Rapidly fatal necrotising fasciitis caused by Streptococcus pyogenes

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Abstract

Aims—To describe the morbid anatomical and bacteriological features in a series of five cases of rapidly fatal Streptococcus pyogenes necrotising fasciitis.

Methods—Post mortem and bacteriological examinations were made of five patients dying within 48 hours from rapidly fatal necrotising fasciitis.

Results—All five cases died rapidly from a toxic Streptococcus toxin syndrome as a result of developing necrotising fasciitis following trivial injury.

Conclusions—Necrotising fasciitis caused by Streptococcus pyogenes infection can be rapidly fatal. This is probably the result of a toxic shock syndrome. Rapid, early diagnosis and swift and probably empirical treatment is required to avoid a fatal outcome.

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Subcutaneous soft tissue infections are often caused by mixed organisms. They occur principally in patients who have had surgery and those with predisposing conditions, such as diabetes mellitus or malignancy. But they can occur apparently spontaneously or after minor injury in otherwise healthy people. In most patients they have a relatively indolent course with a prolonged period of recovery.1–4 In more rapidly advancing cases it may take many days before the diagnosis is made and treatment is instigated.5 Mortalities of 30–50% have been reported.5–8 Death sometimes occurs after a prolonged illness,9,10 but often within a week. The rapid and fatal progression of streptococcal necrotising fasciitis in those not otherwise thought to be at risk is rare.

Case reports

In the five cases presented the diagnosis of Streptococcus pyogenes necrotising fasciitis was based on the appearances at post mortem examination together with definitive bacteriological identification either from antemortem culture from the infected site or blood culture or post mortem cultures from the infected site, viscera, or blood. Specimens were cultured for both anaerobic and aerobic organisms. Normal laboratory methods were used for identification, and Lancefield grouping was performed using a commercial system. Further M and T typing was not performed. Sensitivity testing was carried out on isolates. Features noted at post mortem examination were the possible portals of entry of infection, the extent of spread of the fasciitis, the presence or absence of muscle disease and whether there was evidence of disease in tissues distant to the primary site of infection.

CASE 1

A 70 year old previously healthy woman was admitted to hospital, confused and dyspnoeic, with gross oedema of the right orbit extending into the face and neck. The initial diagnosis was angioneurotic oedema. Later the skin started to blister and she had increasing respiratory distress. Single doses of flucloxacillin (500 mg) and benzylpenicillin (1 MU) were given on an empirical basis intravenously within two hours of death. She had become unwell on the day of admission and died eight hours and 35 minutes after admission (17 hours 30 minutes after the onset of symptoms).

Post mortem examination showed small scalp abrasions. Necrotising fasciitis affected the whole scalp and most of the face and neck, especially on the right side. There was a line of demarcation on the upper third of the chest anteriorly. An underlying myositis was present. The pleura showed evidence of petechial haemorrhaging. The larynx, trachea, and oesophagus were oedematous and the stomach contained bloodstained fluid. Medullary haemorrhage in the adrenals was present. Lymphadenopathy was confined to the neck nodes draining the site of infection.

CASE 2

A 71 year old previously healthy woman was seen in the accident and emergency department with a small laceration of the scalp after a fall. An x-ray picture revealed no fracture and there was no history of loss of consciousness. The laceration was sutured. She re-presented the following day with nausea, vomiting, headache and chest pain. Bruising of the face and severe oedema of the face and neck were seen. These were thought to be the result of the fall before admission. An initial diagnosis of a myocardial infarct or a pulmonary embolus was made. She was treated with oxygen and parenteral morphine. The patient’s condition rapidly deteriorated, however, with death occurring 14 hours 45 minutes after admission. No antibiotics were given.

Post mortem examination showed similar
features affecting the head and neck to those in case 1. There was a sutured laceration on the scalp. No underlying fracture was seen. The arachnoid was oedematous but the brain appeared normal. The lungs were congested and there was oedema of the larynx and trachea.

CASE 3
An 82 year old woman, while an inpatient for investigation and treatment of a macrocytic anaemia, developed a hot swollen lower left leg. A diagnosis of cellulitis or possible deep vein thrombosis was considered and oral erythromycin was given. There was no response to this and death occurred on the second day within 48 hours of onset of the swollen leg.

Post mortem examination showed oedema of both legs, mainly the left in which there was a necrotising fasciitis with overlying blistering. A sharp line of demarcation was present over the inguinal ligament. The left calf muscle showed a myositis with foci of pus. The myocardium was pale and flabby and the spleen and lungs were congested.

CASE 4
An 81 year old woman presented with an eight hour history of diarrhoea. On admission she was very confused and a small laceration was seen at the right elbow with surrounding oedema. There was a rapid decline in her clinical condition and death ensued 11 hours after admission. The only treatment given was intravenous saline and dextrose and oral chloramphenicol edisylate.

Post mortem examination showed oedema, discoloration, and blistering of the skin of the wrist, the right forearm, and the lower half of the right upper arm. Small abrasions were present on the right elbow. The infective process extended into underlying muscle and affected various muscle compartments. The heart was flabby and the myocardium had areas of softening. Infarction was not seen. Evidence of septicema was present with the spleen and lungs showing focal liquefaction.

CASE 5
A 29 year old man was admitted to hospital with severe respiratory distress and a painful swollen right thigh. A pulmonary embolus was suspected. He had pulled his right hamstring playing football and had had his thigh strapped. Following admission his condition rapidly deteriorated and he sustained respiratory and cardiac arrests. These were treated with cardiorespiratory support and appropriate drugs. He was also given large doses of benzylpenicillin on an empirical basis. No specific diagnosis was made and he died eight hours 40 minutes after admission.

Post mortem examination showed a necrotising fasciitis affecting the right thigh and upper third of the lower leg. The underlying quadriceps femoris was necrotic. No venous thromboses or pulmonary emboli were identified. A small bloodstained pericardial effusion was noted and small subendocardial haemorrhages were present. The stomach contained bloodstained fluid.

The clinical features and bacteriological investigations for all five cases are shown in table 1. All streptococcal isolates were fully sensitive to penicillin.

Discussion
Necrotising fasciitis is a progressive, usually rapid, necrotising process of subcutaneous fat, superficial fascia, and superficial deep fascia.10,11 Initially the skin is intact, but secondary gangrene follows, possibly due to thromboses in underlying vessels. Most cases occur either as a result of postoperative infection or in patients with debilitating underlying conditions including malignancies.4,12 Necrotising fasciitis has been divided into two types.13 Type I comprises infection caused by a mixture of anaerobes often with enterobacteriaceae and occasionally with facultative anaerobes (but not including *Streptococcus pyogenes*). Type II involves infections with either pure group A *Streptococcus pyogenes* infection or *Streptococcus pyogenes* with *Staphylococcus aureus*. Many cases of necrotising fasciitis are perineal in site and resemble Fournier’s gangrene.4,8

Historically, streptococcal necrotising fasciitis (streptococcal gangrene) was first extensively reported during the American Civil War. The only available treatment was
Table 2  Summary of previously reported fatal cases of streptococcal fasciitis

<table>
<thead>
<tr>
<th>Age/Sex</th>
<th>Duration of illness (days)</th>
<th>Site</th>
<th>Anaerobic blood culture</th>
<th>Predisposing conditions?</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unknown</td>
<td>7</td>
<td>Left arm</td>
<td>Positive</td>
<td>Unknown</td>
<td>15</td>
</tr>
<tr>
<td>54 M</td>
<td>22</td>
<td>Head/arm</td>
<td>Positive</td>
<td>Yes</td>
<td>14</td>
</tr>
<tr>
<td>14 M</td>
<td>19</td>
<td>Foot</td>
<td>Positive</td>
<td>Yes</td>
<td>14</td>
</tr>
<tr>
<td>37 M</td>
<td>44</td>
<td>Arm</td>
<td>Positive</td>
<td>Yes</td>
<td>14</td>
</tr>
<tr>
<td>23 M</td>
<td>9</td>
<td>Chest/abdomen</td>
<td>Negative</td>
<td>Yes</td>
<td>14</td>
</tr>
<tr>
<td>45</td>
<td>12</td>
<td></td>
<td></td>
<td>Yes</td>
<td>7</td>
</tr>
<tr>
<td>35</td>
<td>7</td>
<td></td>
<td></td>
<td>Yes</td>
<td>7</td>
</tr>
<tr>
<td>67</td>
<td>3</td>
<td></td>
<td></td>
<td>Yes</td>
<td>7</td>
</tr>
<tr>
<td>58</td>
<td>3</td>
<td></td>
<td></td>
<td>Yes</td>
<td>7</td>
</tr>
<tr>
<td>63</td>
<td>3</td>
<td></td>
<td></td>
<td>Yes</td>
<td>7</td>
</tr>
<tr>
<td>27 F</td>
<td>2</td>
<td>Left leg</td>
<td>Positive</td>
<td>Yes</td>
<td>16</td>
</tr>
<tr>
<td>1-6 F</td>
<td>5</td>
<td>Hip</td>
<td>Positive</td>
<td>Yes</td>
<td>16</td>
</tr>
<tr>
<td>53 F</td>
<td>5</td>
<td>Hip</td>
<td>Positive</td>
<td>Yes</td>
<td>16</td>
</tr>
<tr>
<td>47 M</td>
<td>5</td>
<td>Left leg</td>
<td>Positive</td>
<td>Yes</td>
<td>16</td>
</tr>
<tr>
<td>39 F</td>
<td>2</td>
<td>Left leg</td>
<td>Negative</td>
<td>No</td>
<td>17</td>
</tr>
<tr>
<td>31 M</td>
<td>15</td>
<td>Left arm/hand</td>
<td>Positive</td>
<td>No</td>
<td>17</td>
</tr>
<tr>
<td>Adult</td>
<td>&lt;1</td>
<td>Finger</td>
<td>Negative</td>
<td>Yes</td>
<td>17</td>
</tr>
<tr>
<td>46 M</td>
<td>6</td>
<td>Right arm/chest</td>
<td>Negative</td>
<td>Yes</td>
<td>18</td>
</tr>
<tr>
<td>54 M</td>
<td>2</td>
<td>Right leg</td>
<td>Positive</td>
<td>No</td>
<td>19</td>
</tr>
<tr>
<td>32 M</td>
<td>20</td>
<td>Right elbow</td>
<td>Positive</td>
<td>Unknown</td>
<td>20</td>
</tr>
<tr>
<td>48 F</td>
<td>5</td>
<td>Right hand</td>
<td>Positive</td>
<td>Unknown</td>
<td>20</td>
</tr>
<tr>
<td>77 F</td>
<td>3</td>
<td>Left elbow</td>
<td>Positive</td>
<td>No</td>
<td>5</td>
</tr>
<tr>
<td>72 M</td>
<td>&gt;2</td>
<td>Left ankle</td>
<td>Positive</td>
<td>Yes</td>
<td>5</td>
</tr>
<tr>
<td>35 M</td>
<td>8</td>
<td>Right eyelid</td>
<td>Positive</td>
<td>No</td>
<td>5</td>
</tr>
<tr>
<td>62 F</td>
<td>3</td>
<td>Right foot</td>
<td>Positive</td>
<td>Yes</td>
<td>21</td>
</tr>
<tr>
<td>39 M</td>
<td>20</td>
<td>Left leg</td>
<td>Unknown</td>
<td>Yes</td>
<td>22</td>
</tr>
<tr>
<td>57 F</td>
<td>5</td>
<td>Thigh/right iliac fossa</td>
<td>Positive</td>
<td>Yes</td>
<td>22</td>
</tr>
<tr>
<td>43 M</td>
<td>12</td>
<td>Face</td>
<td>Positive</td>
<td>Yes</td>
<td>23</td>
</tr>
</tbody>
</table>

Only two cases showed a similarly rapid course to that reported in this paper. The first case was a 39 year old woman who was dead on arrival at hospital. She had had increasing swelling in her leg for a day before she sought medical attention. The second case was a 54 year old man who presented initially with an infective myositis with overlying oedema and subcutaneous changes that may have been early necrotising fasciitis. Interestingly, neither case had recognisable predisposing conditions. These two cases and the five recorded in this paper had a rapidly fatal course with a systemic toxicamia condition in addition to the localised area of fasciitis.

Recently the concept of a toxic shock-like syndrome due to S pyogenes has been proposed. This shows features similar to those of Staphylococcus aureus toxic shock syndrome. Barter et al illustrated a generalised severe multisystem disorder with positive cultures for S pyogenes. The only cutaneous feature was a mild peeling rash akin to scarlet fever. In 20 cases described by Stevens et al with a toxic shock-like syndrome 11 had necrotising fasciitis. Six of the 20 cases (and four of the 11 necrotising fasciitis cases) died (five within 96 hours and three of these within 36 hours). It is not clear whether the fatal cases had underlying predisposing conditions. No specific T or M type was implicated and the only common factor was scarlet fever toxin A. Shaunak et al describe three cases of S pyogenes cellulitis and septic scarlet fever of which two died. These were all of a similar serotype and all had similar rashes. Erythrogenic toxins, however, were not specifically investigated.

The cases we describe had a rapidly fatal fulminating course. Deep muscle was affected without penetrating injury and there was evidence of either spread of infection away from the primary site or of systemic toxic effects. No scarlet fever-like rash was noticed in life, although at post mortem examination the fasciitic areas showed an erysipelas-like appearance with a sharply demarcated edge. This demarcation is accentuated after death, perhaps in a manner similar to the way bruises and marks of violence are often more readily identifiable at necropsy as a result of increased post mortem autolysis in the affected area.

Four of our cases had gastrointestinal features that were noted either as symptoms during life or changes at postmortem. Barter et al noted such features as frequent findings in their "toxic Strept syndrome".

Several recent reports have noted an apparent increase in virulent streptococcal infections. This increased virulence seems to be manifest as either a "toxic Strept syndrome", a fulminating rapidly progressive fasciitis, or a severe, often fatal, scarlet fever. It has been suggested that these are different host responses to either the same or very similar toxins. An alternative suggestion is that the different clinical appearances may, at least in part, be the effects of different toxins. Some reports show scarlet fever toxin A production, but others did not detect this toxin in serious S pyogenes infections.

The rapid fatal course in the cases we describe was probably caused by a toxic shock syndrome induced by S pyogenes. Such a syndrome is probably mediated by cytokines. A wide variety of such molecules have potent biological effects and the type and quantity of cytokine produced may determine clinical outcome. Both the host response and the virulence of the infecting organism may be important influences on cytokine production. The importance of these mediators of inflammation is indicated by the suggested therapeutic use of anticytokine antibodies. These alone, however, even in large doses, do not often work.

The cases we have described of fulminating streptococcal necrotising fasciitis reinforce the message that Streptococcus pyogenes can be fatal in a very short period of time. If this form of necrotising fasciitis is suspected then early aggressive treatment is essential to reduce the chances of progression to a severe toxic shock syndrome and a likely fatal outcome.


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