A 33-Year-Old Man with a Facial Rash
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DESCRIPTION of CASE

A 33-year-old man presented to his primary care practitioner with a rash beginning around the left ear and spreading into the periorbital region. He was known to have eczema (atopic dermatitis), and the diagnosis of secondary bacterial infection and periorbital cellulitis was made.

Because of a history of penicillin allergy, the patient was started on erythromycin. This treatment had no effect, and the rash extended. On day 4, he presented to the hospital accident and emergency department. He was systemically unwell, complaining of drenching sweats and rigors. On examination he was alert, he was pyrexial at 39.2 °C, his pulse was 100 bpm, and his blood pressure was 128/70 mm Hg. There was a widespread erythematous rash covering his face, chest, and arms, which was described as wet with a yellowish exudate. The rash extended around both eyes, which could not be opened (Figure 1).

The patient had a history of atopic eczema (since childhood), rhinitis, and asthma. He was taking inhaled corticosteroids for asthma and had last received a course of systemic steroids one year previously. There were no risk factors for HIV infection.

Which Investigations Were Now Indicated?

In many patients with a rash, the morphology of the rash will lead to a provisional clinical diagnosis, and it may be sufficiently characteristic for no confirmatory tests to be needed. An example is the typical rash of shingles. There are two broad reasons for doing investigations in a patient presenting with fever and a rash. Firstly, specific tests—such as blood tests, cultures, or a skin biopsy—may be required to

Figure 1. Appearance of Part of the Face and Shoulder at Presentation to Hospital
There are multiple shallow ulcers with copious creamy exudates and some crusting. A few intact vesicles are also visible. The right eye was closed by exudates.

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Abbreviations: HSV, herpes simplex virus; PCR, polymerase chain reaction

The Learning Forum discusses an important clinical problem of relevance to a general medical audience.

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help establish the diagnosis. In this 33-y-old patient, the rash was thought likely to be a skin infection, and so the specific tests that were indicated included viral and bacterial cultures. A skin biopsy would have been considered if the diagnosis remained unclear and the patient was not responding to empirical antimicrobial therapy. Secondly, investigations are used to evaluate how ill the patient is and whether there is any organ involvement beyond the skin. In this case, we were most concerned about severe sepsis with a risk of organ failure.

Investigations showed the following: haemoglobin, 128 g/L (normal range, 135–170 g/L); white blood cell count, 9.9 × 10⁹/l (normal range, 3.5–12.5 × 10⁹/l); and differential white blood cell count, 90% neutrophils with a left shift. The patient was hyponatraemic (his sodium was 126 mmol/l [normal range, 135–145]), but renal and liver function tests were normal. C-reactive protein was 140 mg/l (normal level, <10 mg/l). Chest X ray was normal. Blood cultures and skin swabs were taken along with samples for viral culture and polymerase chain reaction (PCR).

What Was the Provisional Diagnosis?

A provisional diagnosis of bacterially infected eczema was made, and, in view of his history of penicillin allergy, the patient was started on intravenous vancomycin. He was admitted and referred for dermatology, infectious diseases, and ophthalmology reviews.

On closer inspection of the rash, it was apparent that there were multiple small vesicles 1–2 mm in diameter and shallow ulcers over the face and periorbital region (Figure 1). There was extensive exudate on the skin of the eyelids of both eyes. It was not possible to open the right eye, but in the left eye, the cornea was clear and there was no evidence of disease.

How Did This Information Affect the Likely Diagnosis?

In view of the characteristic picture and underlying eczema, the diagnosis was revised to one of severe eczema herpeticum. The patient denied any previous history of oral cold sores or genital ulceration. However, the severe degree of skin inflammation, high fever, raised C-reactive protein, and left-shifted neutrophils suggested co-existent bacterial sepsis.

What Was the Management Approach?

High-dose intravenous aciclovir (10 mg/kg every 8 h) was started. Aciclovir inhibits thymidine kinase, which is an essential enzyme for several herpes viruses. Aciclovir has excellent activity against herpes simplex virus (HSV), and, although less potent, it is also effective against varicella zoster virus [1]. It has only weak activity against cytomegalovirus and Epstein-Barr virus [1].

This man had severe skin involvement with a high likelihood of complicating bacterial sepsis, which is most commonly due to *Staphylococcus aureus* [2]. Erythromycin had originally been prescribed, but increasing erythromycin resistance makes this a poor choice in many parts of the world. In view of his penicillin allergy, vancomycin was continued and ciprofloxacin added to broaden the antibacterial spectrum. Vancomycin disrupts the peptidoglycan bonding of the gram-positive bacterial cell wall and has no activity against gram-negative bacteria. Ciprofloxacin is a DNA gyrase inhibitor with excellent activity against many gram-negative bacteria, but it is less effective for gram-positive organisms. Aciclovir and chloramphenicol were administered topically to both eyes, and this treatment was successful in preventing corneal involvement.

Two separate sets of blood cultures subsequently grew *S. aureus*, which was resistant to penicillin, erythromycin, and clindamycin but sensitive to all other agents. Skin and eye swabs also grew *S. aureus*. HSV DNA was identified by PCR on fluid taken from the face. Viral cultures were positive for HSV-1. Serology taken on admission was positive for HSV-1 IgG.

Progress

The patient rapidly defervesced, and the vesicles desquamated on day 6 (Figure 2). He was discharged after a total hospital stay of 16 d. He returned to the clinic 2 wk later, at which point the skin was healing well (Figure 3).

What Complications Should Be Looked Out for?

In the acute stage of his presentation, our two main concerns for this patient were the extent of involvement of the eyes beneath the eyelids and the positive blood cultures for *S. aureus*. As mentioned above, the eyes were proactively managed to avoid corneal involvement. The *S. aureus* bacteraemia could have progressed to severe sepsis or led to metastatic spread of infection. Echocardiogram was normal with no evidence of endocarditis, and intravenous vancomycin was continued for a period of 14 d to minimize the risk of metastatic spread. Close attention to infection control procedures is essential to prevent hospital-acquired infection of the damaged skin or intravenous line sites.

DISCUSSION

Eczema Herpeticum

Kaposi’s varicelliform eruption describes the widespread dermal infection caused predominantly by HSV-1 in patients with a variety of skin conditions [3]. It is most commonly seen in patients with pre-existing atopic eczema, in which case it is known as eczema herpeticum. Disease severity varies from mild, transient disease to a fulminating fatal
be considered, although there are insufficient data to
With frequent recurrences, prophylactic aciclovir may
diagnosed and treated rapidly, as both the patients and
therapy is an option [1]. In addition to the treatment
and can be considered as alternative antivirals where oral
Oral aciclovir is effective for mild cases, which can be
prompt use of antiviral therapy is highly effective in
controlling HSV replication. Aciclovir is the antiviral agent
choice and is usually given for 7 d. Patients with moderate
to severe disease require admission for intravenous aciclovir.
oral aciclovir is effective for mild cases, which can be
managed on an outpatient basis [5]. Bacterial superinfection
is common in severe eczema herpeticum [2], and antibiotic
therapy is required in severe cases. Valaciclovir (a pro-drug of
aciclovir) and famciclovir are available in oral preparations
and can be considered as alternative antivirals where oral
therapy is an option [1]. In addition to the treatment
of systemic infection, skin and eye lesions require very
careful management, and specialised dermatology [6] and
ophthalmology input are essential [7].

A proportion of patients may experience recurrent attacks
of eczema herpeticum [4]. Recurrences are generally
diagnosed and treated rapidly, as both the patients and
their physicians have become familiar with the disease.
With frequent recurrences, prophylactic aciclovir may be
considered, although there are insufficient data to
recommend its use routinely. Good control of eczema is also
important to reduce the risk of recurrence [3].

Which Patients with Atopic Eczema Are at Risk of
Eczema Herpeticum?
A recent retrospective analysis of 100 cases of eczema
herpeticum in patients with atopic eczema highlighted some
preexisting factors. The analysis found that patients with
eczema herpeticum had developed atopic eczema earlier and
had higher total serum IgE levels than control patients with
atopic eczema alone [3]. In addition, 75% of the patients
with eczema herpeticum had not received corticosteroid
therapy in the 4 wk preceding onset of eczema herpeticum.
The authors of the analysis concluded that most cases of
eczema herpeticum occurred in patients with untreated
atopic eczema. Thus, effective control of eczema is important
to prevent eczema herpeticum. Such control is particularly
important in our patient to prevent further attacks of eczema
herpeticum.

Making the Correct Diagnosis
The rapidly progressive, widespread, crusted papules,
vesicles, and erosions in a patient with atopic eczema are
characteristic, and an experienced physician who has
seen eczema herpeticum will make a rapid clinical
diagnosis. However, some patients present with atypical
or purely crusted lesions and no obvious vesicles, making a
clinical diagnosis more difficult. Thus, a high index of clinical
suspicion is required, and both viral and bacterial cultures are
essential when a patient with atopic eczema presents with a
spreading vesicular or crusting rash [4]. Rapid confirmation
of cutaneous HSV can be achieved with immunofluorescent
techniques or PCR, but these are not yet available in many
centres [8].

Smallpox Vaccination
A similar and potentially fatal disease may follow smallpox
vaccination [9,10]. Until recently, this was only of academic
interest, given the global eradication of smallpox. Recent
events have raised the spectre of smallpox returning, however,
and some countries have begun stockpiling vaccine and
inoculating key health-care workers. Smallpox vaccination
involves the intradermal inoculation of live attenuated variola
virus by scarification, and the site may shed live virus for 2–3
wk until the lesion heals. In a person with eczema, the variola
virus can cause widespread eczema vaccinatum. As the variola
virus is shed into the environment from the vaccine site, it
can also spread to close contacts with eczema, which can lead
to secondary cases of eczema vaccinatum. This risk is greatly
diminished with the use of an appropriate occlusive dressing
to the vaccination site. It is reassuring that, so far, no cases
of eczema vaccinatum have been reported in the United
States following the recent smallpox vaccination programme,
but this disease may well return if there is need for more
extensive smallpox vaccination.■

Key Learning Points
• Eczema herpeticum is an uncommon but potentially fatal
disease that can present to primary care practitioners or to the
emergency department.
• Diagnostic delay is common and may increase morbidity.
• First-line therapy is with acyclovir; intravenous high-dose
therapy is required in severe cases.
• Patients should be referred to a dermatologist for specialist
care and follow-up to optimise eczema management, so that
recurrence is less likely.
• Intensive nursing care is indicated to minimise scarring and
promote rapid healing.
• If the periorbital region is involved, refer urgently to an
ophthalmologist.

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