Evaluation and Management of Necrotizing Soft Tissue Infections

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KEYWORDS

• Necrotizing fasciitis • Soft tissue infection • Sepsis • Gangrene

KEY POINTS

- Necrotizing soft tissue infections (NSTI) are generally severe and rapidly progressive and accompanied by sepsis, multisystem organ failure, and often death.
- Rapid recognition and early surgical intervention form the mainstay of management of NSTIs. Most cases require more than 1 debridement. Imaging can facilitate diagnosis and the decision to operate should not delay treatment in unequivocal cases; direct exploration remains the gold standard for diagnosis.
- Initial surgical debridement should be promptly performed, preferably at the presenting hospital when adequate surgical infrastructure and personnel exist. Transfer of the patient to a referral center may be necessary for definitive surgical and complex wound care.
- Broad-spectrum empiric antibiotics directed at the likely organisms are essential early in the treatment course but do not substitute surgical management. Antibiotic therapy should be subsequently tailored to the etiologic agent. In cases of documented NSTI due to group A *Streptococcus*, clindamycin should be administered in addition to penicillin.
- There are insufficient data to warrant routine use of adjuvant hyperbaric oxygen. Adjuvant intravenous immunoglobulin is an expensive intervention that is not likely to improve survival or physical quality of life and is best reserved for use on a case-by-case basis.

INTRODUCTION

Necrotizing soft tissue infections (NSTIs) are rapidly progressive skin and soft tissue infections that cause widespread tissue necrosis and are associated with systemic illness.[1] The term NSTI has been increasingly used in lieu of the term necrotizing fasciitis, originally coined by BL Wilson[2] in 1952 to encompass cases in which necrosis

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extends beyond the fascia and can involve the muscle, skin, and surrounding tissues. The incidence and prevalence of NSTIs varies by season, location, and patient population. It is known from the active surveillance operations of the Centers for Disease Control and Prevention that the incidence of NSTI due to invasive group A streptococcal (GAS) infections in the United States is 0.4 per 100,000.[3] The estimated incidence of all-cause NSTI remains less clear due to wide variability in reporting practices. Despite advances in the care, mortality from NSTI has remained relatively high at 25% to 30% for the past 30 years, and has only recently seen a decrease to just over 20%.[4–8] Case fatality rates remain highest when NSTI is accompanied by shock and/or host factors such as advanced age, comorbidities, or immunocompromised state.[1]

Necrotizing soft tissue infections can be classified based on microbiology, location, or depth of tissue involvement. Giuliano and colleagues[9] originally described 2 distinct microbiologic profiles in NSTI; however, the classification system has evolved over time with the recognition of additional pathogen classes (**Table 1**). Type 1 is the most common infection seen, and describes polymicrobial infections, often including anaerobes. Type 2 infections are monomicrobial and typically involve GAS or, less commonly, *Staphylococcus aureus*. Monomicrobial NSTI can also be caused by *Clostridium* spp and, rarely, by *Vibrio vulnificus* (from exposure to warm coastal seawater or consumption of raw oysters; classified by some as type III), *Aeromonas hydrophila* (from exposure to leech therapy or traumatic lesions in fresh water),[10] and fungi (classified by some as type IV) such as *Apophysomyces* spp. Certain monomicrobial causes have presented as local outbreaks (eg, community-associated methicillin-resistant *Staphylococcus aureus* [MRSA] in Los Angeles)[11] or exhibited geographic clustering (eg, *Klebsiella pneumoniae* among diabetic patients with NSTI in Taiwan).[12] Terminology varies by anatomic site as well. Fournier gangrene is used to describe NSTIs of the perineum, which is generally polymicrobial. Diabetic foot infections are polymicrobial and associated with an anaerobic milieu and compromised microvasculature and can sometimes progress to a necrotizing pattern. Finally, the depth of necrosis can also help classify NSTI, with necrotizing cellulitis describing an infection involving the dermis and subcutaneous tissue, necrotizing fasciitis involving the fascia, and pyomyositis or myonecrosis describing involvement of the muscle fascicle without necessarily having overlying skin infections.

PATHOPHYSIOLOGY

The vicious cycle of fulminant infection, toxin production, cytokine activation, microthrombosis and ischemia, and tissue dysfunction and death, and, in turn, greater dissemination of infection is central to the rapidly progressive necrosis seen in NSTI and differentiates it from that of uncomplicated skin and soft tissue infections (**Fig. 1**).[13] Inoculation may be related to trauma or surgery; injured skeletal muscle cells have demonstrated greater adherence to bacteria.[14] The pathogen first spreads in the tissue, releasing a variety of toxins. In the case of GAS and *S aureus*, these are exotoxins.[15] Toxins mediate an inflammatory change in the walls of the microvasculature that facilitates microvascular thrombosis. Pyrogenic exotoxins act as superantigens that bind to antigen-presenting cells and cause rapid proliferation of T cells, and, in turn, production of cytokines that perpetrate shock and multiorgan failure. This is the mechanism for development of toxic shock syndrome (TSS), which is seen with up to half of the NSTI cases due to GAS[16] and can also be seen in cases due to *S aureus*. All the clinical criteria of TSS, including macular rash and desquamation of palms and soles, are not always present, making TSS difficult to distinguish from septic shock by the bedside; the latter can be associated with all causes of NSTI.