CASE REPORT

Cutaneous vasculitis overlap with acute generalised exanthematous pustulosis (AGEP)

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SUMMARY

A man in his 40s developed a severe cutaneous adverse reaction following treatment of septic arthritis with flucloxacillin. The eruption had overlap features of cutaneous vasculitis and acute generalised exanthematous pustulosis which was complicated by renal and liver impairment. This case heightens the variation in presentation of a severe drug eruption.

CASE PRESENTATION

A man in his 40s was admitted for treatment of an infected prosthesis of the left knee secondary to methicillin sensitive *Staphylococcus aureus*. He was otherwise healthy. Three days after starting flucloxacillin and clindamycin, he developed a purpuric rash involving the distal extremities (figure 1A). Within 48 h he developed a diffuse non-follicular pustular eruption on his trunk and proximal limbs involving 60% of his body surface area (figure 2A). There was no mucosal involvement. He had fever (38.5°C) and tachycardia.

Figure 1 (A) Purpuric eruption involving distal legs. (B) Extensive papillary dermal red blood cell extravasation and acute neutrophilic fibrinoid vasculitis involving superficial and deep dermal vascular plexus (H&E, original magnification $\times 20$).

Figure 2 (A) Diffuse non-follicular pustular eruption on the trunk and proximal limbs. (B) Intraepidermal pustules and spongiosis of the epidermis with polymorphonuclear inflammatory infiltrates in the dermis (H&E, original magnification $\times 20$).

INVESTIGATIONS

Laboratory investigations showed an increase in inflammatory markers: white cell count $31.2 \times 10^9/L$ (normal range 4–11), neutrophilia ($28.1 \times 10^9/L$; normal range 2–7) and C reactive protein 297 mg/L (normal range <7). Renal and liver function were impaired: creatinine 203 $\mu\text{mol/L}$ (normal range 64–74), alkaline phosphatase 207 U/L (normal range 40–129), γ -glutamyl transpeptidase 330 U/L (normal range 10–71) and albumin 25 g/L (normal range 35–55). Urine protein/creatinine ratio was normal. Swab from pustule, serial blood and urine cultures were negative. Vasculitis screen was also negative. Skin biopsy from the leg demonstrated extensive papillary dermal red blood cell extravasation and acute neutrophilic fibrinoid vasculitis involving superficial and deep dermal vascular plexus (figure 1B). Histology from his trunk demonstrated multiple intraepidermal pustules and

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spongiosis of the epidermis with polymorphonuclear inflammatory infiltrates in the dermis (figure 2B).

DIFFERENTIAL DIAGNOSIS

The patient had cutaneous vasculitis overlapped with a definite diagnosis of acute generalised exanthematous pustulosis (AGEP) based on the EUROSCAR diagnostic criteria.¹ The history, clinical appearance and distribution of the eruption were not typical for psoriasis, pustular vasculitis or subcorneal pustular dermatosis. Drug reaction with eosinophilia and systemic symptoms was less likely in the absence of eosinophilia and the pustules are usually less pronounced.

TREATMENT

Clindamycin was stopped initially and he received intensive emollient therapy. The eruption progressed and he developed a severe facial swelling 2 days later. In view of the progression, flucloxacillin was stopped and he was started on intravenous methylprednisolone 500 mg once daily.

Parenteral daptomycin was started to replace flucloxacillin for the treatment of his septic arthritis.

OUTCOME AND FOLLOW-UP

His condition improved significantly after 3 days of treatment with desquamation noted on all affected areas. His inflammatory markers and renal function had also normalised. He continued on reducing doses of steroids for a period of 10 days. Improvement following cessation of flucloxacillin excluded infection as a possible cause for the eruption.

DISCUSSION

AGEP is characterised by pustular eruption, fever and elevated circulating neutrophils. In 90% of patients, AGEP is usually caused by a medication although infective causes such as *Chlamydia pneumoniae*, parvovirus B19, Epstein-Barr virus infection have been reported.² Although it usually has a benign course, systemic involvement has been described. The incidence of renal impairment in AGEP ranges between 7.6% and 32% which is transient and normalises following treatment of the underlying cause.³ The clinical features of severe cutaneous adverse reactions could overlap or early signs can mimic other reactions. Both scenarios have been reported and pose a challenge in making the diagnosis and initiating appropriate therapy.^{4 5} Our patient had a further rise in inflammatory markers after starting antimicrobials. However, several blood

cultures were negative and the isolated *S. aureus* from his knee aspirate was confirmed to be flucloxacillin sensitive. These suggest that it is more likely due to a drug eruption rather than a severe systemic inflammatory reaction syndrome secondary to sepsis. The patient was treated with systemic steroids because the eruption worsened despite intensive topical therapy. Progression of the eruption with multiorgan dysfunction could have been halted by systemic steroids but it was also possible that it may have improved as part of the self-resolving course of AGEP.

Learning points

- ▶ Detailed drug history is an important part of the management of severe cutaneous adverse reactions.
- ▶ Acute generalised exanthematous pustulosis usually has a benign course but systemic involvement has been reported. Abnormalities in organ function are usually transient and improve following discontinuation of the offending drug.
- ▶ Awareness in variation of clinical presentation helps in the definitive management of severe drug eruptions.

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Competing interests None.

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