A negative test does not exclude the responsibility of the drug, since patch testing is not a rechallenge and since penetration of the drug may be insufficient with a non-standardized patch test.

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