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A man in his forties with a rash and hallucinations

EDUCATIONAL CASE REPORT

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Acute exacerbation of rash is common in patients with atopic dermatitis and has diverse aetiology. We describe a patient with atopic dermatitis who developed a pruritic, burning and weeping rash. The rash quickly worsened and developed into a serious condition for which early diagnosis and treatment are crucial.

A man in his forties developed pruritic sores on his throat that were burning and weeping. He had a history of mild atopic dermatitis (eczema), which he occasionally treated with cortisone cream, but was otherwise in good health. Over the next few days, his condition deteriorated rapidly. He developed fever and diarrhoea, and his rash became increasingly widespread and painful. Four days after symptom onset, he called his general practitioner, who suspected a bacterial skin infection and prescribed oral dicloxacillin 500 mg × 4 for ten days.

Impetigo is a superficial skin infection usually caused by *Staphylococcus aureus*. It occurs in previously healthy skin, typically in the form of moist erosions with honey-coloured crusts. Impetigo is most frequently seen in children, causes mild-to-moderate illness, and can usually be treated with topical agents. Serious cases can be treated with oral antibiotics in combination with topical antiseptics. Skin affected by eczema is at increased risk of infection, particularly by *Staphylococcus aureus*. Infected eczema will weep, itch, and may be covered by yellow crusts reminiscent of impetigo.

The patient did not improve with dicloxacillin, and on day 6 he was admitted to his local hospital. He had severe erythema on his face and neck, diffuse swelling and large crusted erosive areas that were oozing pus. His eyelids were swollen and sticky, and he was unable to open his mouth fully due to pain and swelling. He had small, scattered monomorphic erosions – most of them crusted – on his upper body, arms and thighs, as well as pustules on his palms.

On admission he was febrile with a temperature of 38.5°C, hypertensive with blood pressure 144/85 mm Hg, and tachycardic with a heart rate of 101 beats/min. Blood samples revealed haemoglobin 16.6 g/dL (reference range 13.4–17.0), leukocytes 3.9 × 10^9/L (3.5–10 × 10^9/L), neutrophils 2.9 × 10^9/L (1.5–7.3 × 10^9/L), sodium 129 mmol/L (137–144), potassium 3.6 mmol/L (3.5–4.4), creatinine 103 µmol/L (60–105) and procalcitonin 0.45 µg/L (<0.10). His CRP level was 128 mg/L (<4).

Given the patient's extensive erosions, pain, and signs of infection, the on-call team considered the possibility that he might have a serious condition known as 'staphylococcal scalded skin syndrome'.

Patients with staphylococcal scalded skin syndrome often have fever and cutaneous pain. Their skin becomes erythematous with blisters that rupture easily, leaving behind erosive lesions. The condition is caused by toxin-producing *Staphylococcus aureus*; the toxins lead to the formation of fissures in the epidermis. Staphylococcal scalded skin syndrome most commonly affects neonates and children. Many adults will have developed protective antibodies, but the condition may be seen in individuals with chronic renal failure and in those who are immunocompromised (1).

The patient's medical history revealed no obvious sources of infection. One of his close contacts had recently had cold sores, but the patient himself had never been affected. The treating doctor contacted the dermatology section of the university hospital. The dermatologist agreed that the medical history and clinical findings could indicate an extensive bacterial skin infection, but considered staphylococcal scalded skin syndrome to be less likely.

Given the clinical findings, history of atopic dermatitis, and contact with an individual with cold sores, it was suspected that the bacterial infection might be secondary to another serious condition. After securing microbiological samples of skin and blood, treatment was initiated with intravenous acyclovir 5 mg/kg body weight × 3, intravenous cloxacillin 2 g × 4, and chloramphenicol eye ointment on both eyelid margins x 3–4. Plans were made to transfer the patient to the dermatology section of the university hospital the following day.

That same evening, the patient experienced visual hallucinations of landscapes and people. He also had slight memory impairment. On suspicion of meningitis, a head CT was performed and was found to be normal. Lumbar puncture revealed clear fluid, with normal cerebrospinal fluid (CSF) leukocytes 1.0 × 10^6/L (<4.0 × 10^6/L), a CSF/serum glucose ratio of 68 % (60–70), and CSF protein 0.37 g/L (0.15–0.50). No bacteria were detected by microscopy. The remainder of the CSF sample was sent for bacteriological culture and viral PCR.

Upon transfer to the university hospital the following morning, the patient had a high fever with a temperature of 40.2°C. Other vital signs were normal. He was oriented to time, place and situation, and did not appear to be hallucinating. He had a severe erythematous rash with extensive erosions and weeping eczema on his face, neck and throat. There were numerous circular crusted erosions on the neck, throat, upper body, and upper arms (Figure 1). His hands were swollen, with pustules, fissures and crusted erosions (Figure 2), and the lymph nodes in his neck were swollen and tender.

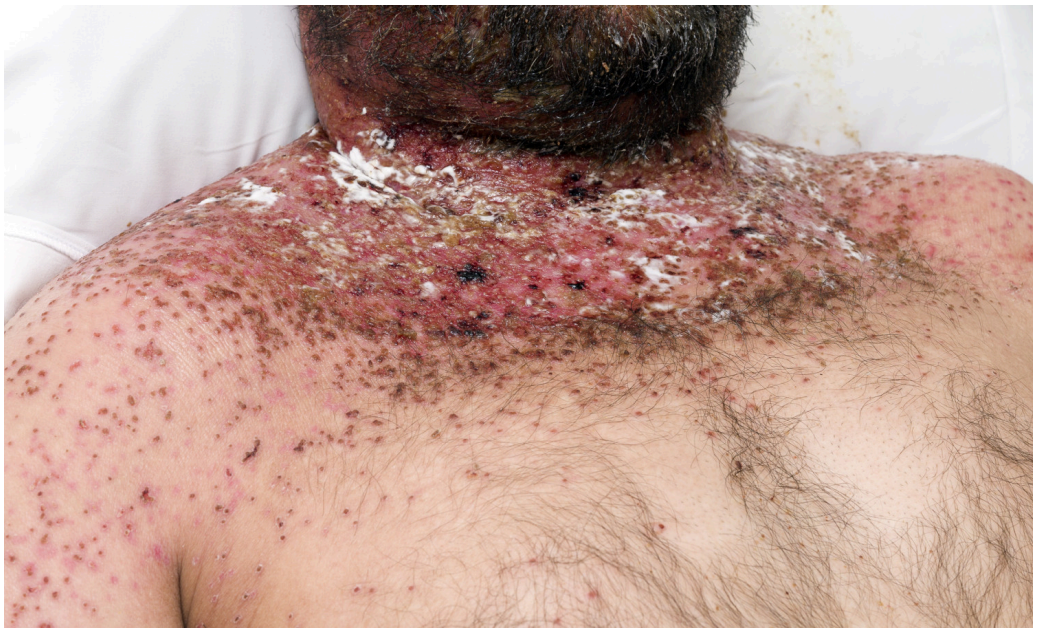

Figure 1 Extensive erosions and weeping eczema on the face, neck and throat, with scattered crusted erosions on the neck, throat, upper body and upper arms. The whitish areas are cream, and the black areas are crusts.

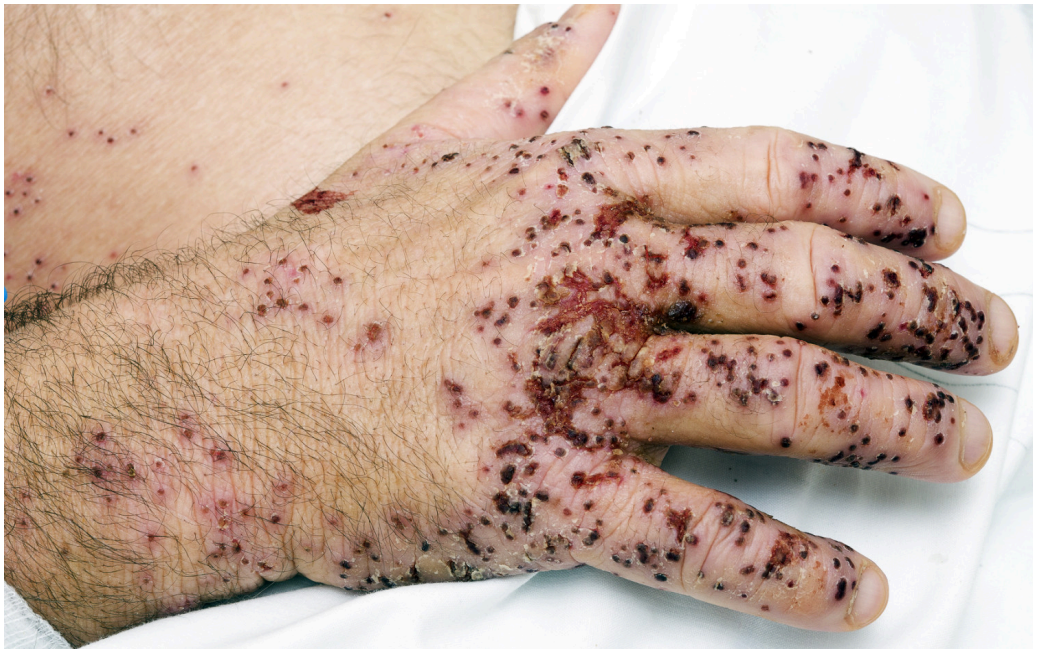

Figure 2 Dorsal hand with multiple crusted erosions and fissures.

His vision was unaffected, but he had swollen, erythematous eyelids, with mild conjunctivitis and yellow discharge. Other mucosae were normal. Blood tests showed elevated CRP of 108 mg/L (<4), cytopenia with Hb 12.8 g/dL (13.4–17.0), leukocytes 1.4 × 10^9/L (3.5–10.0 × 10^9/L), neutrophils 0.9 × 10^9/L (1.5–7.3 × 10^9/L), hypokalaemia 3.0 mmol/L (3.5–4.4), hyponatraemia 131 mmol/L (137–144) and elevated procalcitonin 0.50 µg/L (<0.10). A platelet count could not be obtained due to platelet aggregation.

The findings strengthened suspicion that the patient had a serious skin condition: his known atopic dermatitis, close contact with an individual with cold sores, characteristic rash and other clinical findings were all consistent with eczema herpeticum.

Eczema herpeticum is a serious skin infection caused by the herpes simplex virus (HSV) in patients with atopic dermatitis. The condition is most often seen upon primary infection with the virus. It is characterised by the formation of painful vesicles that rupture easily, leaving behind monomorphic erosions with crusts. Bacterial superinfection is also usually present. Eczema herpeticum requires urgent treatment as the cutaneous infection can quickly spread, and in some cases may disseminate to other organs via the blood. Left untreated, the condition can be life-threatening.

The patient's widespread rash with lymphadenopathy, high fever, abnormal blood test results, and memory impairment led to suspicion of a disseminated viral infection. When the patient arrived in the dermatology section, intravenous acyclovir was therefore increased from 5 mg/kg body weight to 10 mg/kg body weight × 3. Intravenous cloxacillin had previously been initiated to cover bacterial superinfection. This was now switched to intravenous clindamycin 600 mg × 3, due to concern that the patient's leukopenia might reflect cloxacillin-induced bone marrow suppression.
The patient also received 1 L of Ringer's acetate supplemented with 40 mmol potassium chloride to correct his electrolyte imbalance, as well as subcutaneous dalteparin 5 000 IU × 1 as thromboprophylaxis. His skin was treated locally with an aluminium acetotartrate wrap, dibrompropamidine isethionate cream and moisturiser (blended 50:50), plus foam dressings. The patient was examined by an ophthalmologist, who found no evidence of herpetic keratitis or other ocular manifestations. The patient's swollen eyelids were treated prophylactically with saline compresses and chloramphenicol ointment.
The first night after his transfer, the patient again had visual hallucinations. It was thought that these might be fever-related, and incipient viral encephalitis could not be ruled out. The patient was already receiving intravenous acyclovir 10 mg/kg body weight × 3, which would cover viral encephalitis, and his existing treatment was therefore continued. The following night, he had visual hallucinations once again. Another neurological examination revealed slight memory impairment and difficulty performing simple subtraction. This strengthened the suspicion of encephalitis. Blood tests showed increasing CRP of 151 mg/L (<4), persistent leukopenia with leukocytes 1.6 × 10^9/L (3.5–10.0 × 10^9/L), neutrophils 0.8 × 10^9/L (1.5–7.3 × 10^9/L), lymphocytes 0.7 × 10^9/L (1.1–3.3 × 10^9/L) and monocytes 0.1 × 10^9/L (0.2–0.8 × 10^9/L), in addition to new-onset thrombocytopenia, 98 × 10^9/L (145–390 × 10^9/L). A blood smear showed thrombocytopenia with somewhat abnormal cell morphology, as well as granulocytopenia and lymphopenia with normal cell morphologies.
Herpes encephalitis is a serious complication of eczema herpeticum with haematogenous dissemination. It can give rise to diverse symptoms, including confusion, behavioural changes and seizures. Mortality in herpes encephalitis used to be very high but has decreased following the introduction of acyclovir (2).

On days 2 and 3 after transfer, the patient was afebrile. His CRP level had fallen to 83 mg/L, and his cell lines were normalising, with leukocyte levels increasing to 2.5 × 10^9/L, neutrophils 1.4 × 10^9/L, lymphocytes 0.8 × 10^9/L

and platelets 141 × 10^9/L. PCR tests confirmed the presence of herpes simplex 1 virus (HSV-1) in the samples of blood and wound secretions taken on admission. He tested negative for HSV-1 immunoglobulin G (IgG) antibodies, and his immunoglobulin M (IgM) antibody level was borderline, consistent with primary HSV-1 infection. Bacterial wound drainage cultures showed growth of Staphylococcus aureus *and* Pseudomonas aeruginosa. *Head MRI showed no pathology and EEG was normal, and cerebrospinal fluid bacterial culture was negative. The delivery of the cerebrospinal fluid sample for viral PCR had been delayed, but PCR testing was now performed and showed a weak positive for HSV-1.*

Over the next few days, the patient gradually improved. His rash dried up and the swelling subsided, his electrolyte disturbances stabilised, and his memory improved. One week after transfer, the patient was mobilised and was able to fully open his eyes. On the ninth day after admission, clindamycin was discontinued. HSV-1 could no longer be detected in his blood, and he was switched to oral valaciclovir 1 g × 3. With the herpes infection now in remission, treatment of the patient's atopic dermatitis was intensified with hydrocortisone butyrate cream × 2 and moisturiser.

Twelve days after admission, the patient was discharged. He remained on oral valaciclovir 1 g × 3 for one week, followed by 1 g × 2 for two weeks, and finally 500 mg × 2 as prophylaxis for two months. He was thoroughly informed about the importance of effective local treatment of his atopic dermatitis, and follow-up was arranged with a local dermatologist. Today the patient has no long-term sequelae and is back at work full-time.

Discussion

Eczema herpeticum is a potentially fatal condition that occurs when skin with atopic dermatitis becomes infected with the herpes simplex virus (3, 4). The condition is characterised by cutaneous pain and by clusters of punched-out erosions with crusting (Figures 1 and 2) or intact vesicles. The vesicles rupture easily and will not necessarily be present on examination. Fever, lymphadenopathy and reduced general condition are common. The lesions occur most frequently on the skin of the face, neck, throat and upper body, but can also occur on the limbs and genitals (4, 5).

Primary infection with the herpes simplex 1 virus often gives rise to more severe eczema herpeticum compared to reactivation, and the rash usually develops 5–12 days after contact with an infected person. Our patient had a borderline HSV-1 IgM level and was negative for IgG, indicating probable primary infection. His close contact with cold sores (herpes labialis) may have been the source of infection. Eczema herpeticum can also occur upon viral reactivation, but the disease course is then usually milder.

Eczema herpeticum has a prevalence of 3 % in patients with atopic dermatitis (5), with an average age at onset of 23 years (4). Impaired barrier function, immunological changes and an altered microbiome may contribute to the development of eczema herpeticum in atopic skin (4, 5). Our patient also had a bacterial superinfection. Superinfection with *Staphylococcus aureus* occurs

frequently in patients with atopic dermatitis (4), and it is also common for a herpes rash to become superinfected. Our patient had large erosive areas that posed a risk of serious bacterial superinfection.

The severity of eczema herpeticum ranges from mild localised outbreaks to a severe and widespread rash with the risk of a disseminated viral infection. Eczema herpeticum is primarily a clinical diagnosis confirmed by HSV-PCR testing of a sample from the cutaneous lesions. Mild cases should be treated with oral antiviral therapy as soon as the condition is suspected, and the patient closely monitored by a general practitioner. Patients with severe illness should be admitted acutely for treatment and observation.

Our patient had signs and symptoms from several organ systems that required interdisciplinary assessment. Given that the area around the eye was affected, it was important to rule out herpes keratitis, which is the most common ocular HSV manifestation. Scarring with potential vision loss can be a serious complication. Fortunately, our patient had no ocular herpes manifestations. In the case of illness affecting multiple body systems, it is important to be on the alert for changes in mental function that may indicate herpes encephalitis, as in the current case report.

The gold standard for the diagnosis of herpes encephalitis is PCR testing of cerebrospinal fluid. The majority of patients also have abnormalities on MRI, usually contrast enhancement in the temporal lobes (2). Our patient had low-grade cerebral involvement, which did not result in changes on MRI, but which was confirmed by a positive cerebrospinal fluid test for HSV-1. It is important to be aware of eczema herpeticum, as early antiviral treatment is crucial for a good prognosis (3–5).

Fortunately for our patient, severe eczema herpeticum was quickly suspected based on his medical history and clinical signs. The local hospital had already begun intravenous treatment with acyclovir, and the dose was increased at the university hospital due to suspected haematogenous dissemination with encephalitis. This may have spared the patient a more serious disease course.

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The patient has consented to the publication of this article.

The article has been peer-reviewed.

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