Massive Infectious Soft-Tissue Injury: Diagnosis and Management of Necrotizing Fasciitis and Purpura Fulminans

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Learning Objectives: After studying the article, the participant should be able to: 1. Describe the most common bacteriology of necrotizing fasciitis and purpura fulminans. 2. Describe the “finger test” in the diagnosis of necrotizing fasciitis. 3. Discuss the three presentation patterns of necrotizing fasciitis. 4. Discuss the pathophysiology of acute infectious purpura fulminans. 5. Discuss the treatment strategies for necrotizing fasciitis and purpura fulminans, including the use of artificial skin substitutes.

Necrotizing fasciitis and purpura fulminans are two destructive processes that involve skin and soft tissues. The plastic and reconstructive surgeon may frequently be called on for assistance in the diagnosis, treatment, and/or reconstruction of patients with these conditions. Understanding the natural history and unique characteristics of these processes is essential for effective surgical management and favorable patient outcome. A comprehensive review of the literature pertaining to these two conditions is presented, outlining the different pathophysiologies, the patterns of presentation, and the treatment strategies necessary for successful management of these massive infectious soft-tissue diseases. (Plast. Reconstr. Surg. 107: 1025, 2001.)

Infections of the skin and soft tissues range from mild pyodermas to life-threatening necrotizing infections. Although most commonly caused by streptococcal and staphylococcal species, other aerobic and anaerobic bacteria have been associated with these conditions. Fungi, viruses, and atypical mycobacteria have also been implicated in soft-tissue infections, as have infestations with scabies and lice. In addition, exotoxin-mediated skin destruction has become more prevalent in the past decade as invasive, toxin-producing streptococcal, meningococcal, and staphylococcal species have become increasingly virulent. The reconstructive surgeon is frequently called on to treat patients with infectious skin destruction. Two such infectious processes, necrotizing fasciitis and purpura fulminans, will be discussed in this article. Although different in pathophysiology and presentation, the treatment goals and reconstructive efforts are similar for these massively destructive conditions.

NECROTIZING FASCIITIS

Smith et al. classified soft-tissue infections as either local or spreading, whereas Lewis further classified such infections as necrotizing or nonnecrotizing. Most local, nonnecrotizing infections start in the skin or adnexa and are easily diagnosed and treated with local measures such as drainage and antibiotic therapy. Cellulitis, the most common spreading, nonnecrotizing infection, is also managed with antibiotic therapy. The relatively uncommon local necrotizing infections, although easily diagnosed, usually require operative debridement in conjunction with antibiotic therapy. Spreading, necrotizing processes represent the hyperacute end of the spectrum of soft-tissue infections and are the subject of this article. Streptococcal gangrene, progressive bacterial synergistic gangrene (Meleney’s gangrene), Fournier’s gangrene, and synergistic necrotizing cellulitis all present with extensive skin and soft-tissue destruction requiring wide debride-
ment, long-term antibiotic therapy, treatment of multisystem dysfunction, and eventual reconstruction. Although each of these processes has unique characteristics, they are often indistinguishable on presentation and are commonly considered variations of necrotizing fasciitis. It is these infections that are often managed by the reconstructive surgeon.

Necrotizing fasciitis is characterized by widespread necrosis of the fascia and subcutaneous tissue. Although once considered a rare entity, necrotizing fasciitis became a topic of worldwide interest in the summer of 1994. At that time, necrotizing fasciitis was touted as a novel entity by the lay community, necrotizing fasciitis was elegantly described by Ambrose Paré in the fifteenth century as follows: “but there can happen no greater than a Gangrene, as that which may cause the mortification and death of the part, and oft times the whole body.” Although the pathogenesis of necrotizing fasciitis is still not completely understood, the rapid and destructive clinical course of necrotizing fasciitis is believed to be the result of multibacterial symbiosis and synergy.

It is implied from the myriad reports in the popular press that necrotizing fasciitis is a new, deadly epidemic caused by one particular bacterium, namely the group A β-hemolytic streptococcus. Historically, this organism has been the common generator of necrotizing fasciitis. These monomicrobial infections usually affect the extremities, with nearly two-thirds of cases in the lower extremities, although cases involving the face have been described. In most cases, an underlying cause such as diabetes, atherosclerotic vascular disease, or venous insufficiency with edema was present. A polymicrobial, synergistic pathogenesis was recently suggested to be more common. Polymicrobial infections are commonly associated with previous surgical procedures, penetrating trauma, decubitus ulcers, perianal abscesses, intravenous drug use, and Bartholin’s or other vulvovaginal abscesses. Our large, unpublished series of 163 consecutive patients with necrotizing fasciitis supports a more common polymicrobial cause: 71 percent of the studied patients had visible skin lesions. The early presentation is one of high fever, tachycardia, stable blood pressure, and normal sensorium. The involved skin reveals erythema, blisters, and intense pain on palpation. The intermediate presentation is similar.
but involves a worsening clinical picture, with a larger area of skin involvement, increasing number and size of skin blisters, and mild disturbances in sensorium. Patients presenting late have high fever, white blood cell counts greater than 25,000, classic skin findings of necrotizing fasciitis (edema with central patches of dusky blue discoloration, weeping blisters, and border cellulitis), systemic sepsis, shock, multisystem failure, and unconsciousness. A patient may progress through these phases with alarming rapidity. Rectal and perineal examinations are mandatory. Appropriate laboratory work-up includes complete blood counts with differential, blood chemistries, arterial blood gases, and tissue and blood cultures. Radiographic studies may be done to identify soft-tissue air. Computerized tomography scans may have utility for difficult areas, such as the abdominal wall, perineum, and neck.22

The “finger test” and rapid frozen section biopsy examinations have been used as complementary steps in the work-up of patients presenting in the early or intermediate stages.22,34 The finger test is performed in the following manner: the area of suspected involvement is infiltrated with local anesthesia. A 2-cm incision is made in the skin down to the deep fascia. Lack of bleeding is an ominous sign of a necrotizing process. On many occasions, a “murky dishwater fluid” has been noted in the wound. A gentle, probing maneuver with the index finger is performed at the level of the deep fascia. If the tissues dissect with minimal resistance, the finger test is positive. Tissue biopsies can be sent for frozen section analysis. The characteristic histologic findings include obliterator vasculitis of the subcutaneous vessels, acute inflammation, and subcutaneous tissue necrosis. If the finger test or the rapid frozen section analysis is positive or if the patient has progressive clinical findings consistent with necrotizing fasciitis, the patient should be resuscitated and taken to the operating room emergently for debridement.

Case Report

A 41-year-old man presented to an outlying hospital complaining of fever, weakness, and severe pain in his extremities 3 days after a fall. When the patient continued to deteriorate, he was transferred to our facility for further evaluation and care. On arrival, he was in florid septic shock with hypotension, a fever of 103°F, and a white blood cell count of 21,000. The diagnosis of extensive necrotizing fasciitis involving the right lower leg and bilateral upper extremities was made clinically after physical examination (Fig. 1). He was intubated in the emergency room, resuscitative efforts were begun, and he was taken emergently to surgery. Empiric broad-spectrum antibiotics were administered. Intraoperatively, the patient underwent extensive debridement of the involved areas, as dictated by the finger test and skin discoloration (Fig. 2). Immediately after surgery, he was taken to the hyperbaric oxygen tank for the first of 20 treatments. Blood cultures revealed group A β-hemolytic streptococci, and the antibiotic coverage was adjusted accordingly. The patient required hemodynamic support in the intensive care unit for several days. Over the course of several weeks, he underwent two series of skin-grafting procedures to close his massive wounds. The

Fig. 1. Extensive necrotizing fasciitis involving the (above) left upper extremity, (center) right upper extremity, and (below) right lower leg. Note the classic skin discoloration and vesicle formation. Because of the patient’s clinical condition, this would be classified as a late presentation.
patient was ultimately discharged from the hospital 3 months after his initial presentation (Fig. 3).

**PURPURA FULMINANS**

Purpura fulminans is a rare syndrome of intravascular thrombosis and hemorrhagic infarction of the skin. It is rapidly progressive and accompanied by vascular collapse and disseminated intravascular coagulation. The syndrome usually occurs in children, but it has also been reported in adults. Two age peaks, infancy and adulthood, are now recognized. Although all patients demonstrate rapid skin necrosis due to dermal thrombosis, three forms of the disease have recently been classified based on the triggering mechanism. Neonatal purpura fulminans is associated with a hereditary deficiency of the natural anticoagulants protein C and S. These vitamin-K-dependent cofactors inactivate clotting factors V and VIII and are also profibrinolytic. Affected neonates present with massive venous thrombosis of the skin and other organs within the first days of life. Purpura fulminans, in these unfortunate babies, is a cutaneous manifestation of systemic disseminated intravascular coagulation. Idiopathic or chronic purpura fulminans follows a viral illness and occurs after a variable latent period. The classic, most common form of the disease occurs superimposed on a bacterial infection and has been termed acute infectious purpura fulminans. This form of purpura fulminans has been associated with an acquired deficiency of protein C. Meningococcus and varicella are the two most common bacterial and viral triggers, although associations with Gram-negative bacilli, staphylococci, streptococci, *Rickettsia*, and measles have been made. The pathophysiologic mechanism involves a...
disturbance in the balance of procoagulant and anticoagulant endothelial cell activities. This disturbance is triggered by bacterial endotoxin and mediated by the inflammatory cytokines interleukin-12, interferon-γ, tumor necrosis factor-α, and interleukin-1, which consume proteins C and S and antithrombin III. Microemboli and direct bacterial damage to vessels have also been associated with this process.

The clinical picture of acute infectious purpura fulminans involves a premonitory illness followed by the rapid development of a septic syndrome with fever, shock, and disseminated intravascular coagulation. The skin lesions begin as petechial rashes that rapidly become large, confluent ecchymotic areas. Hemorrhagic bullae then form which, with further necrosis, form the classic hard eschars that are characteristic of the disease. Extensive tissue destruction and loss is the norm. Bilateral symmetric gangrene is also characteristic of purpura fulminans, and the need for amputation is common. In fact, some studies indicate an amputation rate of 19 percent. Sepsis, disseminated intravascular coagulation, and accompanying multisystem organ failure represent the largest impediments to survival, and mortality rates of up to 50 percent have been reported.

We recently completed a 15-year retrospective review of 28 consecutive cases of purpura fulminans at a single institution. We found that the majority of patients (82 percent) were younger than 7 years of age at the time of presentation. Twenty-five percent of the patients had premonitory upper respiratory infections before presentation. Two patients, one adult and one child, were asplenic. The only identified predisposing factors were age, absence of the spleen, recent surgery or childbirth, and upper respiratory infection. Nearly all of the patients (92 percent) presented with disseminated intravascular coagulation and skin discoloration. The most commonly involved bacteria were Neisseria meningitidis (36 percent), Haemophilus influenzae (11 percent), and Streptococcus pneumoniae (11 percent). Twenty-nine percent of patients died within 2 days of presentation. The overall rate of mortality was 43 percent.

**CASE REPORT**

A 32-year-old asplenic, 3-week postpartum white woman presented to an outlying community hospital with a history of flu-like symptoms and a blue appearance to her distal extremities. On initial presentation, the patient was in septic shock. Blood cultures revealed S. pneumoniae. The patient was transferred to our facility sedated, intubated, and supported hemodynamically with massive fluid infusions and inotropic support. The patient had extensive areas of tissue necrosis and apparently gangrenous upper and distal lower extremities (Fig. 4). Clinical history and physical examination confirmed the diagnosis of acute infectious purpura fulminans secondary to streptococcal sepsis. The patient was taken to surgery and underwent guillotine amputations of both lower extremities (Fig. 5) and the necrotic right hand (Fig. 6). All fingers on the opposite hand underwent amputation as well. The patient was critically ill with continuing sepsis and, the following day, she underwent a massive debridement of approximately 45 percent of her body surface area. She was temporarily covered with an allograft. Three days after this procedure, she underwent revision amputations of the lower extremities and secondary debridement.

The patient continued to be unstable over the next several days. To close this massive wound, we applied more than 1 m² of AlloDerm, a cadaveric, acellular dermal replacement, and ultrathin epidermal grafts (Fig. 7). AlloDerm was chosen to minimize donor site morbidity and the potential loss of precious skin. The grafts took well; however, the patient continued to be septic from other sources. The patient developed multisystem organ failure. Very surprisingly, she began to stabilize over the next several weeks. Further revision procedures were delayed due to a coagulopathy the patient developed secondary to her liver failure and many episodes of disseminated intravascular coagulation. The overall graft take was between 80 and 85 percent. The patient had many episodes of sepsis, hemodynamic instability, and cardiac arrest during the next 9 to 10 weeks. Some additional tissue loss...
required further grafting. Five months after her transfer, she was extubated. Slowly, with speech therapy and physical therapy, the patient began to respond. She was finally discharged from the hospital 9 months after her presentation. On final examination, she had 95 percent closure of all wounds (Fig. 8).

MANAGEMENT OF MASSIVE SOFT-TISSUE INJURY

Both necrotizing fasciitis and acute infectious purpura fulminans represent surgical emergencies. The large amount of necrotic tissue fuels a persistent septic state and recalcitrant hemodynamic instability. When possible, aggressive resuscitative efforts should be made; however, one may not be able to completely stabilize the patient before surgery because the delay may lead to a fatal outcome in these rapidly progressive conditions. The operative team must be aware of this natural history and plan accordingly. The anesthesiologist plays a critical role in this endeavor because continued resuscitative efforts will be made intraoperatively.

Surgery is the primary treatment for these devastating processes. Wide debridement of all obviously necrotic and poorly perfused tissues leads to more rapid overall clinical improvement. In necrotizing fasciitis, fillet-type incisions have been recommended in the past, and there has been controversy regarding how much tissue should be initially resected because the skin may often appear normal. We examined the normal-appearing tissues micro-

Fig. 5. The patient in Figure 4 is shown after guillotine below-knee amputations of necrotic legs and feet.

Fig. 6. A right-hand fasciotomy was performed, revealing complete necrosis of all deep structures. A wrist disarticulation was subsequently performed.

Fig. 7. This photograph demonstrates the application of AlloDerm followed immediately by thin epidermal autografts.

Fig. 8. The patient is shown 36 weeks after presentation. She underwent quadruple distal amputations, debridement, and reconstruction of 45 percent of her total body surface area soft-tissue loss with AlloDerm and autografts.
scopically and found they had extensive early vascular thrombosis and vasculitis, suggesting a high potential for full-thickness loss. We recommend wide, extensive debridement of all tissues that can be easily elevated off of the deep fascia with gentle finger dissection. In purpura fulminans, the demarcation between viable and nonviable tissues is more easily discernible. Deep tissues of the extremities are often involved, which require amputation to adequately debride. In both conditions, the wound must be inspected closely after the initial debridement. Hemodynamic instability usually persists postoperatively, and progressive skin necrosis may occur from infectious spread or hypoperfusion. Affected patients must be returned promptly, as often as necessary, for further debridements.10,29

We have abandoned the classic wet-to-dry dressings in favor of hydrogel for temporary wound care. Allograft or xenograft skin can be used for wound closure until the patient is satisfactorily stabilized for reconstruction. Temporary closure helps to minimize the fluid and protein loss, catabolism, and infection associated with massive open wounds. Antibiotic therapy is paramount in both necrotizing fasciitis and purpura fulminans. In the former, empiric, broad-spectrum coverage has been recommended due to the high incidence of polymicrobial infection.1,2,10,17,27,28,30–32 We use a combination of penicillin G, an aminoglycoside (if renal function permits), and clindamycin to cover streptococci, staphylococci, Gram-negative bacilli, and anaerobes. Clindamycin has been shown to decrease lipopolysaccharide production and peptidoglycan release from toxin-producing strains of Gram-positive and Gram-negative organisms and to minimize cytokine production.51,54 In purpura fulminans, broad-spectrum antibiotic coverage should be initiated to cover the most common causative organisms and then narrowed once culture results are obtained. Polymicrobial involvement is less common.

Hyperbaric oxygen in the treatment of necrotizing fasciitis has been debated.35,36 Our previous study examining hyperbaric oxygen in necrotizing infections found a trend toward increasing survival.37 In this retrospective review, we compared survival rates between 30 patients with necrotizing fasciitis who were treated with hyperbaric oxygen and 33 patients with necrotizing fasciitis who were not treated with hyperbaric oxygen. The standard treatment protocol was used in all treated patients (20 treatments of 90 minutes each at 2 atm of total pressure). There was a 16 percent mortality rate in the treated group and a 35 percent mortality rate in the untreated group ($p < 0.07$). Clark and Moon38 described their successful use of hyperbaric oxygen in life-threatening soft-tissue infections. Gonzalez24 used hyperbaric oxygen as an adjunct treatment for necrotizing fasciitis in the upper extremity. The primary use in that study, however, was for clostridial myonecrosis, where the utility of hyperbaric oxygen has been well-documented.59,61 Hyperoxemia allows for more efficient leukocyte function by providing more substrate for formation of free radicals and by augmenting respiratory burst. The effects of hyperbaric oxygen also include increased fibroblast growth, inhibition of bacterial toxin formation, increased red cell pliability, termination of lipid peroxidation, and reduction of tissue edema.62 Hyperoxia also causes increased neovascularization, which may lead to improved delivery of antibiotics to the infected areas.36 The literature seems to support the use of hyperbaric oxygen as an adjunctive treatment measure in necrotizing fasciitis. Transfer to a hyperbaric oxygen-equipped center should not, however, delay surgical intervention.

Hyperbaric oxygen has been used only rarely in purpura fulminans47,63 and has not been considered an important part of its therapy. Purpura fulminans, however, has other unique treatment considerations when compared with necrotizing fasciitis. Because deeper tissues are involved in this process, compartmental pressures may become elevated. Early literature did not advocate fasciotomy, claiming that disseminated intravascular coagulation leading to vessel thrombosis would cause muscle infarction and that fasciotomy would not alter that process. Brown and colleagues,41 however, described the positive clinical effects of fasciotomy in preventing amputation and extensive debridement. In our retrospective study, we also found an incidence of compartment syndrome (7 percent) in purpura fulminans and, along with others, we espouse an aggressive approach to compartment pressure monitoring and early fasciotomy.50,64 The use of topical nitroglycerin65,66 leeches,67 heparin,68 vitamin K,69 antithrombin III concentrate,70 streptokinase,71 dextran,72 and protein C concentrate73,74 has been described in pur-
Necrotizing fasciitis and purpura fulminans are two skin and soft-tissue infectious disease processes that frequently involve the reconstructive surgeon. Rapid diagnosis and treatment are paramount to patient survival and functional rehabilitation. The following treatment modalities are of paramount importance:

1. Prompt, aggressive surgery is the basic principle of management.

2. Frequent wound examinations and serial debridements are often necessary to halt the disease process.

3. Broad-spectrum antibiotic coverage is an important component of therapy.

4. In purpura fulminans, compartment pressures should be monitored and fasciotomy performed in threatened extremities.

5. Aggressive nutritional support, as in all critically ill patients, is essential.

6. Adjunctive hyperbaric oxygen therapy should be considered, if available, but it should not delay aggressive surgical treatment.

7. Soft-tissue reconstruction can benefit from commercially available skin and dermal substitutes. These products may allow for earlier wound closure and reduced catabolic insult.

Necrotizing fasciitis and purpura fulminans are devastating but survivable illnesses. An aggressive surgical approach is necessary in the treatment and reconstruction of these massive, infectious, soft-tissue injuries.
REFERENCES

1. A CLEARLY IDENTIFIABLE INITIATORY SKIN LESION IS ALWAYS PRESENT IN CASES OF NECROTIZING FASCIITIS.
   A) True
   B) False

2. APPROPRIATE TREATMENT STRATEGIES FOR ADVANCED NECROTIZING FASCIITIS INCLUDE ALL OF THE FOLLOWING EXCEPT:
   A) Surgical debridement
   B) Temporary wound closure with allograft
   C) Nutritional supplementation
   D) Preoperative hyperbaric oxygen treatments

3. THE MOST COMMON BACTERIUM ASSOCIATED WITH PURPURA FULMINANS IS:
   A) Group A β-hemolytic streptococcus
   B) Staphylococcus aureus
   C) Neisseria meningitidis
   D) Pseudomonas aeruginosa

4. THE MOST COMMON BACTERIUM ASSOCIATED WITH MONOMICROBIAL NECROTIZING FASCIITIS IS:
   A) Group A β-hemolytic streptococcus
   B) Staphylococcus aureus
   C) Neisseria meningitidis
   D) Pseudomonas aeruginosa
   E) Escherichia coli

5. WHICH OF THE FOLLOWING ANTIBIOTICS USED IN NECROTIZING FASCIITIS IS DIRECTED TOWARD TOXIN PRODUCTION?
   A) Penicillin G
   B) Azactam
   C) Gentamicin
   D) Metronidazole
   E) Clindamycin

6. EFFECTS OF HYPERBARIC OXYGEN INCLUDE ALL OF THE FOLLOWING EXCEPT:
   A) Elimination of free radicals
   B) Fibroblast proliferation
   C) Reduced tissue edema
   D) Decreased endotoxin production

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