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A Case of Infectious Purpura Fulminans: An Unusual Organism and Method of Diagnosis

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Abstract:

Infectious purpura fulminans is a rapidly progressive skin necrosis that has a mortality rate of 30%[1,2]. Here, we describe a case of infectious purpura fulminans caused by *Capnocytophaga*, diagnosed by a blood film.

Keywords: Capnocytophaga, purpura fulminans, bacillus, sepsis

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Introduction

Infectious purpura fulminans is a rapidly progressive skin necrosis that has a mortality rate of 30%[1,2]. Here, we describe a case of infectious purpura fulminans caused by *Capnocytophaga*, diagnosed by a blood film.

Case report

A previously healthy 66-year-old man presented to the emergency department with a history of less than 24 hours of feeling unwell, fever, non-productive cough and vomiting. He had not been exposed to anyone sick in the recent past and had no past medical history.

On admission, he was pyrexic at 38.3°C, tachycardic at 125 beats per minute and tachypnoeic at 33 breaths per minute. His blood pressure was 88/61 mmHg. On auscultation, there were minimal

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crepitations at both lung bases. All other physical examinations were normal. Biochemistry results demonstrated a raised white cell count with left shift, acute kidney injury, deranged liver function and disseminated intravascular coagulation (*Table 1*).

	Laboratory value	Reference range
Biochemistry		
C-reactive protein	284 mg/l	<5 mg/l
Sodium	143 mmol/l	135–145 mmol/l
Potassium	3.4 mmol/l	3.5–5.0 mmol/l
Creatinine	240 µmol/l	45–120 µmol/l
eGFR corrected for ethnic group	21	>90 ml/min/1.73 m^2
Urea	8.1 mmol/l	3.3–6.7 mmol/l
Phosphate	1.76 mmol/l	0.80–1.40 mmol/l
Corrected calcium	2.09 mmol/l	2.15–2.60 mmol/l
Total protein	66 g/l	60–80 g/l
Albumin	36 g/l	35–50 g/l
Globulin	30 g/l	25–35 g/l
Bilirubin (total)	26 µmol/l	3–20 µmol/l
Alkaline phosphatase	159 IU/l	30–130 IU/l
Aspartate transaminase	515 IU/l	10–50 IU/l
Gamma-glutamyl transferase	251 IU/l	1–55 IU/l
Haematology		
White blood cells	16	4–11×10^9 cells/l
Red blood cells	4.08	4.5–5.8×10^{12} cells/l
Haemoglobin	10.8	13–16.5 g/dl
Mean corpuscular volume	88.2	77–95 fl
Platelets	24	150–450×10^9cells/l
Neutrophils	10.46	2.2–6.3×10^9 cells/l
Lymphocytes	1.08	1.3–4×10^9 cells/l
Monocytes	0.55	0.2–1. 0×10^9 cells/l
Basophils	0.06	0–0.1×10^9 cells/l
Fibrinogen	5.5	1.5–4 g/l
INR	2	1.0–1.5

Table 1: *Initial blood test results of the patient during admission*

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Chest radiograph showed possible right basal consolidation. A computed tomography of his chest, abdomen and pelvis showed features of an infarcted spleen, with no evidence of intra-abdominal collections. A diagnosis of sepsis of unknown origin was made and intravenous Tazocin (piperacillin and tazobactam) was commenced at 4.5 g twice a day. Five litres of intravenous saline, 1 l of colloid and 15 ml/kg of fresh frozen plasma were administered. Continuous haemodialysis was instigated in the Medical Critical Care Unit (MCCU). Despite all therapeutic efforts, the patient became progressively hypotensive and was intubated, mechanically ventilated and treated with milrinone and noradrenaline. Within the first few hours in the MCCU, he developed cutaneous blistering, initially on the left arm, later progressing rapidly, forming areas of widespread ecchymosis involving the thorax, abdomen, digits, lower limbs and nose tip (*Figs. 1 and 2*).

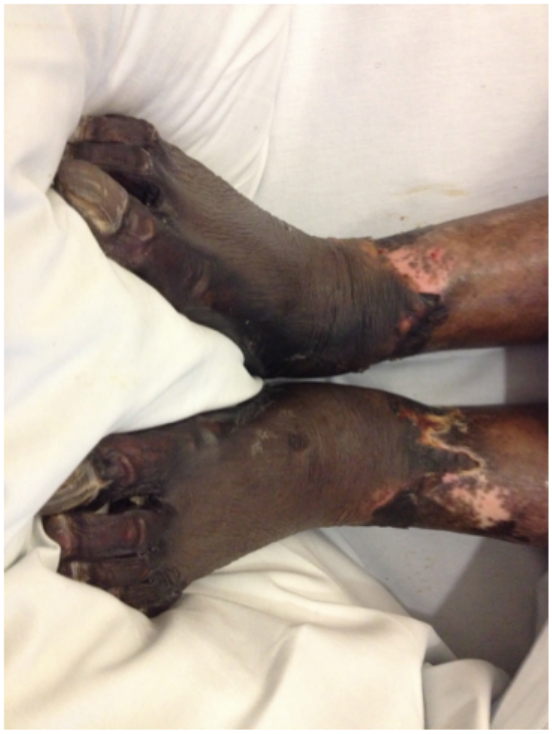

Figure 1: Purpura fulminans leading to peripheral gangrene in the feet.

Figure 2: Purpura fulminans leading to peripheral gangrene in the hands.

Sepsis due to meningococcal disease or staphylococcal/streptococcal infection was suspected and antibiotic treatment was escalated to intravenous clindamycin, ciprofloxacin, Tazocin and linezolid.

Investigations

The initial blood cultures showed no growth. These blood cultures were sent for prolonged incubation on chocolate agar and again no growth was detected. The urine culture and wound swab showed no growth. His retroviral test was negative. The combined nose and throat swab showed absence of influenza A, influenza B, respiratory syncytial virus, parainfluenza virus type 1, 2 and 3 and adenovirus. Cytomegalovirus, Epstein–Barr virus and hepatitis screens were negative. Sputum culture showed no acid-fast bacilli. Urine pneumococcal antigen was negative.

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A second set of blood cultures grew *Candida glabrata*. The positive fungal culture suggested a possible occult infection although fundoscopy examination was normal and neither the transthoracic echocardiogram nor transoesophageal echocardiogram showed any vegetations.

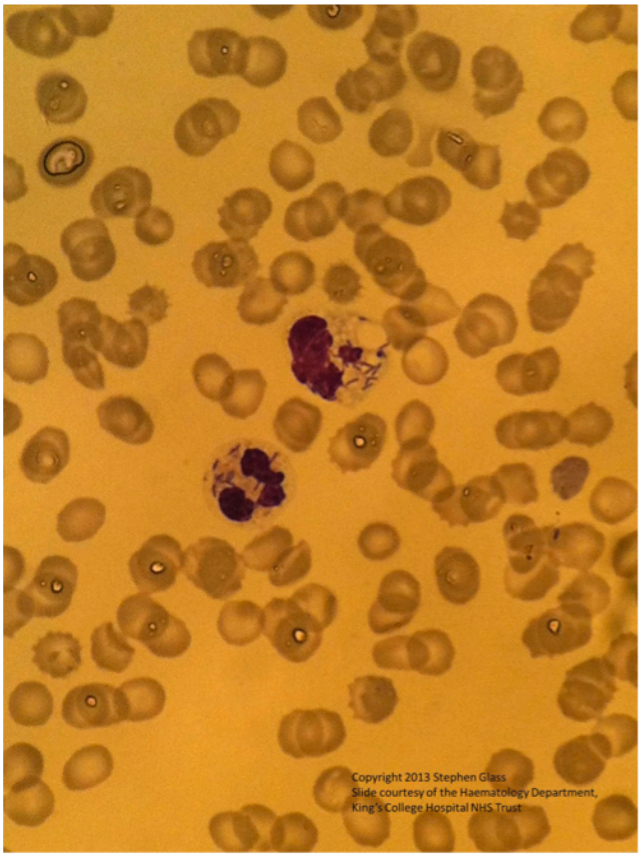

Figure 3: A peripheral blood smear showing intracellular bacilli in neutrophils

The central venous line, peripheral line and nasogastric line tips were negative for bacterial and fungal growth. Intravenous amphotericin B was added to the antibiotic regimen but it was agreed that the fungal growth was not the primary focus of infection.

The focus of infection remained unclear, until results of a peripheral blood smear (*Fig. 3*) showed rod-like inclusions consistent with an intracellular bacterium, raising a suspicion of *Capnocytophaga canimorsus* septicaemia. This was supported by the patient's history. A family dog had bitten the patient 48 hours prior to the onset of symptoms; the bite marks were superficial. The dog was up to date with vaccinations. Antibiotic therapy was changed to meropenam, given reports of beta-lactam-resistant strains of the *Capnocytophaga* species. The areas of ecchymoses on the nose, lower limbs and fingertips became necrotic, requiring surgical debridement.

Outcome

The patient had 14 days of intravenous meropenam. He eventually had bilateral below-knee amputations and became wheelchair bound, requiring ongoing rehabilitation.

Discussion

C. canimorsus is a gram-negative, non-spore-forming bacillus found in the gingival flora of cats and dogs. It is transmitted to man by bites (54% of cases), scratches (8.5%) or by mere exposure to animals (27%)[2,3]. Human infection with this bacterium is rare. It tends to occur at greater frequency in those who are immunocompromised (5%) and those with asplenia (33%), alcoholism (24%), chronic lung disease and cirrhosis[4,5]. Despite its low virulence, 50% of patients suffering from *C. canimorsus* septicaemia develop severe purpura fulminans. The mortality rate is 30% and prompt diagnosis is essential[3-5].

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Patients with *C. canimorsus* infections present with nonspecific signs such as nausea, vomiting and shortness of breath and progress rapidly to septic shock. Few develop a maculopapular rash at the site of the animal bite[4,5]. Some patients develop haemorrhagic adrenal insufficiency[6]. There are also rare instances of *C. canimorsus* endocarditis or meningitis[7,8].

As *C. canimorsus* is a fastidious, slow-growing organism, isolation of this organism is difficult. Culturing of *C. canimorsus* involves using an enriched agar such as chocolate, 5% sheep blood, heart or brain–heart infusion agar with 5% rabbit blood at 37°C. Colonies may not be visible for up to 7 days. Even with meticulous culture conditions, blood cultures are negative in 30% of cases[9,10]. Some authors have suggested identification of *C. canimorsus* through polymerase chain reaction (PCR) and 16s ribosomal RNA gene sequencing[11], but such facilities are not readily available in all centres.

C. canimorsus infection can cause organ failure. The mechanisms involve widespread inflammatory response secondary to endotoxin production. The systemic influx of the local inflammatory mediators causes tissue toxicity, microvascular ischaemia and cell death[12]. Treatment involves early targeted antibiotic therapy and intensive organ support[12,13]. *C. canimorsus* infection responds well to penicillin and β-lactam–β-lactamase inhibitor combinations. Other active agents include clindamycin, linezolid, tetracycline, carbapenems and chloramphenicol[14]. Due to the increasing frequency of β-lactamase-resistant strains, meropenam was chosen[14,15]. Though monoclonal anti-endotoxin antibodies have been used in gram-negative sepsis, there are still insufficient clinical studies to prove its benefit[16,17].

Learning Points

- *C. canimorsus*-induced septicaemia, though rare, should be considered in any patients presenting with sepsis.
- A history on animal exposure, previous foreign travel and recent contacts is vital.
- Waiting for blood culture could delay treatment. Alternative methods of diagnosis should be considered.

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