CASE REPORT

Baboon syndrome: an unusual complication arising from antibiotic treatment of tonsillitis and review of the literature

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SUMMARY

A 40-year-old man presented with sore throat and fevers associated with bilaterally enlarged and inflamed tonsils. A clinical diagnosis of tonsillitis was made and the patient received intravenous benzylpenicillin. Over subsequent days, the patient developed a macular rash over both groins, buttocks and axillae, with necrotic patches in the groins. An assumptive diagnosis of necrotising fasciitis was made. The patient underwent urgent groin biopsy and was started on broad spectrum antibiotics. No organisms were seen on Gram stain. Following a multidisciplinary discussion, the patient was diagnosed with baboon syndrome (symmetrical drug-related intertriginous and flexural exanthema). He was treated with oral steroid along with topical agents. Baboon syndrome can develop following penicillin administration. Given the widespread use of penicillin antibiotics to treat tonsillitis and many other conditions, it is important that medical staff recognise the side effects of these medications.

BACKGROUND

Acute respiratory tract infections including tonsillitis are one of the most common problems dealt with in primary care.¹ Only one episode of sore throat in 18 leads to a general practitioner (GP) consultation in those aged 20-years to 44-years, however.² The burden of illness due to tonsillitis on the population is therefore vast.

In cases presenting with stridor, difficulty with swallowing, increasing pain or severe systemic symptoms, emergency admission to ear, nose and throat (ENT) service is indicated.³ In our institution, patients with tonsillitis can constitute up to half of the emergency admissions in any given week.

In severe cases of tonsillitis, antibiotics may be required. Sore throats and tonsillitis account for 60% of antibiotic prescribing in general practice.¹ Penicillin V is the most commonly used antibiotic.³ Ampicillin-based antibiotics (eg, co-amoxiclav) may cause a rash when used in the presence of glandular fever and hence should not be used.³

Skin complaints constitute up to 24% of primary care consultations.⁴⁻⁵ Dermatitis makes up to 23% of diagnoses made in patients presenting with skin complaints.⁶ One study looking at referrals to secondary-care dermatology services in Scotland demonstrated a 134% increase in new referrals in the past 30 years, with a referral rate now of 23.2/1000 population per annum.⁷ Fifty-eight per cent

of referrals were for diagnosis,⁷ and hence some of this increase in the number of patients seen could be attributed to a lack of dermatology training in undergraduate medical curricula and in postgraduate training programmes with a consequent lack of knowledge in primary and secondary care.⁷⁻⁸

'Baboon syndrome,' or symmetrical drug-related intertriginous and flexural exanthema (SDRIFE) as it is more correctly termed, is a rare type IV hypersensitivity reaction causing a maculopapular rash.⁹⁻¹⁰ The original name (*baboon syndrome*) stems from the rash of the patient's buttocks being reminiscent of the buttocks of a baboon.

Given the frequency of presentation to primary care and ENT services and the frequent use of penicillins, it is important that clinicians recognise possible side effects, and especially dermatological problems, arising from this treatment.

CASE PRESENTATION

A 40-year-old man presented to the ENT department in May 2013 with a 1-week history of sore throat and fevers. Prior to attending, he had been started on penicillin V for 2 days by his GP, but was now unable to swallow due to odynophagia. He reported no significant medical history, was on no regular medications and reported no drug allergies. While he was not certain of the specific drug name, he stated that he had received penicillin as a child without incident. On examination his airway was clear and inspection of his throat revealed bilaterally inflamed, enlarged tonsils and a thin film of exudate. A clinical diagnosis of tonsillitis was made and the patient was started on intravenous benzylpenicillin 1.2 g four times a day and received a single dose of intravenous dexamethasone 8 mg.

The following morning the patient was noted to have developed a macular rash over the groin and antecubital fossae. His antibiotic was changed to clarithromycin on the assumption that this was a drug reaction.

On the third day the patient reported that his throat had markedly improved and he was now able to swallow liquids and soft solids. However his rash had extended and become painful; it now included both axillae, buttocks, lower abdomen and upper thighs. There was also the presence of black necrotic areas in both groins (figure 1A–D).

INVESTIGATIONS

► At time of admission the patient was feverish at 38.5°C. His white cell count (WCC) and C

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Figure 1 (A–D) Pictures taken at the time of skin biopsy demonstrating rashes to buttocks, groins, upper thighs, flanks and axillae. The areas of erythema were marked on day 2 postadmission, and hence these pictures demonstrate the rapid progression of erythema.

reactive protein (CRP) levels were elevated ($13.5 \times 10^9/\text{L}$ and 73 mg/dL , respectively) with a predominant neutrophilia ($11.41 \times 10^9/\text{L}$).

- On the third day of admission, the patient's WCC had worsened to $28.9 \times 10^9/\text{L}$ and CRP to 86 mg/dL .

DIFFERENTIAL DIAGNOSIS

While the patient was haemodynamically stable, these features raised the concern of necrotising fasciitis. The team was therefore faced with a difficult differential: Was this a case of severe drug reaction which would likely improve with conservative treatment, or was it necrotising fasciitis requiring urgent, major debridement with the associated physical and psychological ramifications that would involve? The patient was promptly started on broad-spectrum antibiotics (meropenem 2 g and clindamycin 1.2 g). The plastic surgery, dermatology and microbiology teams were urgently involved. Although the patient looked well, necrotising fasciitis could not be excluded and a biopsy from his right groin was taken by the plastic surgical team and sent to pathology. During the procedure no pus or fluid was seen but the skin appeared hyperaemic and oedematous. Gram staining revealed no organisms.

Following a multidisciplinary discussion, and having excluded necrotising fasciitis, a diagnosis of baboon syndrome (SDRIFE) was made.

The biopsy was subsequently reported to show extensive subcorneal pustule formation with incipient necrosis of the superficial epidermis and a moderately dense superficial perivascular and interstitial lymphohistiocytic infiltrate with neutrophils and scattered eosinophils. The histological features were those of a pustular dermatitis in an acute eruptive phase in keeping with an acute generalised exanthematous pustulosis (AGEP) or other unusual pustular drug reaction, such as baboon syndrome/SDRIFE.

TREATMENT

The patient's antibiotics were stopped and he was started on oral prednisolone 20 mg daily along with oral fexofenadine, 0.1% mometasone cream, Dermol 500 skin wash and Dermovate ointment.

OUTCOME AND FOLLOW-UP

He was discharged 11 days after admission on a reducing steroid regimen. He remained well at last follow-up with generalised xerosis of the skin, but with resolution of the original eruption.

DISCUSSION

A diagnosis of baboon syndrome or SDRIFE is made on the basis of involvement of at least one great flexure, symmetry, sharply demarcated erythema of buttocks and/or thighs, absence of systemic symptoms and occurrence after re-exposure to systemic drugs.⁹ Involvement of mucosal surfaces or the face is rare.¹⁰ There is a male predominance with a latency of hours to 2 days from intake to eruption.¹⁰ In the above case, the initial fever was felt to be secondary to his tonsillitis, and not to systemic upset from his skin reaction.

Histology demonstrates a superficial perivascular infiltrate of mononuclear cells, in particular CD3 and CD4 T cells in the dermis, and more unusually neutrophils and eosinophils.^{9–11} Subcorneal pustules (as in the case above) have also been reported.¹²

The syndrome is most commonly associated with penicillins, but it has also been associated with exposure to nickel and mercury, omeprazole, clozapine and to biological and chemotherapeutic agents.^{13–16} The syndrome is rarely observed in children, but has been reported in an 18-month-old patient as a side effect of erythromycin for sore throat,¹⁷ and in a 5-year-old patient treated with co-amoxiclav for acute otitis media.¹⁸

Why the rash particularly affects the flexural surfaces is unknown. Theories include that it is a form of recall phenomenon from a previous unrelated dermatitis¹⁹ or that metabolites of the causative agent are excreted preferentially from eccrine glands found in flexures.²⁰

Diagnosis is made clinically and having excluded other causes of such a rash. Controlled drug-provocation testing is the gold-standard clinical test,¹⁰ but clearly is of no value in the acute setting. The condition is self-limiting and topical or parenteral

steroids may hasten recovery and provide symptomatic relief.^{21 22} Recovery may take up to 3 weeks.¹⁰

Unlike baboon syndrome/SDRIFE, patients with AGEP have numerous pinhead-sized pustules on a background of erythematous macular rash. The face is frequently involved.²³ Skin symptoms usually arise within hours,²⁴ the patient is feverish and the neutrophil count is elevated.²³ Resolution is typically associated with desquamation.²³ AGEP has similar histological features to baboon syndrome/SDRIFE, with subcorneal pustules, papillary oedema and perivascular infiltrates of neutrophils and eosinophils.²³

The pathogenesis for AGEP is better understood than that of SDRIFE, but is likely to be similar. Initial activation of drug-specific T cells is associated with their expansion and migration to skin. T cell migration is also associated with drug-antigen presentation by major histocompatibility complex molecules on keratinocytes. This activates apoptosis of keratinocytes, with subsequent development of subcorneal blisters, and leads to neutrophil migration.²⁵

Penicillins are the most commonly prescribed antibiotics and the most common cause of drug allergies.^{26 27} The development of a maculopapular rash starting over the trunk and spreading symmetrically over limbs and neck 1–2 weeks after ampicillin-containing antibiotics (eg, co-amoxiclav) in patients with glandular fever has long been recognised.^{28 29} Again this is a delayed-type IV allergic reaction involving drug-specific T cells (CD4) which settles with cessation of the use of the causative agent.³⁰ Other skin reactions associated with penicillins include type I urticarial reactions, Stevens-Johnson syndrome and toxic epidermal necrolysis.

Given the widespread use of penicillin antibiotics to treat tonsillitis, it is important that GPs, otolaryngologists and other medical professionals recognise the side effects of these medications.

Learning points

- ▶ 'Baboon syndrome,' or symmetrical drug-related intertriginous and flexural exanthema, is an unusual complication of penicillin therapy.
- ▶ The appearance of 'baboon syndrome' can mimic that of necrotising fasciitis.
- ▶ 'Baboon syndrome' is self-limiting. Steroid therapy may hasten recovery.
- ▶ It is important to recognise side effects of penicillin antibiotics given their widespread use.
- ▶ This case reinforces the importance of multidisciplinary discussions to patient management.

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Contributors JPB and SL were involved in clinical care of the patient by the otolaryngology and plastic surgery teams, respectively. DECB was the otolaryngology consultant involved in clinical care and management of the patient. All authors were involved in writing and review of the case.

Competing interests None.

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