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R Sullivan

G Fulde

University of Notre Dame Australia, Gordian.Fulde@nd.edu.au

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A middle-aged man with cellulitis

RICHARD SULLIVAN MB BS

GORDIAN FULDE MB BS, FRACS, FRCS(Ed), FRCS/FRCP(A&E)Ed, FACEM

A middle-aged man presents with an extremely painful swollen red leg and signs of sepsis. He has a history of chronic venous insufficiency, obesity, diabetes, hypertension and obstructive sleep apnoea. What are your differential diagnoses and how should he be managed?

As a GP working in both your own practice and the local emergency department, you commonly assess and treat patients of all ages with infections of the skin.

The case

Late one evening, a middle-aged man limps into the emergency department. You note that he is pale and does not look well. His left leg is extremely erythematous. You immediately admit him to a bed in the emergency department. His blood pressure is 80/40 mmHg, heart rate 150 beats/minute and irregularly irregular, respiratory rate 28 breaths/minute and temperature 39.2°C.

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Dr Sullivan is a Conjoint Associate Lecturer in the Prince of Wales Clinical School, UNSW Australia; and an Infectious Diseases Advanced Trainee, Prince of Wales Hospital, Sydney, NSW. Professor Fulde is Director of Emergency Medicine at St Vincent's Hospital, Sydney; Professor in Emergency Medicine at the University of Notre Dame, Sydney; and Associate Professor in Emergency Medicine at UNSW Australia, Sydney, NSW.



You assess the patient and quickly note he has sepsis from a skin source. While you take a history, you insert an intravenous cannula and prescribe a one litre bolus of normal saline. You take samples for a full blood count, venous blood gas, electrolytes and creatinine measurements and blood cultures. The patient has no allergies and after brief history-taking you prescribe flucloxacillin empirically.

The history

You learn that the patient has had recurrent episodes of cellulitis over the past 20 years. He has a history of chronic venous insufficiency, obesity, hypertension, type 2 diabetes and obstructive sleep apnoea. He states he has been treated three times in the past year for cellulitis and has tried compression bandaging for his venous insufficiency but could not tolerate this. He has no history of deep venous thrombosis (DVT). He reports increasing erythema in his left leg over the past three days, starting at the foot and spreading to the knee. This is very painful.

His regular medications include perindopril and metformin and he uses continuous positive airway pressure (CPAP) to treat obstructive sleep apnoea. He has no history of immunosuppression, and his family history is unremarkable.

Physical examination

You note that both the patient's legs show changes consistent with chronic venous insufficiency, with haemosiderin deposition and peripheral oedema to the mid-calf. His left leg is extremely erythematous up to the knee. His dorsalis pedis and posterior tibial arteries are palpable bilaterally, and his leg is diffusely tender. There are no ulcers and no crepitus. You consider whether

this is cellulitis, necrotising fasciitis or a DVT. The patient has a full range of movement in his ankle and knee without tenderness, making septic arthritis less likely.

Results of the remainder of the examination are unremarkable.

Provisional diagnosis and management

When the patient's venous blood gas results are returned, they show a pH of 7.33 and a lactate level of 3.5 mmol/L. The creatinine level is elevated at 150 µmol/L. An ECG shows that he has atrial fibrillation with a rapid ventricular response at 130 beats/minute. His blood pressure remains 80/40 mmHg despite the administration of one litre of fluid.

As the patient's leg is extremely tender, his blood pressure is not responsive to fluid and he has acute kidney injury, you consider necrotising fasciitis and toxic shock syndrome as possible diagnoses. Necrotising soft tissue infections are extremely serious and associated with high mortality. Consequently you prescribe meropenem, clindamycin and vancomycin, and request early surgical review.¹ You also prescribe another litre bolus of normal saline and call the high dependency unit (HDU) to request the patient be assessed for admission.

On completion of the second intravenous fluid bolus, the patient's blood pressure has improved to 88/45 mmHg, but he remains tachycardic with a heart rate of 120 beats/minute. You request another 500 mL of intravenous normal saline to be given as a bolus and order a CT scan of the left lower limb.

The patient's vital signs continue to improve and the pain in his leg is gradually decreasing. After the 500 mL fluid bolus, his blood pressure has risen to 100/60 mmHg and his heart rate is 95 beats/minute. You prescribe another 500 mL of normal saline to be given at a rate of 125 mL/h and continue to monitor his blood pressure closely.

The CT scan does not show any features suggesting a necrotic infection (such

Infection	Extent	Treatment
Erysipelas	Infection involving more superficial dermal structures, distinguished clinically by a clear border between infected and uninfected skin	Antibiotics
Cellulitis	Infection of dermis and subcutaneous tissue	Antibiotics
Abscess	A collection in the soft tissues	Incision and drainage ± antibiotics
Necrotising soft tissue infections	A necrotising infection that involves any soft tissue layer and can be as deep as the muscle	Debridement and antibiotics ± hyperbaric therapy

as gas in the deep tissues) and no abscess or myositis, but there is significant subcutaneous oedema.² There is no disruption of the bone cortex to suggest underlying osteomyelitis.

Over the next two hours, the leg pain improves. A surgeon reviews the patient and deems he does not require urgent surgery at present given his clinical response but is happy to reassess him at

Circumstance	Considerations and typical organisms	Consider (always consult local guidelines and consider allergies)
Hypersensitivity to penicillin (non-immediate)	NA	Cefalexin or cefazolin
Hypersensitivity to penicillin (immediate)	NA	Vancomycin or clindamycin
Suspected MRSA or community-associated MRSA	MRSA	Consider vancomycin or clindamycin (assess sensitivities)
Freshwater exposure	<i>Aeromonas</i> spp.	Add ciprofloxacin
Saltwater exposure	<i>Vibrio</i> spp.	Add doxycycline
Chronic diabetic foot infection	Polymicrobial	Amoxicillin + clavulanate or piperacillin + tazobactam (if limb or life threatening)
Animal bites	Polymicrobial	Amoxicillin + clavulanate or piperacillin + tazobactam (if severe)
Necrotising soft tissue infection	Monomicrobial (<i>Streptococcus pyogenes</i> , <i>Clostridium perfringens</i> , <i>Staphylococcus aureus</i> , <i>Vibrio</i> spp., <i>Aeromonas</i> spp.) or polymicrobial	Meropenem + vancomycin + clindamycin

Abbreviations: MRSA = methicillin-resistant *Staphylococcus aureus*; NA = not applicable.

1. CLINICAL FEATURES SUGGESTING SEPSIS, NECROTISING SOFT TISSUE INFECTION OR TOXIC SHOCK SYNDROME^{1,7}

Sepsis

- Infection with features that may include:
 - fever
 - hypothermia
 - tachycardia
 - tachypnoea
 - hypotension
 - altered conscious state
 - elevated white cell count

Necrotising soft tissue infection

- Severe pain and tenderness
- Skin necrosis or bleeding into the skin
- Bullae or vesicles
- Crepitus
- Systemic toxicity
- Rapid spread
- Oedema or tenderness extending beyond the erythema
- Cutaneous anaesthesia

Toxic shock syndrome

- Isolation of *Streptococcus pyogenes*,* hypotension unresponsive to fluid administration and two of:
 - acute kidney injury
 - acute respiratory distress syndrome
 - coagulopathy
 - hyperbilirubinaemia
 - generalised rash or soft tissue necrosis

* Can also be caused by *Staphylococcus aureus* (case definition differs).

any time if his condition deteriorates. The HDU registrar reviews the patient and accepts him for observation. Empirical treatment with meropenem, clindamycin and vancomycin is continued.

Discussion

There is a wide spectrum of skin and soft tissue infections, and your patient highlights some of the concerns prompted

TABLE 3. RELEVANT CLINICAL CHEMISTRY AND FULL BLOOD COUNT RESULTS IN A PATIENT WITH CELLULITIS

Test	Test result	Normal range
Haemoglobin (g/L)	150	≥130
Platelets (x 10 ⁹ /L)	437	150 to 400
White cell count (x 10 ⁹ /L)	25.2	4.5 to 11.0
Neutrophil count (x 10 ⁹ /L)	19.1	2.0 to 7.5
Potassium (mmol/L)	3.8	3.5 to 5.2
Sodium (mmol/L)	146	135 to 145
Urea (mmol/L)	13.8	3.0 to 8.0
Creatinine (µmol/L)	150	60 to 110
International normalised ratio	1.0	<1.1

by a presentation with apparent cellulitis and sepsis. Establishing the extent and depth of infection can help guide treatment (Table 1).³ The incidence of DVT in patients presenting with cellulitis and no other risk factors is low, and routine screening by Doppler ultrasound examination is not generally recommended.⁴

A wide range of organisms can cause cellulitis, the most common of which are *Streptococcus* species and *Staphylococcus aureus*.⁵ Australian guidelines recommend empiric treatment with flucloxacillin monotherapy.¹ Additional or alternative agents may be required in specific circumstances (Table 2).^{1,6}

Your patient had sepsis and features suggestive of necrotising fasciitis as well as toxic shock syndrome early in the presentation (Box 1).^{1,7} However, he responded quickly to antibiotic treatment, and his blood pressure eventually improved with fluid administration, making the latter two diagnoses less likely. Necrotising fasciitis and toxic shock syndrome are medical emergencies, and the benchmark treatment is early surgical debridement and antibiotics. Intravenous immunoglobulin may also be considered in patients with toxic shock syndrome, and hyperbaric oxygen may be considered

in those with necrotising soft tissue infections.¹

Progress

The patient is admitted to hospital. He remains normotensive, the atrial fibrillation spontaneously reverts and the left leg erythema becomes less prominent and reduces in extent over the next 48 hours. His fever also settles. Relevant investigation results are listed in Table 3 and show prominent neutrophilia and an acute kidney injury. These resolve over the course of the admission.

Results of blood cultures taken at presentation show *Streptococcus pyogenes* (Group A streptococcus) that is sensitive to penicillin and clindamycin. Subsequent blood cultures have negative results, demonstrating quick clearance. The patient's antibiotic treatment is changed to benzylpenicillin and clindamycin on day 2 and he continues to make clinical improvement. Research suggests clindamycin decreases mortality in patients presenting with invasive group A streptococcus infection.⁸

Outcome

After seven days of antibiotic treatment, your patient is much improved and the cellulitis has completely resolved. In

2. DIFFERENTIAL DIAGNOSES IN PATIENTS PRESENTING WITH LEG SWELLING AND ERYTHEMA

- Chronic venous insufficiency
- Dermatitis
- Gout
- Lymphoedema
- Vasculitis

uncomplicated cases of cellulitis, five to 10 days of antibiotic treatment is generally sufficient, but up to 14 days may be needed in severe cases.^{1,5}

You consider preventing future episodes of cellulitis in your patient. You encourage compression bandaging of his lower legs and organise community nursing to deliver this care. You note that he has tinea between the toes and treat this to re-establish the skin barrier.

You note that if the cellulitis recurs then you would need to consider other differential diagnoses (Box 2). If recurrent cellulitis is confirmed then you would consider prescribing prophylactic phenoxymethylpenicillin, as this has been shown to reduce the recurrence of cellulitis.⁹ You also consider treating any recurrences

with antibiotics delivered in the community when safe (e.g. hospital in the home), to prevent future hospital admissions and improve patient satisfaction.^{10,11}

Conclusion

Most patients with soft tissue infections can be managed in the community. However, patients can present with sepsis, deeper infection and occasionally toxic shock syndrome. Patients with systemic symptoms and those who are not responding to oral antibiotics after 48 hours should be considered for intravenous antibiotic therapy.¹ Patients with sepsis, features suggestive of necrotising fasciitis or toxic shock syndrome should be transferred to hospital as these conditions are life-threatening emergencies. **MT**

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