Necrotising fasciitis in systemic lupus erythematosus: a case report and literature review

Y Tung Chen,1 D Isenberg2

ABSTRACT
Necrotising fasciitis (NF) is a rare infection of the subcutaneous tissue, known to be rapidly progressive and potentially fatal. Patients with systemic lupus erythematosus (SLE) may be predisposed to this condition, and early clinical recognition can be difficult. We report a case of necrotising fasciitis in a 26-year-old woman with SLE. She presented with painful swelling of her left leg, then developed clinical features of septic shock. Emergency debridement was performed. Intraoperative findings revealed NF and cultures grew Pseudomonas aeruginosa. The patient survived after a lengthy hospital admission, following several further debridements complicated by recurrent chest sepsis and multiorgan failure. We also review and discuss the published cases of NF in SLE patients.

INTRODUCTION
Necrotising fasciitis (NF) is a serious soft tissue and life threatening infection, primarily involving the skin and superficial fascia, characterised by a rapid and extensive necrosis of the subcutaneous tissue. Most patients have associated comorbidities, such as diabetes, HIV infection or treatment with immunosuppressive drugs, but it can also affect previously healthy individuals. Infection is one of the common causes of morbidity and mortality in patients with systemic lupus erythematosus (SLE). It is associated with immunosuppressive agents, renal failure, and increased disease activity. Despite the increased propensity of SLE patients to develop common and opportunistic infections, NF has rarely been reported. To our knowledge, only 31 cases are described in the literature to date (see table 1). NF has also been described in other rheumatic diseases including polymyositis, dermatomyositis, systemic sclerosis, rheumatoid arthritis and ankylosing spondylitis, but it appears that this association is more common in SLE.1 2

We describe the case of a NF caused by Pseudomonas aeruginosa, complicated by recurrent sepsis and multiorgan failure in a young patient with a history of SLE.

CASE REPORT
A 26-year-old Asian woman with a complex history of SLE, diagnosed at age 14 years when she presented with malar rash, arthralgia, mouth ulcers, pulmonary vasculitis, strongly positive anti-nuclear antibody and anti-dsDNA antibodies. Subsequently, she had idiopathic detrusor overactivity with repeated urinary tract infection. Linked to her corticosteroid treatment she developed avascular necrosis of her elbow (at that time, on prednisolone 6 mg daily). The patient was also treated with hydroxychloroquine (HCQ), azathioprine (AZA) (100 mg from 1999 to 2009) and had 14 courses of cyclophosphamide (CYC) (a cumulative dose of 14 g) and two of rituximab (RTX) (two 1 g intravenous infusions separated by 2 weeks), the last being given in March 2012 for a SLE flare manifested by severe vasculitic rash. Immediately prior to B-cell depletion, her C3 level was 0.33 g/L (normal: 0.65–1.65), cluster designation (CD) 19 count was 0.146/µL (0.11–0.69), and immunoglobulin G level was 23.4 g/L (7–16).

In May 2012, she presented to her local hospital with painful swelling of her left lower limb, she denied a history of trauma, and her inflammatory markers and ultrasonography were normal, and she was discharged. Within 12 h she was found at home with a Glasgow Coma Scale of 6, and was admitted to the intensive care unit (ICU). On examination, the patient was in septic shock with hypotension (systolic blood pressure 60 mm Hg), tachycardia (135/min), and respiratory failure (SaO₂ 70%). Poorly demarcated discolouration and blistering purpuric patches on her left lower limb were noted. Laboratory results showed erythrocyte sedimentation rate 96 mm/h (normal: 1–7),
Table 1 Clinical features of NF in systemic lupus erythematosus

<table>
<thead>
<tr>
<th>n</th>
<th>Race/age/sex</th>
<th>Organ involvement</th>
<th>Medications</th>
<th>Comorbidities</th>
<th>Reported anaemia</th>
<th>Alb (g/dl)</th>
<th>WBC (×10³/mm³) (Lym)</th>
<th>Classification of NF</th>
<th>Isolated micro-organism</th>
<th>Presentation</th>
<th>Outcome</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A 26F</td>
<td>Lung and cutaneous vasculitis, myositis, Raynaud, thrombopenia, ART, hepatitis</td>
<td>CS, HCQ, CYC, RTX, Doxycycline</td>
<td>Detrusor overactivity, AVN of elbow, digital ischaemia. <em>Escherichia coli</em> urinary tract infections</td>
<td>Yes</td>
<td>1.7</td>
<td>15.4 (1.9%)</td>
<td>1</td>
<td><em>Pseudomonas</em></td>
<td>Leg pain, purpuric patches</td>
<td>S</td>
<td>Current report</td>
</tr>
<tr>
<td>2</td>
<td>NA 39F</td>
<td>N, ART, thrombopenia</td>
<td>CS, HCQ</td>
<td>DM</td>
<td>No</td>
<td>NA</td>
<td>16.7 (NA)</td>
<td>1</td>
<td><em>Aeromonas</em></td>
<td>Leg pain, blisters</td>
<td>S</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>NA 28F</td>
<td>Cerebral lupus, N, ART</td>
<td>CS</td>
<td>Mental retardation, AVN hips</td>
<td>No</td>
<td>NA</td>
<td>10.5 (9.5%)</td>
<td>1</td>
<td><em>Streptococcus, Serratia marcescens, Aeromonas, Morganella</em></td>
<td>Leg pain, fever</td>
<td>S</td>
<td>1</td>
</tr>
<tr>
<td>4</td>
<td>Aboriginal 34F</td>
<td>N, APS</td>
<td>CS</td>
<td>Renal failure</td>
<td>No</td>
<td>NA</td>
<td>3.3 (4.3%)</td>
<td>2</td>
<td><em>Streptococcus</em></td>
<td>Thigh skin sore</td>
<td>S</td>
<td>4</td>
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<tr>
<td>5</td>
<td>H 48F</td>
<td>Photosensitivity, oral ulcers, leucopenia, pleural effusion, haemolytic anaemia.</td>
<td>CS, anticoagulation.</td>
<td>PE, APS, DM.</td>
<td>Yes</td>
<td>NA</td>
<td>Normal</td>
<td>1</td>
<td><em>SA</em></td>
<td>Thigh swelling, pain</td>
<td>S</td>
<td>5</td>
</tr>
<tr>
<td>6</td>
<td>A 58F</td>
<td>NA</td>
<td>CS</td>
<td>Hepatitis C, cirrhosis</td>
<td>No</td>
<td>NA</td>
<td>21.6 (NA)</td>
<td>1</td>
<td><em>SA, Serratia</em></td>
<td>Swelling leg</td>
<td>D</td>
<td>6</td>
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<tr>
<td>7</td>
<td>A 28F</td>
<td>Anaemia</td>
<td>None</td>
<td>None</td>
<td>Yes</td>
<td>NA</td>
<td>17 (NA)</td>
<td>1</td>
<td><em>Pseudomonas</em></td>
<td>Facial swelling, pain, fever</td>
<td>S</td>
<td>8</td>
</tr>
<tr>
<td>8</td>
<td>H 34F</td>
<td>ART, seizures</td>
<td>CS</td>
<td>None</td>
<td>No</td>
<td>3.3</td>
<td>15.6 (2.6%)</td>
<td>2</td>
<td><em>Streptococcus</em></td>
<td>Leg pain, swelling</td>
<td>S</td>
<td>9</td>
</tr>
<tr>
<td>9</td>
<td>H 43F</td>
<td>ART, N</td>
<td>CS, CYC</td>
<td>None</td>
<td>No</td>
<td>2.2</td>
<td>1.6 (23%)</td>
<td>1</td>
<td><em>Escherichia</em></td>
<td>Leg pain and oedema</td>
<td>D</td>
<td>9</td>
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<tr>
<td>10</td>
<td>AA 53F</td>
<td>ART, N</td>
<td>CS</td>
<td>Hypertension</td>
<td>No</td>
<td>1.9</td>
<td>1.3 (23%)</td>
<td>1</td>
<td><em>Pseudomonas, Enterococcus</em></td>
<td>Thigh ecchymosis, bullous lesion</td>
<td>S</td>
<td>9</td>
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<tr>
<td>11</td>
<td>AA 12M</td>
<td>ART, N</td>
<td>CS</td>
<td>None</td>
<td>No</td>
<td>2.9</td>
<td>4.3 (28%)</td>
<td>1</td>
<td><em>Streptococcus pneumoniae</em></td>
<td>Neck pain, swelling</td>
<td>S</td>
<td>9</td>
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<tr>
<td>12</td>
<td>AA 20F</td>
<td>ART, vasculitis, haemolytic anaemia</td>
<td>CS, AZA, HCQ, napro-xen</td>
<td>None</td>
<td>Yes</td>
<td>NA</td>
<td>NA (NA)</td>
<td>2</td>
<td><em>Streptococcus pneumoniae</em></td>
<td>Streptococcus</td>
<td>NA</td>
<td>S</td>
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<tr>
<td>13</td>
<td>H 30F</td>
<td>Vasculitis, neph</td>
<td>CS, AZA, HCQ</td>
<td>None</td>
<td>No</td>
<td>3.3</td>
<td>NA (0.5 ×10³/mm³)</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>S</td>
<td>9</td>
</tr>
<tr>
<td>14</td>
<td>H 38M</td>
<td>ART, rash</td>
<td>CS, uuburo-fen</td>
<td>None</td>
<td>No</td>
<td>2.9</td>
<td>7.6 (9.2%)</td>
<td>—</td>
<td>Negative</td>
<td>NA</td>
<td>S</td>
<td>9</td>
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<tr>
<td>15</td>
<td>H 57F</td>
<td>Neph, ART, cerebritis</td>
<td>CS</td>
<td>CAD, hypertension</td>
<td>No</td>
<td>2.2</td>
<td>25.6 (3.9%)</td>
<td>2</td>
<td><em>Streptococcus</em></td>
<td>NA</td>
<td>D</td>
<td>9</td>
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<td>16</td>
<td>Canadian 30F</td>
<td>Serositis, purpuria, ART, malignant hypertensio, N</td>
<td>CS, CYC</td>
<td>None</td>
<td>Yes</td>
<td>NA</td>
<td>NA (NA)</td>
<td>1</td>
<td><em>Streptococcus pneumoniae</em></td>
<td>Face and neck swelling, erythema</td>
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<th>n</th>
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<th>Classification of NF</th>
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<th>Presentation</th>
<th>Outcome</th>
<th>Reference</th>
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<td>NA 18F</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>No</td>
<td>NA (NA)</td>
<td>1</td>
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<td>Streptococcus pneumonia</td>
<td>Dyspnoea, dysphagia, neck stiffness Fever, lumbar pain Thigh swelling, tenderness, pain</td>
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<td>18</td>
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<td>ART</td>
<td>CS, CYC</td>
<td>Transverse myelitis</td>
<td>No</td>
<td>NA (NA)</td>
<td>4 (8%)</td>
<td>1</td>
<td>Salmonella</td>
<td>S</td>
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<td>Alopeica, oral ulcers, photosensitivity, ART, rash, thrombopenia</td>
<td>Etodolac</td>
<td>NA</td>
<td>Yes</td>
<td>NA (NA)</td>
<td>3.7 (NA)</td>
<td>Streptococcus pneumonia</td>
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<td>S</td>
<td>13</td>
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<tr>
<td>20</td>
<td>A 35F</td>
<td>N, thrombopenia</td>
<td>CS</td>
<td>Diarrhoea</td>
<td>Yes</td>
<td>NA (NA)</td>
<td>15 (3%)</td>
<td>1</td>
<td>Salmonella</td>
<td>Fever, thigh pain, swelling and haemorrhagic bleb</td>
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<td>14</td>
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<tr>
<td>21</td>
<td>French 66F</td>
<td>Anaemia</td>
<td>AZA</td>
<td>DM</td>
<td>Yes</td>
<td>NA (NA)</td>
<td>1.8 (NA)</td>
<td>Streptococcus</td>
<td>Abdominal pain, leg swelling, haemorrhagic bleb</td>
<td>D</td>
<td>15</td>
<td></td>
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<tr>
<td>22</td>
<td>NA 40M</td>
<td>N</td>
<td>CS</td>
<td>NA</td>
<td>No</td>
<td>NA (NA)</td>
<td>2.1 (20%)</td>
<td>1–2</td>
<td>Serratia</td>
<td>Leg cellulitis</td>
<td>S</td>
<td>16</td>
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<tr>
<td>23</td>
<td>NA 46F</td>
<td>Pleuritis, ART</td>
<td>CS</td>
<td>None</td>
<td>Yes</td>
<td>NA (NA)</td>
<td>1.9 (9%)</td>
<td>Gram-positive cocci in chains</td>
<td>Thigh ecchymosis, oedema, bullae Bartholin abscess Arm pain, swelling Dysphagia, dyspnoea, trigus neck pain, oedema</td>
<td>S</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>A 21F</td>
<td>N</td>
<td>CS</td>
<td>Chronic renal failure</td>
<td>No</td>
<td>2.3</td>
<td>16 (40%)</td>
<td>Bacteroides, Morganella Salmonella</td>
<td>S</td>
<td>S</td>
<td>18</td>
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<tr>
<td>25</td>
<td>A 31F</td>
<td>N, thrombopenia</td>
<td>CS, CYC</td>
<td>DM, chronic watery diarrhoea</td>
<td>Yes</td>
<td>1.9</td>
<td>6.1 (9%)</td>
<td>1</td>
<td>Streptococcus, Staphylococcus</td>
<td>S</td>
<td>S</td>
<td>19</td>
</tr>
<tr>
<td>26</td>
<td>H 23F</td>
<td>NA</td>
<td>CS</td>
<td>Deeply carious tooth</td>
<td>No</td>
<td>NA (NA)</td>
<td>16.5 (NA)</td>
<td>2</td>
<td>Streptococcus pneumonia</td>
<td>S</td>
<td>S</td>
<td>20</td>
</tr>
<tr>
<td>27</td>
<td>NA 21M</td>
<td>N</td>
<td>CS, RTX, plasma-pheresis.</td>
<td>TTP, mesenteric vasculitis, C. difficile-associated colitis</td>
<td>No</td>
<td>NA</td>
<td>NA</td>
<td>1</td>
<td>Acinetobacter</td>
<td>S</td>
<td>S</td>
<td>21</td>
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<tr>
<td>28</td>
<td>NA 36F</td>
<td>Raynaud, APS, heart block, aseptic meningitis</td>
<td>CS, HCQ</td>
<td>Hip AVN</td>
<td>No</td>
<td>NA</td>
<td>8.2 (8.5%)</td>
<td>2</td>
<td>Streptococcus</td>
<td>Back, abdominal pain, fever</td>
<td>S</td>
<td>22</td>
</tr>
<tr>
<td>29</td>
<td>NA 14F</td>
<td>NA</td>
<td>CS, AZA</td>
<td>NA</td>
<td>No</td>
<td>NA (NA)</td>
<td>1</td>
<td>Streptococcus pneumonia Enterobacter, Enterococcus</td>
<td>S</td>
<td>S</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>A 40F</td>
<td>Photosensitivity, Raynaud, oral ulcer</td>
<td>CS, HCQ, AZA</td>
<td>Systemic sclerosis, cutaneous ulcers</td>
<td>Yes</td>
<td>NA</td>
<td>2.3 (NA)</td>
<td>1</td>
<td>Enterococcus</td>
<td>Face and neck swelling, pain, fever</td>
<td>S</td>
<td>S</td>
</tr>
</tbody>
</table>
c-reactive protein 281 mg/dL (0–5), white blood cells 15 400/µL (3000–10 000) (97% neutrophils; 1.9% lymphocytes), haemoglobin 9.6 g/dL (11.5–15.5), platelet 50 000/µL (150 000–400 000), Na 138 mmol/L (135–145), creatine kinase 474 IU/L (26–140), urea 16.8 mmol/L (1.7–8.3), alanine transaminase 384 IU/L (10–35), total bilirubin 11 mg/dL (0.3–1.9), albumin 17 g/L (34–50), creatinine 290 µmol/L (49–92) and proteinuria 2.30 g/L (0–0.10). Anticardiolipin antibodies were negative. Her C3 level was 1.0 g/L (0.65–1.65), CD19 count was 0.001/µL (0.11–0.69), and immunoglobulin G level was 9.32 g/L (7–16).

She had aggressive debridement and a diagnosis of NF was made. Cultures of muscle tissue only grew *P aeruginosa*, resistant to piperazillin-tazobactam; therefore, she was treated with meropenem, teicoplanin and clindamycin. As her clinical condition gradually improved, the antimicrobial therapy was stopped by the 2nd week. However, 1 week later, she deteriorated, with thick yellowish sputum, fever, respiratory distress and the chest X-ray showed right consolidation. Ciprofloxacin and teicoplanin were empirically started, and the patient’s clinical condition gradually improved. A week after this treatment had finished, the patient became worse with a new left lower lobe consolidation, so the antibiotic therapy was changed to ceftazidime. Her lupus flared with a marked malar rash over both cheeks, so her steroids (prednisolone) were increased to 20 mg per day and HCQ was restarted.

She was in the ICU from May to August 2012, but made a remarkable recovery and was discharged home with a steroid-tapering regimen and HCQ. Later, she developed two more SLE flares, which were treated again with CYC and RTX, achieving good response. At 18 months follow-up, there is no evidence of new recurrent or severe ongoing infections.

**DISCUSSION**

Since 1883, more than 500 cases of NF have been reported. Most patients with NF ranged from 38 years to 44 years, with a male to female ratio of 2–3 : 1, and apparently an increased incidence in African and Asian countries. The true incidence is not known (it is estimated to be approximately 0.4 cases per 100 000), with a reported mortality from 20% to as high as 80%. The causative agents of NF vary and include two main categories, polymicrobial (type 1) and infection of group A streptococcal (type 2).

Patients with SLE have an increased risk of infections, due to immunological dysfunction and the use of steroids and immunosuppressive agents. Other factors, such as the presence of a variant form of the Fc receptor are also believed to contribute to the risk of pneumococcal infection.

NF due to *Pseudomonas* has very rarely been reported. The clinical presentation of patients with NF may be deceptively benign at onset, and it may not be possible to
associated conditions have been identi
corticosteroids and 7 HCQ (22%). Additionally, use of
required, and surgical exploration should not be
anaemia, low serum albumin levels, immunosuppressive
suggests that active disease, nephropathy, lymphopenia,
most patients responded to therapy, but 8 of the 32
episode of infection: urinary, Bartholin abscess, diarrhoea,
before the admission, 9 (28%) reported a previous
albumin levels and 12 (37%) had anaemia. Interestingly,
fl

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