

CASE REPORT

Necrotising myositis: significance of early diagnosis, radical surgery and aggressive antibiotic therapy

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Abstract - Necrotising myositis is an extremely rare infection caused by *Streptococcus pyogenes*. Since the disease can mimic several other conditions, the diagnosis is often delayed.

We describe a case of necrotising myositis necessitating amputation of both legs in a previously healthy 40 year-old man. Although the use of clindamycin and immunoglobulin treatment may improve outcome, necrotising myositis is a surgical emergency.

Keywords - Necrotising myositis, streptococcal necrotising myositis, fasciitis necroticans, invasive GAS infection, streptococcal toxic shock syndrome, Meek-Wall technique

Introduction

Streptococcal necrotising myositis is an extremely rare and life-threatening soft-tissue infection. We present a case of necrotising myositis necessitating amputation of both legs of a previously healthy 40 year-old man. This case emphasizes that early diagnosis and radical surgery with aggressive antibiotic therapy are crucial for patient survival.

Case-report

A 40 year-old man with a medical history of asthmatic bronchitis presented at our emergency department with a two-day history of an acutely painful left knee despite the use of nonsteroidal anti-inflammatory drugs (NSAID). This excruciating pain was preceded by a five-day prodromal flu-like disease with malaise, pyrexia, chills and dry cough. There was no history of recent injury. The family history was non-contributory with the exception that the patient's father had survived a necrotising fasciitis many years previously.

Physical examination revealed an otherwise healthy man with a temperature of 37.9 °C. His left knee joint was painful, warm, and swollen. No skin changes were noted. Synovial fluid aspiration of the left knee yielded one millilitre of cloudy, light brown fluid. Samples were sent for urgent microscopy, which showed no crystals. The Gram stain was positive for Gram+-cocci. Laboratory studies included leucocytosis of $16.7 \times 10^9/L$ on the admission and several hours later massive elevated C-reactive protein (CRP) of 346 mg/l and creatinine phosphokinase (CK) plasma level of 28640 U/L.

Surgical joint irrigation was performed and empiric antibiotic treatment was initiated with intravenous flucloxacillin 6 dd 2000 mg and gentamicin 1 dd 400 mg. After several hours, a sepsis with

rapidly progressive multi organ failure developed and required inotropic support and mechanical ventilation.

The skin overlying his left knee rapidly became progressively erythematous. Emergency surgical exploration revealed a marked blue-purple discoloration of the muscles (Figure 1). The greyish necrotic fascia with 'dishwater' subcutaneous pus usually associated with the classical presentation of fasciitis necroticans, was notably absent. Blood cultures and muscle specimens grew group-A haemolytic *Streptococcus*. The isolate was sensitive to clindamycin. Histopathology revealed extensive myonecrosis with infiltration of polymorphonuclear cells in muscles and fascial tissue, fascia necrosis and bacterial load (Figure 2). A clinical diagnosis of streptococcal necrotising myositis with streptococcal toxic shock syndrome was made. Antibiotic therapy with intravenously administered penicillin (6 dd 2 ME), clindamycin (3 dd 900 mg) and a 5 day course of immunoglobulines (1 dd 45 gr.) was initiated.

Figure 1. First surgical exploration. There is a marked blue-purple discoloration of the muscles.



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Five hours after initial surgery he returned to the operation room for a second debridement of the left leg. There was marked, progressive erythema with skin blistering and pockets of necrosis and small pockets of pus were present in various muscle groups. Fascial planes were grey-coloured. Since the limb was deemed to be unsalvageable, an amputation was performed.

Eight hours later, during the third exploration, involvement of the right leg, with progressive muscle necrosis was seen (Figure 3). Extensive debridement of the necrotic musculature was necessary, finally resulting in a high right thigh amputation. Subsequently erythematous skin with blistering was found on post-operative examination on both arms. A small exploratory incision was therefore performed, revealing vital muscles (Figure 4).

Despite haemodynamic and respiratory support, organ dysfunction progressed to acute renal failure, requiring veno-venous hemofiltration. Over the next two weeks, inotropic support was tapered off and the patient started to wean from the ventilator (Figure 5).

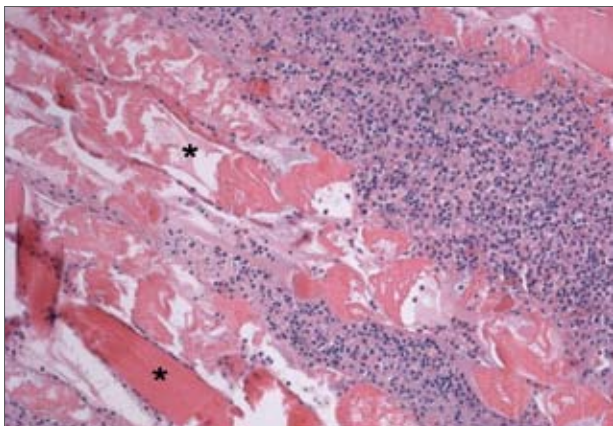
Nineteen days after admission the patient was transferred to a burn centre for skin micrografting with Meek-Wall technique (Figure 6). After three weeks the patient was successfully weaned off the ventilator and renal replacement therapy was discontinued. He remained hospitalised in a rehabilitation clinic for almost three months.

Currently, the patient is working part-time and drives an adapted car. He is able to take part in family life and participate in core social activities. Therefore, despite of his disability, the patient describes his quality of life as high.

Discussion

Group A streptococci (GAS) are common human pathogens capable of causing a broad spectrum of clinical illnesses ranging from pharyngitis and skin infections (impetigo, erysipelas and cellulitis) to invasive fatal soft-tissue infections.

Figure 2. Muscle biopsy showing massive infiltration of polymorphonuclear cells in necrotic muscle fibers. Vital striated muscle fiber (lower asterisk), necrotic muscle fiber (upper asterisk)



Streptococcal myositis primarily involves skeletal muscle, resulting in myositis and myonecrosis. This entity has the highest mortality rate of all invasive streptococcal soft-tissue infections, at least 80 % [1].

Group A streptococci (GAS) express a broad range of virulence factors including M-protein, several superantigens, proteases and adhesion proteins. M-protein protects GAS from phagocytic cells and acts as a superantigen [2]. Superantigens are proteins which possess the ability to trigger massive systemic inflammatory response through stimulation of T-cells to proliferate and to produce a large amount of cytokines [2]. These virulence factors contribute to adherence, colonisation and dissemination of invasive GAS infection.

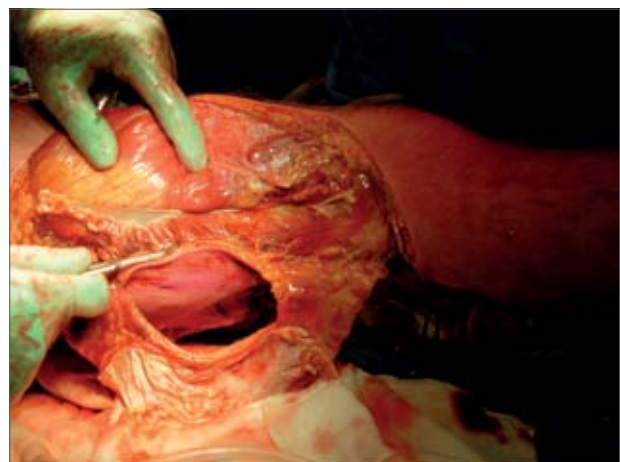
The infection likely starts spontaneously in the pharynx or the skin after a minor, nonpenetrating trauma or muscle strain [1,3]. Infecting organisms then probably reach the musculature via hematogenous spread.

Streptococcal myositis is an extremely rare soft-tissue infection. A literature review reported only 21 cases from 1900 to 1984 [1] mostly between the ages of 30 years and 60 years. A single muscle group is involved in most cases, however, because of hematogenous spread, multiple sites of myonecrosis can occur [1]. Most patients have evidence of both necrotising myositis and fasciitis [1].

Predisposing factors for streptococcal myositis include malnutrition, diabetes mellitus, and drug or alcohol abuse. The male-female ratio is equal. The role of the use of NSAIDs in the pathogenesis of necrotising fasciitis is controversial [5]. As NSAID's are commonly used as analgesics by patients suffering these painful infections, this could delay the diagnosis, but a correlation may exist between the use of NSAIDs and the development of invasive streptococcal infections [4,5].

A remarkable feature of this case is that the patient's father also suffered from severe GAS necrotising fasciitis, which presumes genetic predisposition or influence of social environment. Host susceptibility to invasive streptococcal infections and streptococcal

Figure 3. Showing discoloured muscles above the knee and wrinkled skin as a sign of epidermolysis.



toxic shock syndrome may be related to a lack of protective antibodies against M-protein and exotoxins [6]. Furthermore, the streptococcal exotoxins act as superantigens which activate T-cells by binding to human leukocyte antigen class II molecules (HLA). Increased susceptibility to invasive infections and streptococcal toxic shock syndrome may correlate with certain HLA polymorphisms [7].

Necrotising myositis often starts with early non-specific 'flu-like' symptoms like malaise and fever [3]. The pathognomonic symptom is an acute intense pain in the involved muscle compartment that is disproportional to visible skin changes. The pathogenesis of this excruciating pain is not clear, but microvascular thrombosis mediated by bacterial toxins, leading to reduced tissue perfusion, hypoxemia, and subsequent regional tissue necrosis has been proposed as a possible causative mechanism [8].

Symptoms are rapidly progressive, with escalation of pain and skin changes from erythema and swelling followed by the formation of blisters developing within hours.

Necrotising streptococcal myositis can be associated with marked systemic symptoms including septic shock, acute respiratory distress syndrome, and acute renal failure. This has been defined as a streptococcal toxic shock syndrome [9] (Table 1). Streptococcal toxic shock syndrome is a negative predictor for survival [10].

Laboratory values supporting the diagnosis are: massively elevated serum CK levels indicative of muscle damage, usually accompanied by a leucocytosis and increased serum C-reactive protein, lactic acidosis, and signs of progressive multi-organ failure [1,3].

Radiologic imaging studies such as CT or MRI can confirm the diagnosis. Swelling, oedema of the soft tissues, fat stranding or myonecrosis are usually noted.

Treatment

Surgery

Early and aggressive surgical debridement and resection are imperative in the management of necrotising myositis, since a conservative approach has proved invariably fatal [1,11].

Figure 4. Demonstrates erythematous skin with blistering and vital muscles on small incision.



During convalescence, extensive reconstructive surgery including split skin grafts, muscle flaps or, as in our case, a micrografting technique, is often necessary.

Antibiotics

Surgical therapy is complemented by a combination of penicillin G with clindamycin. Penicillin G inhibits a proliferation of *Streptococcus pyogenes* cell wall. Toxin synthesis by bacterial ribosomes is suppressed by clindamycin. Clindamycin continues to work against even the non-dividing streptococci that are immune to penicillins [12]. Furthermore, clindamycin inhibits production of M-protein, one of the major virulence factors for GAS. Combination therapy has a significant effect on outcome and appears to be superior to monotherapy with penicillin G [12,13].

Immunoglobulins

Despite prompt surgical and antimicrobial therapy, the mortality of invasive GAS and streptococcal toxic shock syndrome infection (STSS) is high. Patients with invasive GAS infection and STSS lack protective humoral immunity against M-proteins and superantigens. Adjunctive therapy has been suggested with immunoglobulins (IVIG) because of its ability to neutralise superantigens, facilitate opsonisation of streptococci and modulation of cytokine response. Several case-reports and small studies provide support for use of immunoglobulins to reduce the mortality rate and accelerate resolution of organ dysfunction [14,15].

However, there is too little evidence for clinical efficacy of immunoglobulins in invasive streptococcal infections to provide clear recommendations for use in routine clinical practice, because of low incidence of disease and slow patient recruitment in clinical trials [16]. If considered, a dosage recommendation is a single dose of 2 g/kg IVIG, with a repeated dose at 48 hours if the patient remains unstable [15]. In our case, the patient was treated with 0,4 g/kg for 5 days.

Figure 5. Skin defects are covered up with Vacuum-Assisted Closure (VAC) sponges.



Conclusion

Early diagnosis, quick decision making, surgical treatment and selection of appropriate antibiotics are crucial in treating streptococcal myositis. Combining several aggressive treatment modalities improve the chances for survival.

Figure 6. Demonstrates a situation 6 month after the amputation and Meek-Wall micrografting.



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Table 1. Case Definition for the Streptococcal Toxic Shock Syndrome⁹

I. Isolation of group A streptococci (<i>Streptococcus pyogenes</i>)	
A.	From a normally sterile site (eg, blood, cerebrospinal, pleural, or peritoneal fluid, tissue biopsy, surgical wound, etc)
B.	From a nonsterile site (eg, throat, sputum, vagina, superficial skin lesion, etc)
II. Clinical signs of severity	
A.	Hypotension defined by a systolic blood pressure less than or equal to 90 mm Hg for adults or less than the fifth percentile by age for children aged less than 16 years
B.	Multi-organ involvement characterized by two or more of the following:
1.	Renal impairment: Creatinine greater than or equal to 2 mg/dL (greater than or equal to 177 µmol/L) for adults or greater than or equal to twice the upper limit of normal for age. In patients with preexisting renal disease, a greater than twofold elevation over the baseline level.
2.	Coagulopathy: Platelets less than or equal to 100,000/mm ³ (less than or equal to 100 x 10 ⁶ /L) or disseminated intravascular coagulation, defined by prolonged clotting times, low fibrinogen level, and the presence of fibrin degradation products.
3.	Liver involvement: Alanine aminotransferase, aspartate aminotransferase, or total bilirubin levels greater than or equal to twice the upper limit of normal for the patient's age. In patients with preexisting liver disease, a greater than twofold increase over the baseline level.
4.	Acute respiratory distress syndrome: defined by acute onset of diffuse pulmonary infiltrates and hypoxemia in the absence of cardiac failure or by evidence of diffuse capillary leak manifested by acute onset of generalized edema, or pleural or peritoneal effusions with hypoalbuminemia.
5.	A generalized erythematous macular rash that may desquamate.
6.	Soft-tissue necrosis, including necrotizing fasciitis or myositis, or gangrene.

* An illness fulfilling criteria IA and II (A and B) can be defined as a definite case. An illness fulfilling criteria IB and II (A and B) can be defined as a probable case if no other etiology for the illness is identified.

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