

CONTACT POINT

Acute generalized exanthematous pustulosis induced by oxacillin confirmed by patch testing

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Acute generalized exanthematous pustulosis (AGEP) is a rare and severe skin condition typically caused by drugs.¹ Generalized pustular psoriasis (GPP) is a rare variant of psoriasis that can be fatal and has several clinical features similar to those of AGEP. An added difficulty is the fact that AGEP has been reported to occur more frequently in patients with a history of psoriasis. We report a case of GPP complicated with severe AGEP caused by oxacillin and confirmed by a positive patch test reaction. To best of our knowledge, oxacillin as the causative agent in AGEP has not been reported before.

CASE REPORT

A 32-year-old female presented with a 4-day history of fever with a generalized eruption of non-follicular pustules and erythema, which had started 2 days after the intake of oxacillin and tiaprofenic acid for treatment of acute otitis. Otherwise, she had a 4-year history of acute generalized pustular eruptions clinically and histologically diagnosed as GPP. A severe disease course with repeated flare-ups of sterile pustules and a prolonged course was noted; no prior drug intake was reported. Psoriasis was under control with mild local steroids when the patient developed the above-mentioned acute skin eruption. This was most pronounced in the major flexures, with widespread erythema covered by numerous pinpoint pustules (Figure 1).

Investigations showed an elevated white blood cell count with neutrophilia ($12.8 \times 10^9/L$), an elevated C-reactive protein level

(120 mg/L), and negative microbiological findings in repeated samples from pustules and blood. A skin biopsy showed the histological features of a drug-induced pustular eruption, such as subcorneal splitting, neutrophilic spongiosis, sporadic apoptotic cells, normal rete ridges, massive superficial dermal oedema, and moderate mixed infiltrates, also containing some eosinophils (Figure 1C). Our patient was diagnosed with AGEP according to the EuroSCAR criteria.² Discontinuation of oxacillin and initiation of treatment with systemic corticosteroids led to rapid resolution of this episode within 10 days. A patch test with oxacillin and tiaprofenic acid (the commercialized form used by the patient diluted to 30% pet.) was performed 10 weeks later on the patient's back, with exposure for 2 days according to ESCD guidelines.³ This showed a +++ (vesiculo)pustular skin reaction to oxacillin on day 4 (Figure 2). No reactions to tiaprofenic acid were seen. As recent findings have shown that genetic defects involving the interleukin-36 receptor antagonist may be associated with several pustular skin eruptions and even some forms of severe AGEP,⁴ we carried out genetic analysis to determine whether there was mutation of the *IL36RN* gene, but we did not find such a genetic defect in our patient.

DISCUSSION

Our patient presented with a generalized pustular eruption with clinical and histopathological features that were more suggestive of AGEP than of an episode of GPP. In particular, the flexural distribution of the pustular rash, the abrupt onset after the use of medication, the

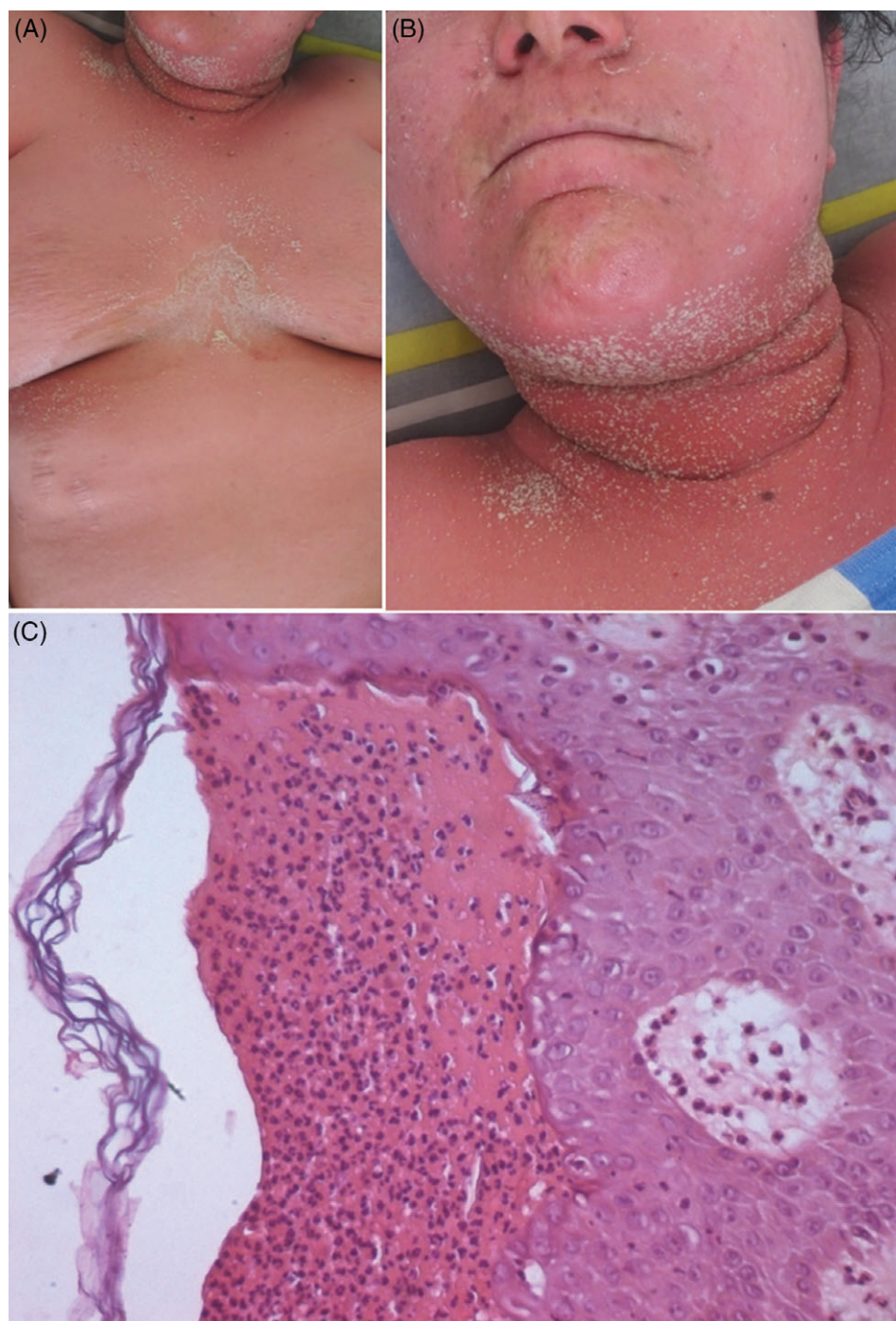


FIGURE 1 A and B, Typical acute generalized exanthematous pustulosis with accentuation on flexural areas. C, Histopathological examination shows a subcorneal pustule with neutrophilic spongiosis, few necrotic keratinocytes, and a papillary infiltrate including eosinophils (haematoxylin and eosin; magnification: $\times 200$)

rapid resolution after oxacillin cessation and the presence of eosinophils and necrotic keratinocytes favour the diagnosis of AGEP.^{1,2} Although the diagnosis of AGEP is mainly based on clinical and histopathological features, patch tests may be necessary to identify the offending drug. They have recently been confirmed to be safe and useful for assessing drug imputability in AGEP, with a high proportion of positive results as compared with other drug-related eruptions.⁵ In the present case, patch testing with oxacillin reproduced the original lesional pattern, strongly supporting the specific immunological nature of this reaction. Drugs are incriminated in >90% of AGEP cases.¹ β -Lactams account for 80% of the antibiotics implicated in AGEP. Flucloxacillin, a drug that is related to oxacillin, has also been reported to induce severe AGEP in many cases.⁶

To the best of our knowledge, we present the first report of AGEP induced by oxacillin. Our case raises questions about the mechanistic link between AGEP and GPP, and suggests that genetic factors other than *IL36RN* mutation may contribute to the pathogenesis of pustular skin disease.

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FIGURE 2 Positive patch test reaction to oxacillin on day 4

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