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Time is Tissue: A Representative Case Report Highlighting the Importance of Early Clinical Diagnosis of Necrotizing Fasciitis

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INTRODUCTION

Necrotizing fasciitis is an uncommon but potentially rapidly fatal infection. The mortality rate is estimated to be 23–29%[1] and when it affects the limbs, the amputation rate is 11–14%.[1] There are 4 types of necrotizing fasciitis: Type 1 (polymicrobial in immunocompromised patients), type 2 (group A streptococcus [GAS] in healthy people), type 3 (gas gangrene due to clostridium), and type 4 (marine organisms and fungal infections). Notably, necrotizing fasciitis type 2 (NF2) associated with GAS is associated with septic shock and multiorgan failure, and therefore, early recognition and treatment are critical to a good prognosis.[2] Delays in diagnosis are unfortunately common due to the nonspecific nature of cutaneous signs and symptoms, radiological findings that lag behind the progressive and extensive soft tissue destruction, and the low frequency with which first responders and primary care and emergency medicine physicians encounter this entity.[3,4]

We report a case of NF2 that firstly benefited from early diagnosis and treatment, which resulted in a favorable outcome, and secondly demonstrated unexpected oral antibiotic failure due to a GAS M-protein variant.

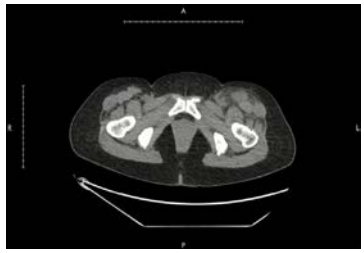
Case Report

A previously healthy 50-year-old woman presented to the emergency room with severe pain in her left thigh for 4 days, limited weight-bearing capacity, and associated fever, fatigue, general body aches, and diarrhea. The patient did not report a history of injury to the affected area, nor any observed visible changes prior to presentation. Recent past medical history was pertinent for tonsillitis approximately 10 days preceding the leg pain, empirically treated with a 7-day course of amoxicillin/clavulanate potassium. There was no microbiological confirmation of GAS with a throat swab. The patient did not report any other new medications nor any history of illicit drug use. The patient did not report any other new medications nor any history of illicit drug use.

FIGURE 1. Left thigh with minimal cutaneous changes on day 1 before the operation.

On examination, the left leg revealed minimal erythema (Figure 1) and was exquisitely tender to palpation on the medial aspect of the left thigh. The patient was initially normotensive on arrival, but suddenly developed tachycardia (120 bpm) and hypotension (79/50 mmHg). Initial labs revealed white cell count to be 17.1 K/UL and serum creatinine to be 4.6 mg/dL, though the blood cultures were negative. The presumed diagnosis was acute renal failure associated with sepsis of unknown origin, though the disproportionate soft tissue pain raised the possibility of necrotizing fasciitis. Broad-spectrum antibiotics, including vancomycin, piperacillin-tazobactam, and clindamycin were initiated. Ultrasound of the left thigh was within normal limits, and a CT scan demonstrated soft tissue edema in the anterior aspect of her left thigh (Figure 2). Surgical exploration of her thigh revealed edema localized to the sartorius muscle with no

FIGURE 2. CT scan – Left thigh on presentation with edema, no other signs of necrotizing fasciitis.



evidence of necrosis. The diagnosis of early necrotizing fasciitis was confirmed. The area was lavaged, and cultures of the site were taken, which eventually grew GAS sensitive to penicillin and cephalosporins. The wounds were left open to drain and heal by secondary intention. The patient continued to improve with IV antibiotics and was discharged with oral cefuroxime.

However, six days after discharge, the patient noticed a recurrence of the pain in her left thigh and was re-admitted. Intravenous vancomycin, clindamycin, and piperacillin-tazobactam were initiated. Repeat cultures and sensitivities in this admission confirmed GAS sensitivity to cefuroxime, which the patient took prior to this administration. The failure of the cefuroxime was ultimately attributed to GAS with a highly virulent antigenic variant M-protein. She was discharged on an additional 4 weeks of high-dose IV ceftriaxone 2 g BD and oral linezolid. On follow-up after the 4 weeks of home therapy, the episode resolved, and she continues to remain well at the time of this report.

DISCUSSION

This case highlights the importance of early diagnosis and rapid institution of broad-spectrum antibiotics to ensure a successful outcome in necrotizing fasciitis. Front-line physicians in primary care and emergency rooms need to have a high index of suspicion because the absence of clinical and diagnostic signs in the early stage of the disease can make the diagnosis difficult.[5] Investigations, such as bedside ultrasound and CT scan, can also be negative for classic signs of necrotizing fasciitis in the early stages of disease.[6] Ultimately, surgical exploration will reveal the diagnosis.

Another important issue highlighted by this case report is the potential role of the hypervariable GAS M-protein in antibiotic treatment failure. The M-protein is a surface protein of GAS that is normally attached to the cell wall. It is the key virulence factor that helps the bacteria survive in human tissues and fluids primarily by preventing phagocytosis by polymorphonuclear leukocytes, allowing the GAS bacteria to persist in infected tissues. As there are over 200 serotypes, this can lead to variable efficiency of the GAS in evading the host's immune defences.[7]

In this case, the infection responded to high-dose broad-spectrum intravenous antibiotics. However, on two occasions, there was failure of oral antibiotics to fully eradicate all the GAS bacteria, leading to the initial episode of necrotizing fasciitis following tonsillitis and the flare of the infection after the first hospital discharge. Although M-protein mutation testing was not performed, it was presumed that the GAS had an antigenic variation of M-protein, which was extremely efficient in evading host immune cell phagocytosis, given the patient had no history of immunodeficiency. Therefore, the successful treatment strategy in this case was to utilize high-dose intravenous antibiotics for a prolonged period. Other potential treatment options being investigated currently include a vaccine to the M-protein[8] and intravenous immunoglobulins.[9]

CONCLUSION

Recognizing and having a high index of suspicion of necrotizing fasciitis in the setting of febrile illness and disproportionate soft tissue pain is critical as clinical and radiological signs may be absent at this early stage. Given the rapid fulminant course of this infection, early diagnosis and intervention are key to achieving a positive outcome. Furthermore, the possibility of a highly virulent M-protein variant GAS bacteria should be considered in the setting of antibiotic treatment failure with a sensitive pathogen, and to institute prolonged high-dose antimicrobial therapy.

DISCLOSURES

The authors have no conflicts of interest to disclose.

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