



Dermatological emergencies

How to recognise them and what to do



Key points

- Dermatological emergencies are uncommon but can cause devastating complications if not recognised and treated early.
- Many patients require early referral to a tertiary hospital with a dermatology department.
- Staphylococcal scalded skin syndrome is a spot diagnosis in children aged under 5 years and responds well to flucloxacillin.
- In toxic epidermal necrolysis, identification and cessation of the causative drug is key, which requires a careful history of any prescribed and over-the-counter medications the patient is taking.
- In pyoderma gangrenosum, clues to the diagnosis include pain disproportionate to lesion morphology and rapid progression; however, pyoderma gangrenosum is a diagnosis of exclusion and infective causes must be ruled out.

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Emergencies in dermatology are uncommon but can cause significant long-term morbidity or even be life-threatening. Three patients illustrate the need for early recognition and urgent referral for treatment of staphylococcal scalded skin syndrome, toxic epidermal necrolysis and pyoderma gangrenosum.

Emergencies in dermatology are rare but have the potential to cause significant morbidity and a major impact on quality of life. We describe three patients with dermatological emergencies. They illustrate the importance of early recognition and urgent referral to a dermatology service in a tertiary hospital for treatment.

PATIENT 1. STAPHYLOCOCCAL SCALDED SKIN SYNDROME

A previously well 4-year-old girl presented to the emergency department (ED) of a large teaching hospital with tender erythematous

patches affecting the axillae, inguinal folds and flexural aspect of the neck (Figure 1). She was not taking any medication.

On examination, the child was irritable, had a fever and complained of pain on palpation of the affected flexural sites. She had periorificial scaling and erythema as well as superficially eroded patches where the tender erythematous areas came into contact with each other. No lymphadenopathy, organomegaly or mucosal lesions were noted.

Investigations

Results of routine blood tests were normal,

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Figure 1. A young child with staphylococcal scalded skin syndrome showing periorificial and flexural scaling and erythema.

flexurally distributed skin lesions, commonly associated with periorificial involvement. Practice points about SSSS are summarised in Box 1.

Pathophysiology

The epidermal changes of SSSS are produced by exfoliative toxin secreted by a strain of *Staphylococcus aureus* infecting the skin, eye, throat or mucosa. SSSS is seen mostly in children but can affect adults in rare cases, particularly if they have compromised renal function. The initial event is usually a localised staphylococcal infection, often quite trivial, which may be on the skin or at a distant site. A few days later, the patient develops fever, irritability and skin tenderness, which progresses without treatment to erosive lesions. The condition usually heals within seven to 14 days of commencing antibiotic treatment for the staphylococcal infection.¹

Diagnosis

SSSS is a unique condition that should be a spot diagnosis. The differential diagnoses listed above relate only to a patient in the early stages where the disease has not yet declared itself. The hallmarks of SSSS are:

- patient age usually under 5 years
- recent staphylococcal infection
- severe pain
- lack of mucosal lesions
- flexural erythema with superficial erosions.

Treatment

Management of SSSS includes:

- oral flucloxacillin 50 mg/kg daily in four divided doses (intravenous flucloxacillin may be required if the patient is not taking oral fluids)
- minimal handling and avoidance of dressings (if possible) to avoid causing pain
- analgesia with regular paracetamol with or without oxycodone
- cultures to determine the source of the septic focus, including culture of

including full blood count, measurement of serum urea, electrolytes and creatinine levels and liver function tests. Blood cultures, urine cultures, chest x-ray and bacterial microscopy, culture and sensitivity tests of swabs from affected skin also gave normal results. Polymerase chain reaction (PCR) tests of axillary swabs were negative for herpes simplex virus.

Management

A provisional diagnosis was made of staphylococcal scalded skin syndrome (SSSS). The differential diagnosis included:

- streptococcal toxin-mediated erythema
- drug reaction
- viral exanthema.

The patient showed clinical improvement within 24 hours of commencing oral flucloxacillin. She rapidly improved over the following two to three days and was subsequently discharged from hospital. The septic focus was found to be undiagnosed otitis externa.

Discussion

SSSS is a toxin-mediated dermatosis that presents with erythematous, tender,

1. STAPHYLOCOCCAL SCALDED SKIN SYNDROME PRACTICE POINTS

- Staphylococcal scalded skin syndrome typically presents with:
 - skin pain, flexural erythema and superficial blistering
 - periorificial erythema and scaling
 - irritable and/or febrile child
- Negative skin swabs do not exclude the diagnosis
- Treatment does not always require intravenous flucloxacillin unless the child is not taking oral fluids; the condition responds well to oral antibiotics

samples taken from any obvious skin lesions, ears, throat and the conjunctiva.

PATIENT 2. TOXIC EPIDERMAL NECROLYSIS

A 33-year-old woman presented to the ED with tender, violaceous, targetoid macules in association with 'gritty-feeling' eyes, pharyngitis and painful vulval erosions. Two weeks before the onset of symptoms, she had begun taking clarithromycin to treat sinusitis. Over the 24 hours after her arrival in the ED, she developed blisters involving 75% of her body surface area (Figure 2).

Investigations and management

A skin biopsy confirmed confluent epidermal necrosis consistent with toxic epidermal necrolysis (TEN). The patient was transferred to the intensive care unit (ICU) for high-dependency nursing care and appropriate analgesia, eventually requiring intubation and an induced coma for pain management.

In the ED, the patient was immediately commenced on intravenous immunoglobulin 1g/kg. She received a second immunoglobulin dose the following day, as well as intravenous hydrocortisone 100 mg daily for three days.



Figure 2. A woman with toxic epidermal necrolysis showing Nikolsky-positive generalised erosions affecting more than 75% of the body.

The patient was reviewed daily by dermatology and ophthalmology specialists and the burns team. She was commenced on daily vaginal dilatation and intravaginal prednisolone suppositories to prevent vaginal fusion.

The patient's hospital stay was complicated by *Pseudomonas aeruginosa* pneumonia and staphylococcal bacteraemia. She required ICU treatment for three weeks. She recovered and was discharged home after 31 days.

Discussion

TEN is an acute life-threatening mucocutaneous reaction characterised by extensive necrolysis and detachment of the epidermis. It is almost invariably a drug reaction, and involves more than 30% of the body surface area.²

Although survival rates in patients with TEN have improved over the past 20 years, some long-term sequelae may occur and are often devastating, including vision loss, oesophageal strictures and vaginal stenosis. Patients' quality of life may be severely compromised. Practice points about TEN are summarised in Box 2.

Pathophysiology

The pathophysiology of TEN remains unclear, but it is well established that drugs are the most important aetiological factor, with more than 100 different drugs being reported as possible causes. The drugs with the highest risk of TEN include

antibacterial sulfonamides, aromatic anti-convulsants, allopurinol, oxicam NSAIDs, lamotrigine and nevirapine. A significant but much lower risk has also been reported for nonsulfonamide antibiotics, such as aminopenicillins, quinolones, cephalosporins and tetracyclines.³ The reaction usually occurs on first exposure to the medication.

Clinical signs and symptoms

TEN typically begins within eight weeks (usually four to 30 days) of first exposure to the drug. Nonspecific symptoms, including fever, pharyngitis, headache, rhinitis and myalgia may precede the mucocutaneous lesions by one to three days. The initial skin lesions are characterised by irregularly shaped erythematous, dusky red, purpuric macules that progressively coalesce. The Nikolsky sign (dislodgement of the epidermis by lateral pressure) is positive on erythematous zones. At this stage, the lesions evolve to superficial flaccid blisters that spread with pressure and break easily. The necrotic epidermis is easily detached at pressure points or by frictional trauma, revealing large areas of exposed, erythematous dermis.²

Treatment

The most important element of the treatment of patients with TEN is cessation of the causative drug. If a diagnosis of TEN is suspected then any potential causative medications should be ceased and the

patient should be immediately referred to a tertiary hospital with a dermatology department and a burns unit.

Intubation is often necessary for pain management and dressing changes, and most patients spend some time in the ICU in an induced coma because of pain. Patients should also have regular specialist ophthalmology review, nanocrystalline silver dressings of wounds and supportive care, including mouth care. Nanocrystalline silver dressings have an important role through their antibacterial and anti-inflammatory properties.

Intravenous immunoglobulin has been found to arrest progression of the disease, allowing re-epithelialisation. Treatment with systemic corticosteroids and other immunosuppressive agents, particularly cyclosporin A, has been described but is controversial because of a possible increased risk of sepsis and the lack of grade A supporting evidence.

Infection is the most common cause of death in TEN, with *S. aureus*, *P. aeruginosa* and *Candida* spp. being the most typical isolates.⁴ Other potentially fatal complications include pulmonary embolism, adult respiratory distress syndrome, gastrointestinal haemorrhage and cardiac and renal failure.⁵

Follow up involves ensuring that the offending medication (and closely related medications) are never readministered to the patient as this could lead to a recurrence of TEN. Long-term morbidity is often related to ocular, dermatological, gynaecological and renal complications.

PATIENT 3. PYODERMA GANGRENOSUM

A 52-year-old woman with a history of type 2 diabetes and hypertension presented to her private dermatologist with a two-week history of very painful, rapidly enlarging ulcers on her left foot, a toe on her right foot and her calves (Figure 3a).

Investigations and management

Swabs were collected from the ulcers for microscopy and culture and the patient was

commenced on oral antibiotics. A biopsy was also performed, which showed a neutrophilic dermal infiltrate consistent with pyoderma gangrenosum. Cultures were negative for bacteria, mycobacteria and fungi.

The patient was referred to the dermatology department at her local hospital where she was commenced on prednisolone 60 mg daily and cyclosporin 5 mg/kg daily. She was advised to apply simple dressings daily to existing ulcers and betamethasone dipropionate 0.05% ointment to any new ulcers.

Initially she was managed as an outpatient. However, she developed osteomyelitis as a complication and required hospital admission to receive intravenous antibiotic treatment.

Within weeks of the patient commencing treatment, the ulcers improved significantly (Figure 3b). The patient was able to mobilise and perform activities of daily living independently. Prednisolone was withdrawn, but cyclosporin was continued until all ulcers had healed completely. The patient was at risk for below-knee amputation because of the osteomyelitis but fortunately responded well enough to antibiotic treatment to avoid this.

Discussion

Pyoderma gangrenosum is a rare, non-infectious neutrophilic dermatosis, which is associated with underlying systemic disease in 50% of cases. Diagnosis is based on typical clinical features and the exclusion of other cutaneous ulcerating diseases, including infection, trauma and cancer.⁶

Common associations of pyoderma gangrenosum include inflammatory bowel disease, rheumatoid arthritis, systemic lupus erythematosus, haematological malignancies and monoclonal gammopathies. The exact aetiology of pyoderma gangrenosum is unknown, but it is best thought of as an autoimmune process characterised by a sterile neutrophilic infiltrate. Practice points about pyoderma gangrenosum are summarised in Box 3.

Clinical signs and symptoms

Clinical features of pyoderma gangrenosum include:

- rapid progression of painful, necrotic ulceration with an irregular, undermined, violaceous border, often preceded by a papule, pustule or bulla, and causing severe pain out of proportion to the size of the ulcerated area

2. TOXIC EPIDERMAL NECROLYSIS PRACTICE POINTS

- Toxic epidermal necrolysis (TEN) is an acute, life-threatening, mucocutaneous drug eruption with extensive necrolysis and detachment of the epidermis
- If there is any suspicion of TEN, patients must be urgently referred to a tertiary hospital; a multidisciplinary team approach is necessary with dermatology, burns, ophthalmology, gynaecology and sometimes intensive care involvement
- Cessation of the causative drug, wound care and pain management are the cornerstones of treatment
- Intravenous immunoglobulin is frequently used to arrest progression of the disease, allowing re-epithelialisation

- history of pathergy (lesions occurring at sites of mild trauma)
- cribriform (crater-like) scarring as the ulcer heals
- an underlying condition, particularly inflammatory bowel disease.



Figures 3a and b. An older woman with pyoderma gangrenosum affecting the left foot. (a, left). At initial presentation, showing deep ulceration of the foot with a violaceous edge. b (right). After treatment with oral prednisolone showing the healing ulcer.

3. PYODERMA GANGRENUMUS PRACTICE POINTS

- Pyoderma gangrenosum is characterised by:
 - disproportionate pain
 - rapid ulcer progression
- No evidence of infection is found on histopathology, polymerase chain reaction tests and culture
- Pyoderma gangrenosum fails to respond to antibiotics
- Ulcers worsen after debridement or trauma (pathergy)
- Pyoderma gangrenosum is associated with underlying disease

There are four main clinical subtypes of pyoderma gangrenosum, comprising:

- classic/ulcerative
- pustular/superficial
- bullous
- vegetative.⁷

Diagnosis

Histopathological findings in patients with pyoderma gangrenosum are often variable and nonspecific, but typical findings include central necrosis and ulceration of the epidermis and dermis, surrounded by an intense, acute inflammatory cell infiltrate consisting of neutrophils.⁸ A skin biopsy is not diagnostic of pyoderma gangrenosum but can rule out other conditions, particularly infection and malignancy.

Diagnosis of pyoderma gangrenosum is essentially based on clinical characteristics. PCR tests and microscopy with specific histopathology stains for mycobacteria, fungi and bacteria should be performed to exclude an infectious aetiology before commencing immunosuppression. Tissue should be sent for mycobacterial and fungal culture but treatment should not be delayed while waiting for culture results if there is no histopathological evidence that the ulcer could be caused by an infection.

Treatment

In patients with early or mild cases of pyoderma gangrenosum, topical therapy such as potent corticosteroids or tacrolimus 0.1% ointment can be used. Minocycline and dapsone have also been used in milder cases. More severe or resistant disease responds quickly to oral corticosteroids (1 to 2 mg/kg daily).

A number of immunosuppressive agents have been found useful in corticosteroid-unresponsive pyoderma gangrenosum, either given alone or as corticosteroid-sparing agents, and should be commenced immediately in a patient in whom oral corticosteroids present a relative risk. Cyclosporin has been widely used in the past because of its rapid onset of action. It is not ideal for long-term therapy, but this is usually not needed as the drug can be ceased when the ulcers heal.

Other corticosteroid-sparing options include methotrexate, azathioprine and mycophenolate mofetil. There have also been several reports of tumour necrosis factor- α blockers being efficacious in the treatment of patients with pyoderma gangrenosum, including etanercept, adalimumab and infliximab, and other case reports of intravenous immunoglobulin and plasmapheresis.¹

Treatment of pyoderma gangrenosum can usually be discontinued after complete healing of lesions. Recurrences may occur but are unpredictable and do not justify prolonged maintenance therapy.

CONCLUSION

This article outlines some dermatological emergencies that are important for GPs to be able to identify as possible differential diagnoses and to refer on appropriately. MT

REFERENCES

1. Burns DA, Breathnach SM, Cox N, Griffiths CE. Rook's textbook of dermatology. 8th ed. Chichester, West Sussex: Wiley-Blackwell; 2010.
2. Wolff K, Goldsmith LA, Katz SI, et al, eds.

Fitzpatrick's dermatology in general medicine. 7th ed. New York: McGraw-Hill; 2008.

3. Mockenhaupt M, Viboud C, Dunant A, et al. Stevens-Johnson syndrome and toxic epidermal necrolysis: assessment of medication risks with emphasis on recently marketed drugs. The EuroSCAR-study. *J Invest Dermatol* 2008; 128: 35-44.
4. Roujeau JC, Stern RS. Severe adverse cutaneous reactions to drugs. *N Engl J Med* 1994; 331: 1272-1285.
5. Downey A, Jackson C, Harun N, Cooper A. Toxic epidermal necrolysis: review of pathogenesis and management. *J Am Acad Dermatol* 2012; 66: 995-1003.
6. Powell FC, Su WPD. Pyoderma gangrenosum: classification and management. *J Am Acad Dermatol* 1996; 34: 395-409.
7. Su WPD, Davis MD, Weenig RH, et al. Pyoderma gangrenosum: clinicopathologic correlation and proposed diagnostic criteria. *Int J Dermatol* 2004; 43: 790-800.
8. Crowson NA, Mihm MC Jr, Magro C. Pyoderma gangrenosum: a review. *J Cutan Pathol* 2003; 30: 97-107.

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