Management of Necrotizing Soft Tissue Infection

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Case Presentation

A 50 year-old woman with history of congestive heart failure presented to the emergency room of her local community hospital complaining of progressive right elbow pain and swelling that developed after a minor fall at home 4 days prior. Her husband reported that she had profuse watery diarrhea 1 week prior, while continuing to take her home medications, which included Lasix. Since the fall, she had remained in bed with generalized weakness and poor PO intake. In the ED, her initial systolic blood pressure is 70 mmHg and the right forearm is noted to be swollen and tense, erythematous, warm and exquisitely painful to passive range of motion. Induration extends to the proximal posterior upper arm. WBC is 21, lactic acid 10.8, creatinine 11, sodium 119. She rapidly receives ceftriaxone and clindamycin, 3 L of crystalloid resuscitation and norepinephrine and vasopressin infusions are started.

The orthopedic surgeon on call takes her urgently to the operating room to treat what is strongly suspected to be a necrotizing soft tissue infection. The forearm skin is incised and the superficial volar compartment fascia released, the muscles are noted to be generally viable. No debridement is performed. A wound vacuum dressing is placed and she is transported to the ICU. Overnight, norepinephrine is discontinued, but her WBC increases to 36 and oliguria develops. She is transferred emergently to a tertiary care center, arriving in the emergency department intubated and sedated on mechanical ventilation, systolic blood pressure in the 80's despite ongoing treatment with vasopressin and sodium bicarbonate infusion for progressive metabolic acidosis (pH 7.09). Her sodium level is 131. The Gram stain from blood cultures obtained at the prior facility shows Gram positive cocci in chains.

Question What is the approach that should be applied to guide the management of this patient?

Answer Surgical source control

Norepinephrine is restarted, 3 L of lactated ringers fluid are administered immediately and additional antibiotics (vancomycin) are administered while the general surgeon on call evaluates the patient and arranges for emergent re-exploration. She is taken to the operating room where the wound vac dressing is removed. The wound is thoroughly evaluated, the incisions extended both proximally and distally to facilitate examination of the entire length of the forearm to the hand and the superficial and deep volar

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compartments to the forearm are found to be nonviable (Fig. 85.1).

The general surgeon calls an emergent intraoperative consult to the on-call hand surgeon. Together, the two identify necrotic soft tissue throughout the forearm, with gray dishwasher fluid exuding from the soft tissues. There is dead muscle in both the volar and dorsal compartments and a transition zone of viability just proximal to the elbow; the biceps, triceps, and brachialis appear normal. The two surgeons agree that the forearm cannot be salvaged. Given the degree of swelling that extends through the elbow joint, a mid-humeral amputation is performed in order to gain proximal control and arrest the progressive infection. After achieving hemostasis, the wound is not closed, but is covered with a gauze dressing soaked in Dakin's solution. The patient is transported still intubated and mechanically ventilated to the critical care unit, with blood pressure still supported by norepinephrine and vasopressin. Post-operatively, her WBC remains in the 30's and her oliguria continues. The final cultures are reported as Group A beta-hemolytic *Streptococcus*. Given her ongoing shock and leukocytosis, the patient is taken back to the operating room the following day where additional sharp debridement of the mid-humeral amputation site is performed.

The patient is extubated the following day and vasopressin is discontinued. Antibiotics are narrowed to ceftriaxone. Over the next week, her WBC normalizes, she is weaned off norepinephrine, and her acute kidney injury resolves. On hospital day 8, the amputation site is revised with a formal myodesis and skin closure. She is discharged home on hospital day 10. Eight months later, the patient was fitted for a prosthetic arm.

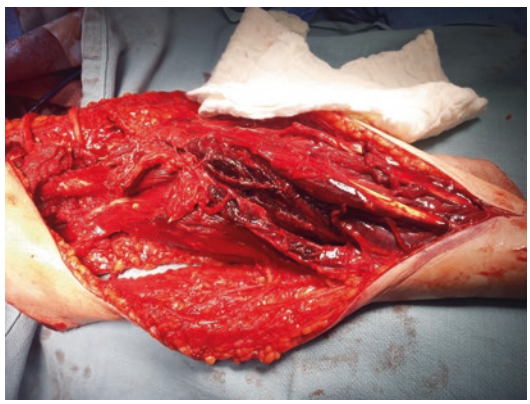

Fig. 85.1 Necrotic muscle visible in superficial and deep volar compartments to distal forearm (rightmost aspect of photo). Transition of viability is noted just below the elbow joint

Principles of Management

Rapid Diagnosis

While necrotizing soft tissue infections (NSTI) are very rare (estimated 1000 cases annually in the United States), because of the potential for rapid escalation to overwhelming septic shock with multisystem organ failure, early recognition of the possibility of necrotizing soft tissue infection is imperative. Even with optimal treatment, mortality ranges as high as 25–35 %. Unfortunately, the early signs and symptoms of NSTI can be identical to those seen with cellulitis or localized abscess. Generally, erythema, pain beyond the obvious margin of infection, swelling and fever are most common. More suggestive of NSTI are skin induration and pain disproportionate to examination findings. The most obvious "hard" clinical signs of skin bullae, ecchymosis and necrosis, cutaneous anesthesia, and gas on clinical or radiographic examination do not appear until much later in the course of the disease. NSTI can affect any region of the body, but the extremities and genito-perineal areas are most common. Inoculation of bacteria through the skin barrier is typically due to history of trauma, injection, insect bites or surgery, but may also occur via systemic dissemination from recent oropharyngeal or gastrointestinal infection.

After suspicion is established with history and physical exam features, laboratory data confirms metabolic derangement, generally with leukocytosis and other signs of acute inflammation (e.g., elevated CRP). Evidence of organ failure may be present on presentation as well, and the more deranged the laboratory values, the

higher the likelihood of a bad outcome. Radiography is seldom helpful in making the diagnosis, but computed tomography may help to define the extent of the disease on presentation. It should be recognized, however, that in the setting of high clinical suspicion, the gold standard for diagnosis of NSTI remains operative exploration *without delay*. In questionable cases, a skin incision carried down to the fascia allows evaluation of adherence of the fascia to other soft tissue layers. In classic necrotizing fasciitis, the diseased fascia is no longer adherent to the adjoining layers, allowing the surgeon to easily slide his or her finger along the fascial plane. Necrotizing adiposities or deep necrotizing myositis may also be diagnosed with local exploration for necrotic tissue.

Empiric Broad Spectrum Antibiotic Therapy and Resuscitation

Even prior to definitive diagnosis, patients with suspected NSTI should receive treatment appropriate for sepsis or septic shock, including empiric administration of broad spectrum antibiotics and fluid resuscitation. As definitive microbiology is not available until after blood and intra-operative tissue cultures are obtained, empiric antibiotics should cover Gram positive, Gram negative and anaerobic organisms. While the site and etiology of infection heavily influences the causative organism, with perineal infections tending to be polymicrobial NSTIs, antibiotics should cover both Type 1 polymicrobial infections (including *Clostridia* spp.) as well as Type 2 Group A Beta-hemolytic *Streptococcus* (GAS) infections. Type 3 infections, caused by marine organisms such as *Vibrio* spp., are more typically seen in warm-water coastal regions, or associated with the ingestion of shellfish. Empiric coverage against MRSA should be included for patients with history of colonization or recent healthcare exposure. Antibiotics may be tailored to final culture results, and generally, antibiotics are continued until operative debridement has been completed and the patient's immune response begins to resolve.

Surgical Source Control

The cornerstone of treatment for NSTI is early and wide surgical debridement of affected tissue, in order to obtain source control and arrest progression of disease. Delay from presentation to initial surgical debridement is associated with increased number of subsequent debridements and a higher incidence of septic shock and acute renal failure [1–5]. With a 24-h delay from presentation, there is an estimated ninefold increase in mortality [6]. As NSTI can continue and advance despite apparent initial adequate debridement, mandatory return to the operating room within 12–24 h is advisable in the most critically ill patients. Worsening of disease as measured by increased leukocytosis or progressive organ failure, or local spread of erythema and/or induration from the debridement site, should also prompt additional debridements until clinical improvement is established.

Evidence Contour

NSTI treatment is not without controversy. The preponderance of evidence available is from retrospective observational studies, and because of the relative rarity of this disease and its high mortality, randomized controlled trials of novel interventions are also challenging and rare.

Predicting NSTI Diagnosis and Outcome

Multiple scoring systems have been developed to facilitate diagnosis, but even the most widely used score, the laboratory risk indicator for necrotizing fasciitis (LRINEC) which uses level of C-reactive protein, white blood count, hemoglobin level, serum sodium level, serum creatinine level, and serum glucose level at admission, has never been validated prospectively [7]. While hyponatremia and extremes of WBC are also helpful in indicating severity of systematic derangement, and may portend poor outcome, these laboratory features are non-specific.

Magnetic resonance imaging has similarly been shown to be fairly sensitive, but lacks specificity as the tissue enhancement on T2-weighted imaging is frequently seen after trauma and other non-infectious inflammatory processes [8]. Finally, ultrasonography can be used to detect superficial abscesses but lacks sensitivity or specificity for NSTIs [9].

Early Amputation

The decision to perform an emergent extremity amputation is difficult, but when life-threatening infection is present, limb sacrifice may be warranted. For example, a 5-year review at our institution revealed that clostridial infection was an independent predictor for both limb loss and mortality [10]. The functional outcomes of early amputation and complex limb salvage have been demonstrated to be equivalent at 7 year follow up in a meta-analysis [11].

Adjunctive Therapies

Immunomodulatory Therapy

In infections caused by staphylococcal and streptococcal spp., exotoxins may engage the body in a especially robust immune response. Through activation of T cells, a polyclonal expansion and release of proinflammatory cytokines ensures that can lead to the combination of septic shock and multiple organ failure known as "toxic shock syndrome." While intravenous immunoglobulin has been used to neutralize antibodies against streptococcal superantigens, IVIG preparations vary, and success of its administration relies upon adequate antibodies from pooled human serum [12]. Two studies suggested a potential reduction in mortality, but these studies were limited by sample size and lack of randomization [13, 14]. A novel drug that selectively inhibits the direct binding of superantigen exotoxins to the CD28 costimulatory receptor on T-helper 1 lymphocytes was evaluated in a phase 2 randomized placebo controlled trial. This study established the drug's safety and pharmacokinetics in a population of patients with NSTI, and demonstrated promising results in decreasing the incidence of organ failure [15]. While not yet available for clinical use, the development of this therapy signals a new hope for targeting this mechanism of disease progression, and mitigation of the morbidity of NSTI.

Hyperbaric Oxygen

Hyperbaric oxygen (HBO) therapy is performed in a high-pressure chamber, resulting in delivery of oxygen at two to three times typical atmospheric pressure. This leads to substantially increased tissue oxygen tension as high as 300 mmHg, which based on animal and human studies, is thought to reduce tissue edema, stimulate fibroblast growth, increase the killing ability of leukocytes by augmenting the oxidative burst, have independent cytotoxic effects on some anaerobes, inhibit bacterial toxin elaboration and release, and enhance antibiotic efficacy. Multiple studies have examined the use of HBO in the treatment of NSTIs with mixed results. Early single-institution and small retrospective studies suggested a mortality benefit for patients with NSTI who were treated with HBO [16, 17]. Recent studies with larger sample sizes have failed to show a beneficial effect on mortality [18–20]. Due to lack of clear benefit, and to significant limitations on care delivery possible in hyperbaric chambers, HBO therapy should be limited to hemodynamically stable patients in whom HBO therapy will not delay surgical debridement.

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