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Necrotizing Infection of the Perineum

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Spontaneous gangrene of the scrotum was described for the first time in 1753 by Boerhaave,[1] who reported on a 40-year-old man with urinary retention. Since that time, several authors have reported similar cases of spontaneous gangrene of the scrotum and penis with associated diseases such as systemic infections, diabetes, urinary extravasations and infiltration, trauma to the perineal area, and inflammatory processes involving the genitalia. In 1883–84, Fournier reported 1 similar case and discussed 4 others from his own experience, all of whom did not have any known risk factor or associated diseases.[2–4] In his landmark paper,[2] he then established the 3 criteria of what became known as Fournier's gangrene:[1] abrupt onset of penile or scrotal gangrene in previously healthy young male patients;[2] rapid progression to fulminating gangrene; and absence of identifiable causes.[3] The first and third criteria were quickly dropped among authors reporting such cases, and the second criterion, namely the rapid progression to fulminating gangrene, became a landmark diagnostic clue. Gangrene starts anywhere in the perineum but progresses to involve the scrotum and penis. The concept of male predilection was broken in 1927 when Narducci[5] reported on a female patient with fulminating gangrene involving the external genitalia. This diversion from Fournier's main definition created confusion in the literature about the name, diagnosis, and treatment of this disease. This article reviews the diagnosis and treatment of Fournier's gangrene in the context of a representative case that illustrates clinical aspects of the disease process.

TAKE HOME POINTS

- Early recognition and therapy are essential for best outcome.
- Expedited resuscitation is necessary to maintain adequate perfusion, and steps should be taken to control hyperglycemia while an operating room is being prepared.
- Blood products should be prepared in anticipation of blood loss during surgery.
- Broad-spectrum antibiotics with methicillin-resistant *Staphylococcus aureus* coverage should be administered initially and targeted to culture-specific organisms later.
- Radical débridement of all necrotic tissues is the mainstay of therapy and must be done expeditiously. Re-débridement is performed as often as necessary to control the spread of infection.
- Fecal and urinary diversion are used selectively.

CASE PRESENTATION

A 52-year-old man presented with a 3-day history of scrotal pain and swelling and the rapid development of necrotic, black lesions on the scrotum, penis, and perineal region (**Figure 1**). There was no history of similar symptoms. The patient denied recent trauma. He had no nausea, vomiting, diarrhea, constipation, abdominal pain, melena, or hematochezia. He also denied dysuria, urgency, and frequency. He was in a monogamous relationship and had no history of sexually transmitted diseases.

The patient's medical history was positive only for type 2 diabetes, which was treated with metformin but poorly controlled. He had no allergies and took no other medications. He reported alcohol abuse for the past 15 years and smoking 2 packs of cigarettes per day during the past 35 years. The patient's family history was noncontributory.

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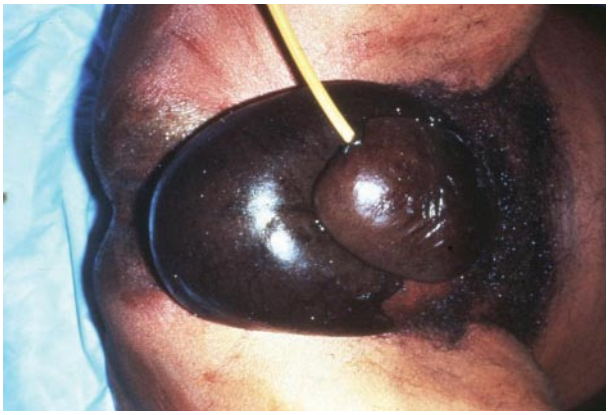

Figure 1. Black discoloration of penile, scrotal, and perineal skin in a patient with necrotizing infection of the perineum. There is also erythema, edema, and severe tenderness over the lower abdomen.

ETIOLOGY

Clinical experience gained over the years confirms the changing etiology of Fournier's gangrene. Although the French venereologist was the first to clearly define this entity, confusion mainly relating to etiology continued to persist. Fournier's gangrene was once thought to be completely idiopathic; however, 103 patients out of 219 (47%) reported during the first 50 years after Fournier's original description were found to have an associated condition or risk factor. In the next 50 years, the proportion with an associated condition increased to 153 out of 186 reported patients (82%). This better detection of an associated condition or risk factor is ascribed by Sharifi et al[6] to the use of more thorough investigative procedures with time. According to Jones et al,[7] it is likely that a source can be identified in most of the idiopathic cases if the patient comes to medical attention early enough and receives the appropriate diagnostic measures.

Patients with a systemic disease such as diabetes or those who are alcoholics are more frequently affected by Fournier's gangrene. It is reported that 32% to 60% of patients with Fournier's gangrene have diabetes and 25% to 66% of them suffer from alcoholism.[8,9] Malnutrition seen in patients with alcoholism can lead to a lack of nutrients and critical enzymatic cofactors involved in the normal cellular response to infection. Other significant risk factors are chronic debilitation and immunosuppression secondary to transplantation, chemotherapy, or HIV infection.[8,9] Another mechanism proposed in the pathophysiology of this disease is that reduced oxygen tension allows pathogens to proliferate. Small vessel disease as seen with diabetes impairs the local blood and oxygen supply. Patients with chronic pulmonary disease have systemic hypoxemia, and those with congestive heart failure or coronary artery disease may be unable to increase their cardiac output in response to infection. In addition, diabetes mellitus inhibits white blood cell function. Each of these patient factors impairs the host response and increases the chances for the development and progression of infection.

As many as 20% of necrotizing soft tissue infections are idiopathic and occur in previously healthy patients who have no predisposing factors and no known portal of entry for infection.[10] Upon careful investigation, a rectal, dermal, or urinary source can often be detected.[9] Presence of anorectal pain, bleeding, a history of anal fissures, anorectal procedures (eg, dilatation, hemorrhoid banding), or rectal perforation from instrumentation usually indicate an anorectal source. Dermal sources are suggested by acute or chronic infections of the scrotum, a recent episiotomy in females, hidradenitis, or balanitis. Dysuria, urethral discharge, recent urinary catheterization or other manipulations of the urinary tract as well as urethral stricture usually point to a urinary source. The most common predisposing conditions are urethral strictures and perirectal abscesses.[11]

CASE CONTINUED

Physical examination showed an ill-appearing man in distress. His vital signs included blood pressure of 105/67 mm Hg, heart rate of 110 bpm, respiratory rate of 13 breaths/min, and temperature of 101.7°F. He was 5'6" and weighed 137 lb. Examination of his head, eyes, ears, nose, and throat was normal. Lungs were clear. The patient was tachycardic with a normal S_1 and S_2 with no murmurs or gallops and no rub. Abdomen was nontender and not distended with normal bowel sounds. He had no edema, and pulses were normal bilaterally in his lower extremities.

Perineal examination revealed the skin of the entire scrotum and perineal area to be gangrenous and necrotic, and there was severe tenderness and no crepitus. There were multiple areas of hemorrhagic necrosis involving almost the entire scrotum. His testicles were normal in size and contour and were nontender. The inguinal area was swollen and erythematous bilaterally (Figure 1).

DIAGNOSIS

The majority of patients present with an acute, rapidly progressive illness and signs of systemic toxicity, and only a few have a more indolent, slowly progressive

form of infection. The following symptoms are often characteristic of patients with Fournier's gangrene: genital swelling, erythema, tenderness beyond the area of erythema, and cutaneous anesthesia. These symptoms are frequently accompanied by fever and systemic toxicity. Crepitus is noted in only 30% of patients with necrotizing tissue infections. Tenderness beyond the borders of the erythematous area is an extremely important clinical sign as it indicates progression of the infection in the deeper layers underneath the skin. Early skin changes may be minimal despite extensive necrosis of the subcutaneous tissue and fascia. Often these changes are not clear, and the diagnosis may not be obvious. Being aware that initial skin findings may be limited is important for making a quick diagnosis, preventing progression, and instituting appropriate treatment.[12]

CASE CONTINUED

The patient's perirectal area was erythematous, but there was no evidence of fissures, fistulae, or external or internal hemorrhoids. Rectal examination did not reveal undue tenderness, a perirectal abscess, abnormalities in the prostate, or masses in the anal canal or rectum. Laboratory data included normal hemoglobin and hematocrit but a markedly elevated white blood cell count to 35,000,000/μL. His chemistry 7 panel was also normal except for a decreased sodium level of 125 mEq/L and an elevated glucose level of 310 mg/dL. His hemoglobin A_{1c} concentration was 12.7% with a glycosylated hemoglobin of 17.5%.

MICROBIOLOGY

Necrotizing infection of the perineum is polymicrobial 70% to 75% of the time (**Table 1**).[13,14] *Staphylococcus aureus*, *Streptococcus pyogenes*, and enterococci are the most common gram-positive aerobes. *Escherichia coli* is the most common gram-negative organism. The most common anaerobes are *Bacteroides* species and peptostreptococci.[14–17] The remaining 25% to 30% of deep necrotizing infections are monomicrobial.[18] These infections are fulminant and are notable for their acute onset, rapid progression, and systemic toxicity. *S. pyogenes* is the causative pathogen in more that half of the monomicrobial infections. *S. aureus*, *Clostridium perfringens*, *Vibrio vulnificus*, and *Pseudomonas aeruginosa* are less common. *S. aureus* has been an uncommon monomicrobial cause of necrotizing fasciitis, but recently there has been an increase in the number of these infections caused by community-associated methicillin-resistant *S. aureus* (MRSA).[19]

The exotoxins produced by gram-positive cocci and some gram-negative bacteria are powerful proteolytic enzymes. *S. pyogenes* produces hemolysins, fibrinolysins, hyaluronidases, and streptolysin. *S. aureus* and *P. aeruginosa* produce coagulases that result in local tissue damage and necrosis. *C. perfringens* produces numerous exotoxins that cause hemolysis, alter capillary permeability, and have a direct cardiotoxic effect.

Infection starts locally at the portal of entry. The inflammation then spreads to the deep fascial planes and results in obliterative endarteritis. This is followed by a cascade of cutaneous and subcutaneous vascular necrosis, local ischemia, and tissue necrosis as well as hypoxia-driven proliferation of anaerobic organisms.[8] These anaerobes elaborate additional enzymes and other coproducts that facilitate tissue invasion and destruction.

Table 1. Organisms Causing Necrotizing Soft Tissue Infection

Aerobes	
Gram-positive	Gram-negative
Group A streptococcus	*Escherichia coli*
Enterococcus species	*Pseudomonas aeruginosa*
Staphylococcus aureus	*Enterobacter cloacae*
Group B streptococcus	*Klebsiella* species
Bacillus species	*Serratia* species
	Acinetobacter calcoaceticus
	Vibrio vulnificus
Anaerobes	
Bacteroides species	
Clostridium species	
Peptostreptococcus species	

Adapted with permission from Malangoni MA, McHenry CR. 3 Breast, skin and soft tissue, 2 soft tissue infection. ACS Surgery Online. New York: WebMD Inc.; 2000.

MEDICAL THERAPY

Having established the diagnosis of Fournier's gangrene, treatment should be instituted immediately. The patient should be resuscitated with intravenous fluids, started on broad-spectrum intravenous antibiotics, and managed properly for pain. Optimizing glycemic control in diabetic patients is crucial to improve clinical outcomes.[20] In this patient with a blood glucose of 310 mg/dL, an insulin drip should be started in the intensive care unit while monitoring levels of electrolytes, especially potassium.[21]

The mainstay of cardiovascular resuscitation is administration of intravenous fluids to increase circulating blood volume, cardiac preload, cardiac output, and systemic oxygen delivery. Lactic acidosis generally responds to administration of fluids. Blood urea nitrogen, urine output, and serum creatinine concentrations are the

Table 2. Intravenous Antibiotic Dosage for Adult Patients with Necrotizing Soft Tissue Infection and Normal Renal Function

Single agents	
Ampicillin-sulbactam	3 g every 6 hr
Imipenem-cilastatin	500–1000 mg every 6 hr
Meropenem	1 g every 8 hr
Piperacillin-tazobactam	3.375 g every 6 hr
Ticarcillin-clavulanate	3.1 g every 6 hr
Agents used in combination regimens	
Aerobic/facultative coverage	
Ampicillin	2 g every 6 hr
Cefotaxime	1–2 g every 8 hr
Ceftazidime	1g every 8 hr
Cefuroxime	1.5 g every 8 hr
Ciprofloxacin	400 mg every 12 hr
Gentamicin	1.7 mg/kg every 8 hr
Vancomycin	1 g every 12 hr
Anaerobic coverage	
Clindamycin	900 mg every 8 hr
Metronidazol	500 mg every 6 hr

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most common criteria for renal function assessment. Myoglobinuria and elevated creatine kinase levels are clear signs of myonecrosis. Patients presenting with anemia should receive packed red blood cell transfusions. Patients with traumatic wounds or other contaminated sites should be immunized with tetanus toxoid or human tetanus immunoglobulin, depending on the patient's immunization status.

Empiric antibiotic therapy in Fournier's gangrene should target the polymicrobial nature of the infection (**Table 2**).[22,23] However, antibiotic therapy is no substitute for prompt and adequate operative débridement. Antibiotic therapy should be adjusted based on the results of intraoperative culture and antimicrobial sensitivity testing. Intravenous antibiotic therapy is continued until operative débridement is complete and there is no further evidence of infection in the involved tissues or signs of systemic toxicity. When patients are able to resume oral intake, they can be switched to oral antimicrobial therapy.[12] With the increasing rates of MRSA skin and soft tissue infections and the recent report of necrotizing perineal myofasciitis caused by MRSA, empiric therapy should now include vancomycin.[19]

The role of hyperbaric oxygen in the treatment of necrotizing fasciitis remains controversial. Authors have advocated its use in addition to operative débridement in order to improve outcome. The principle behind its use is to increase the tissue oxygen tension in hypoxic areas. This prevents extension of the disease and the need for further débridements.[24] On the other hand, others have shown no survival benefit.[25] Further studies therefore are required before this treatment can be definitely recommended.

CASE CONTINUED

In this patient, the diagnosis of Fournier's gangrene was established by the surgical team in the emergency department. A Foley catheter was carefully inserted while checking to rule out a urethral disruption. An abdominal radiograph was performed to evaluate for subcutaneous air and its extent in the abdominal wall. The patient was transferred to the intensive care unit where resuscitation was started with normal saline. Antibiotic therapy consisting of piperacillin, tazobactam, and vancomycin was started. An intravenous insulin drip was initiated concurrently. As soon as the operating room team was ready, the patient was expeditiously moved to the operating room for débridement.

SURGICAL THERAPY

Surgeons should make incisions down to the deep fascia looking for dead tissue and the characteristic "murky dishwater fluid." All nonviable tissue, including fascia, should be débrided. Arterial bleeding usually is indicative of tissue viability. It is best to preserve as much viable skin and subcutaneous tissue as possible as these tissues will be essential for later coverage of the wound. Wound exudates and necrotic tissue should be submitted for Gram stain as well as for aerobic, anaerobic, and fungal cultures and sensitivity testing.[12] If the tissues dissect with minimal resistance, this again favors the diagnosis and the need for additional débridement. Significant blood loss during these extensive débridements is not uncommon, especially if the patient develops systemic intravascular coagulopathy. It is essential to have blood products available.

Further surgical exploration 24 to 48 hours later is necessary to ensure that the infectious process has not progressed. Further débridement should be performed as necessary.[11] The testicles are usually spared because of their independent blood supply, although in rare instances they might be affected as well.[8] The role of suprapubic cystostomy is unclear. If the urethra is disrupted as in obstructive lesions, a suprapubic cystostomy may be necessary. In cases where the infection arises from an anorectal source and especially in cases

where débridement of the anal sphincter muscles is necessary, a diverting colostomy is required. Overall, this measure is required in 25% of cases and facilitates wound care postoperatively.[15]

After débridement, the exposed areas should be treated with 0.9% normal saline wet-to-dry dressings. Early enteral or parenteral nutritional support is essential to support a highly catabolic state.

CASE CONTINUED

All necrotic skin, subcutaneous tissue, fascia, and nonviable muscle were débrided (**Figure 2**) and sent for histologic and microbiologic examination. Viable dermis and soft tissue were preserved to facilitate later closure. To prevent wound problems from fecal soilage, a diverting colostomy was performed. The wounds were then dressed loosely with gauze moistened with saline. After initial débridement, the patient was transferred to the intensive care unit. Invasive monitoring, pain management, fluid therapy, and inotropic support were necessary. Piperacillin/tazobactam was continued while vancomycin therapy was stopped based on culture results. Packed red blood cell transfusion was necessary, and enteral nutrition was started through a dobhoff tube. The patient remained intubated as he required 2 additional débridements in the operating room and daily minor débridements at the bedside.

RECONSTRUCTION

Surgical reconstruction has been advocated to shorten the time of hospitalization, hasten healing, and bring on a more esthetic result. Reconstructive operations should be considered only once the patient has been stabilized and the infection fully eradicated.

If part of the scrotum was débrided, the remaining scrotal tissue can be mobilized and approximated for coverage of the testicles.[26] Split thickness skin grafts should be placed over the remaining area of the wound. If the whole scrotum is lost, several techniques might be used to cover the testicles or reconstruct the scrotum. To cover the testicles, subcutaneous pockets have to be created, most commonly in the anteromedial aspect of each thigh.[27] Alternatively, a rotating flap from each thigh can be used, followed later by detachment of the flaps, remodeling, and suturing around the testes[28,29] or by using bilateral musculocutaneous gracilis flaps that are laid over the testes and cords and sutured together.[30,31] Reconstruction of the scrotum using a flap of penile skin that is distally based and split in the middle also has been described.[32]

Several methods also can be used in the reconstruction of the penis. In uncircumcised males in whom the prepuce is available, a modified circumcision should be performed and a preputial flap based on the frenular vessels is used to cover the bare area followed later by disconnection of the vascular pedicle.[33] Rotation flaps from the scrotum or suprapubic region as well as split thickness grafts to reconstruct the whole penis have been described.[31,34] Other types of reconstruction that can be considered include embedding of the penis in the anterior abdominal wall under a rectangular flap followed by detaching the flap and wrapping it around the penis,[29] or a Cecil repair in which the penis is burrowed into the scrotal skin. Some authors have used fresh frozen porcine xenografts to protect bare débrided areas in preparation for permanent autogenous skin or rotating flap grafting.[30,35]

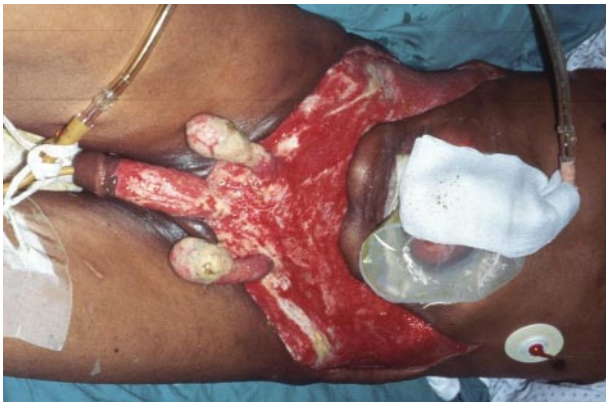

Figure 2. Extensive débridement of the scrotum, penis, perineum, and lower abdomen were performed. A sigmoid loop colostomy was also created.

CASE CONCLUSION

The patient's extensive wound was initially packed, with the intention to close it later by means of skin grafting. To cover the testicles, subcutaneous pockets were created in the anteromedial part of each thigh (**Figure 3**). Later, split thickness skin grafts were placed over the remaining areas of the wound. To reconstruct the scrotum, a rotating flap from each thigh was used followed by detachment of the flaps, remodeling, and suturing around the testes. Rotation flaps from the suprapubic region were used as well as split thickness grafts to reconstruct the whole penis. Spermatogenesis as evidenced by sperm count was normal.

LONG-TERM COMPLICATIONS

The fate of cured patients was unknown in most reports since follow-up was rarely given. In one series,[36] complications of this disease included scrotal deformity, penile deformity, urethral fistula, skin depigmentation,

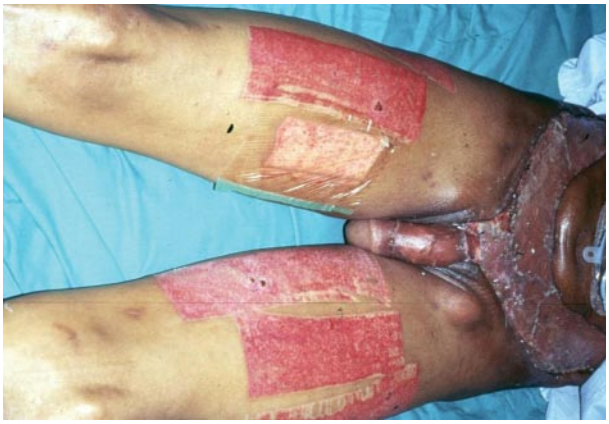

Figure 3. The testicles were lodged in subcutaneous pockets in the anteromedial aspect of each thigh. Split thickness skin grafts from the thighs were used to cover the penis and lower abdomen.

transient painful erection, and toxemia, each occurring in 4% of patients. A transient postinfective impotence was reported in another 8% of patients. The most common complications were anxiety neuroses occurring in 24% of patients. In this same report,[36] semen analyses were carried out in 23 patients. Sixteen had sperm counts of 20×10^6/mL or less with reduced sperm motility. However, 13 of 16 patients had counts above 20×10^6/mL 24 weeks later and the motility had risen appreciably. With serious scrotal or shaft lesions, the counts remained low at 24 weeks. Seven patients had initial counts of 21×10^6/mL or above and maintained these levels. Half of these patients had conservative surgical therapy, while 13 had more radical surgery with reconstructive procedures. In another report, semen analyses were done in 3 cases 4 months after the onset of the disease.[32] There was persistent azoospermia in 1 case and oligospermia in 2 cases. Despite the gradual improvement of sperm count over a period of 4 years, the latter cases still remain infertile. Testicular biopsy in all 3 cases done 4 months after the onset of the disease revealed moderate to severe hypospermatogenesis. Hormonal assays revealed suppression of serum follicle-stimulating hormone and testosterone. All 3 cases had radical surgical débridement and skin grafting.[32]

CONCLUSION

Mortality in patients with Fournier's gangrene is approximately 16%[10] and has not improved much since the original description of this disease. Some of the reasons are the more complicated patient population and the increased average age of patients at diagnosis.[37] The diagnosis of Fournier's gangrene is clinical. The disease has a predilection for patients with diabetes, alcoholism, and nonobvious immune compromise. Interestingly, compared with other patients with this disease, patients with diabetes are not at increased risk of death despite being the highest risk group for developing Fournier's gangrene. However, mortality is increased with age, greater extent of the disease, positive blood cultures, anorectal sources, and renal or hepatic insufficiencies.[9,10] Community-associated MRSA has the potential to cause rapidly progressive disease that is clinically indistinguishable from cases caused by pathogens such as group A streptococcus. Early recognition and surgical débridement of all nonviable tissue have reduced mortality. The role of hyperbaric oxygen therapy in the treatment course of this disease remains unclear. Reconstructive surgical treatment improves outcome and gives acceptable esthetic results. **HP**

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