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Presentation and Diagnosis of Fournier's Gangrene

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Abstract

Necrotizing fasciitis is a severe type of necrotizing soft tissue infection involving the superficial fascia and subcutaneous tissues. Fournier's gangrene, a type of necrotizing fasciitis, affects the genitalia and/or perineum. While a rare health condition, Fournier's gangrene can result in significant morbidity and unnecessary mortality following delay in diagnosis and management. We provide a review of relevant presenting features to aid diagnosis and allow timely surgical management of this serious infectious condition.

Introduction

Necrotizing soft tissue infections (NSTIs) can involve any layer of the soft tissues in the form of fasciitis, cellulitis or myositis, and they are characterized by widespread soft tissue necrosis, systemic toxicity, and possible mortality. Necrotizing fasciitis is a severe form of NSTI that affects the superficial fascia and subcutaneous tissues. Necrotizing fasciitis of the perineal, genital, and/or anorectal region was originally termed Fournier's gangrene after Jean-Alfred Fournier, a Parisian dermatologist who published about the necrotizing infection in 1877[1]; however, the disease was first described by Baurienne in 1764[2]. His original description of the infection was that it (1) affected healthy, young men, (2) resulted in a rapid progression to gangrene, and (3) was idiopathic. The term 'necrotizing fasciitis' was later introduced by Wilson in 1952 as a means to describe the pathognomonic necrosis of the skin fascia that is the hallmark of Fournier's gangrene[3].

Joseph Jones, a Confederate army surgeon was the first person to describe the mortality of Fournier's gangrene among a large population of men[4]. In 1871, he reported a mortality rate of 46% among 2,642 affected Civil War soldiers. In 2000, Eke published a review of 1726 published cases from 1950-1999 and noted the mortality to be 16%[5]. A population-based analysis of the epidemiology of Fournier's gangrene was performed in 2009 using the United States State Inpatient Database and noted the mortality rate to be lower[6]. Among 25 million hospital admissions from 2001 and 2004, Fournier's gangrene constituted only 0.02% of hospital admissions with a 7.5% case fatality rate. Interestingly, 66% of the hospitals in the State Inpatient Database reported no patients

with Fournier's gangrene, and among high volume centers, the admission frequency was only one patient every few months. The overall case fatality rate from these national databases mirrors our NSTI experience in the state of Washington from 2007-2013, where we noted a 6.7% case fatality rate[7].

Based on the rarity of Fournier's gangrene, this manuscript will serve as a review of the presentation and diagnosis of Fournier's gangrene. For those seeking additional information regarding management of Fournier's gangrene, the European Urological Association published guidelines for urological infections in 2013 (https://uroweb.org/wp-content/uploads/18_Urological-infections_LR.pdf; accessed 10/23/2017). A care pathway for Fournier's gangrene was provided (Figure 1).

PRESENTATION

Anatomy

Understanding the fascial anatomy allows a better understanding of how necrotizing soft tissue infections that originate in the urogenital or anogenital region (i.e., Fournier's gangrene) can spread to the abdomen, chest, and flank. Fournier's gangrene spreads across the superficial and deep fascial planes of the urogenital and anogenital region. Infection of the deep tissues results in vascular occlusion, ischemia, and tissue necrosis. The hypoxia will consequently cause infarction of the nerves that initially is painful and eventually leads to localized anesthesia[8]. It is important to note, that the superficial skin is initially spared from the infection while the necrotizing process spreads along the fascial planes, making the extent of the disease difficult to visualize.

Colles fascia is located in the perineum and is attached to the ischiopubic rami. It is continuous with Dartos fascia of the penis/scrotum and Scarpa's fascia of the anterior abdomen/thorax. These fascial planes (Colles, Dartos, and Scarpa's) are in continuity with one another allowing infections to spread in a rapid manner. Of note, the external and internal spermatic fascia and blood vessels from the retroperitoneum, that are independent of the vascular supply of the urogenital/anogenital region, protect the testicles from infectious involvement. Similarly, the deep fascia (Buck's fascia) that envelops the urethra and corpora cavernosa provides additional protection from the spread of Fournier's gangrene.

Demographics

The proportional difference in male:females can vary significantly across the published literature. For example, an analysis of over 25 million patients from the State Inpatient Database identified 1641 male patients and only 39 female patients with Fournier's gangrene (i.e., of those with Fournier's, only 2% were female)[6]. In contradistinction, researchers using the National Surgical Quality Improvement Program noted a much higher male: female ratio of 57%:43%[9]. A theorized difference for their finding is that the latter study relied on CPT codes for 'debridement of skin, subcutaneous tissue, muscle, and fascia' (code 11004, 11006) to identify NSTI patients, which could result in inclusion of other soft tissue infections such as necrotizing myositis and cellulitis. The former study relied on the ICD-9 diagnosis of Fournier's gangrene for patient selection, which is more specific.

Systematic review of published case reports may provide a truer assessment of male: female ratio. A PubMed review of Fournier's gangrene between 1981-2011 that excluded reports with < 30 patients identified 22 manuscripts and a total of 2656 diagnoses[10]. Men were overwhelmingly affected (mean 84%, range 52-100%). Further, most affected individuals were older, as the mean age across the accepted case studies was 51.8 years old (range 47-63).

Risk Factors

While Fournier originally believed that classic presentation was idiopathic, research has proved that there is often an etiology for development of Fournier's gangrene. Between 52%-88% of patients will have at least one co-morbid condition thought to contribute to the development of Fournier's gangrene[11-13]. These comorbidities have similar impairments in microcirculation and/or immunosuppression. Diabetes is the most commonly attributed risk factor (27%-60%)[14-16]. Hypertension, obesity (BMI > 30), congestive heart failure, tobacco use, immunosuppressive conditions, peripheral vascular disease, and alcoholism have also been associated with an increased risk of Fournier's gangrene[6,11-16].

Etiology

Fournier's gangrene is most commonly due to genital/anorectal abscess, pressure sores, or surgical site infections; however, it can also commonly occur following chronic urethral catheterization, urethral instrumentation, genital/anorectal trauma, or genital

shaving[11]. Patients with spinal cord injuries can be particularly susceptible to Fournier's gangrene as a consequence of pressure sores and/or chronic urethral catheterization[17]. Finally, Fournier's gangrene can develop following treatment for urethral, bladder, or rectal cancer therapy[16,18]. In women, Fournier's gangrene has been attributed to Bartholin's duct abscesses or skin infections of the vulva[19].

Microbiology

Fournier's gangrene most commonly presents as a polymicrobial infection[10]. The reported range falls somewhere between 54-80%. The most common pathogen to be isolated is *E. coli*; however, other organisms reported to be present include: *Streptococcus*, *Bacteroides*, *Enterobacter*, *Staphylococcus*, *Enterococcus*, *Pseudomonas*, *Corynebacterium*, *Klebsiella pneumonia*, and *Candida albicans*[10,11]. More recently resistant strains of bacteria, such as methicillin-resistant *Staphylococcus aureus,* as well as extended-spectrum beta-lactamase *Escherichia coli* have been identified as etiologic agents[18,20].

DIAGNOSIS

Necrotizing soft tissue is the most important component of Fournier's gangrene. These infections are characterized a high morbidity/mortality; therefore, a high index of suspicion is paramount. Often clinical findings and the patient's medical condition can facilitate accurate diagnosis; however, laboratory tests and radiographic technology can augment the early diagnosis of Fournier's gangrene.

Classification of NSTIs

Necrotizing soft tissue infections can be categorized into four types based upon microbiology of the infection. Historically, manuscripts focused on the clinical findings of necrotizing fasciitis with limited data about the bacteriological findings. Bacterial cultures from sixteen patients with necrotizing soft tissue infections at various sites on the body were reviewed to better understand the bacteriology of these infections. Based on these findings, Giuliano and colleagues described two types of infections[21]; however, the classification scheme has been expanded to four categories[8].

Type 1 (polymicrobial)

Type 1 necrotizing soft tissue infection is the most common type. Fournier's gangrene is most commonly a result of this microbial type of necrotizing soft tissue infection. Responsible for > 50%% of infections, it is due to the synergistic action of anaerobic, aerobic, and facultative anaerobic bacteria (i.e., *E coli*, *Pseudomonas* spp., and *Bacteroides* spp.)[10]. Immunocompromised patients and others with several co-morbidities are commonly affected. The most likely areas of the body for these infections are the trunk and perineum.

Type 2 (monomicrobial)

These infections are less common but can be more aggressive than type 1 necrotizing soft tissue infections. They more commonly involve necrotizing fasciitis of the extremities with a history of trauma or recent surgery. The most common bacteria is Group A beta-hemolytic streptococcus with or without *Staphylococcus aureus*. Toxic shock syndrome is associated with this microbial type.

Type 3

These infections account for <5% of necrotizing soft tissue infections and are attributed to *Vibrio* species or Gram-negative bacteria. The extremities, trunk or perineum can be involved and they are notorious for extremely rapid spread of disease resulting in multisystem organ failure and mortality if not addressed within 24 hours. These infections are more prevalent in warm water coastal regions in the southeastern Unites States, Central and South America, and Asia. Infections can occur through exposure via an open wound[22]. Gas production resulting in crepitus is also a common finding with these bacteria. Clostridium infections often occur following deep soft tissue wounds or intestinal/obstetric surgical wounds. IV drug users can also present with these microbial necrotizing soft tissue infections.

Type 4 (fungal)

These are rare fungal infections due to *Candida* spp. and Zygomycetes that primarily involve immunocompromised patients following trauma[23]. Similar to type 1 and 3 infections, the extremities, trunk and perineum are the commons affected body regions. Similar to type 3 necrotizing infections, they are aggressive and can progress rapidly.

Clinical Diagnosis

The clinical presentation of Fournier's gangrene can be variable depending on the stage of infection, patient co-morbidities, and overall health status. Tenderness, erythema, and swelling can mimic less severe infections such as cellulitis and erysipelas; however, pain out of proportion to clinical exam should alert the clinician to the strong possibility of necrotizing fasciitis[24]. Cellulitis and erysipelas can present with well-demarcated

areas of erythema/inflammation, while necrotizing fasciitis is characterized by poorly demarcated erythema. In addition, cellulitis and erysipelas commonly present with generalized signs of infection (i.e., fever, lethargy), while necrotizing fasciitis can result in systemic toxicity with associated multi-organ dysfunction. During late stages, blisters and bullae are associated with necrotizing fasciitis, while these skin changes are rare for cellulitis and erysipelas.

While necrotizing infections commonly manifest as an acute process, they can present in a subacute manner. During the subacute process, the patient may experience generalized symptoms such as fever and tiredness. Clinicians may notice skin erythema with indistinct margins, swelling, and tenderness (Figure 2); however, the infection can evolve to an acute phase as bacteria spread along superficial perineal fascial planes to surrounding structures. In some cases, the infection can spread as quickly as one inch per hour along the fascial planes in the absence of skin changes[25]. Localized anesthesia can occur if superficial nerves are damaged from infectious spread, and deeper fascial planes can become affected resulting in thrombosis of blood vessels, ischemia and tissue necrosis (Figure 3). Foul smelling “dishwater” fluid, which can be encountered during surgical debridement, characterizes necrotizing fasciitis as a result of tissue necrosis. Left unchecked, shock and multi-organ dysfunction can quickly ensue increasing the risk of mortality.

Goh and colleagues performed a systematic review of manuscripts from 1980-2013 to ascertain the presentation of necrotizing fasciitis[24]. After excluding studies with < 50

patients and those that did not provide information on presenting symptoms, nine studies were examined which included 1463 patients. Swelling (81%), pain (79%), and erythema (71%) were the most common clinical findings at presentation. Crepitus and soft tissue air on plain tissue radiograph can also occur following anaerobic infections (i.e., *Clostridia* species) as a result of exotoxins that result in tissue necrosis and release of gases. Bullae (26%), skin necrosis (24%), and crepitus (20%) were less commonly noted at initial presentation, as these physical exam findings are associated with later stages of necrotizing infections.

Laboratory Diagnosis

The Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) is a scoring system that was developed to assist diagnosis of necrotizing fasciitis from other soft tissue infections[26]. The authors originally examined age, sex, serum potassium, platelet count, C-reactive protein, leukocyte count, hemoglobin, sodium, creatinine, and glucose from 89 consecutive patients with necrotizing fasciitis compared to 225 controls. The most reliable indicators were C-reactive protein, leukocyte count, hemoglobin, sodium, creatinine, and glucose. The LRINEC score ranges from 0-13. Addition of the six predictive variables allows categorization into low risk (≤5), intermediate risk (6-7), and high risk (≥8) categories. The risks correspond to a <50%, 50-75%, and >75% probability of developing a necrotizing soft tissue infection. Criticisms of the LRINEC scoring system is that it was developed in a retrospective setting among patients with a strong suspicion for necrotizing fasciitis. It is unknown how predictive the scoring system would be among patients with a weaker diagnostic presumption, but the scoring

system has been validated in the literature and is thought to be a useful adjunct to the clinical exam[27].

Little has been published about the predictive ability of the LRINEC scoring system to aid diagnosis of Fournier's gangrene, as most of the published literature has focused on generalized necrotizing fasciitis. In one of the only studies examining the LRINEC scoring system among Fournier's gangrene patients, 16 male spinal cord injury patients with Fournier's gangrene were retrospectively assessed[17]. The median LRINEC value at admission was 6.5 (range 2-9), with eleven patients scoring ≥6 and one patient scoring ≥9.

The intended purpose of the LRINEC system was to aid differentiation of necrotizing fasciitis from other soft tissue infections; however, the LRINEC system has been more commonly used to assess mortality due to necrotizing fasciitis. Of note, the aim of the study in the above paragraph that included spinal cord injured patients with Fournier's gangrene was to examine if a LRINEC score ≥6 predicted for longer time to wound closure and time in the hospital. A LRINEC score ≥6 did predict for this outcome; however, it did not predict for mortality, as all patients survived. A separate study noted that stratification of LRINEC to ≥6 and < 6 in patients with Fournier's gangrene predicted mechanical ventilation requirement and mortality[28]. The Fournier's gangrene severity index (FGSI) was developed as a prognostic indicator[29]. A score on the FGSI scale of > 9 is associated with a 75% probability of death and a score of 9 or less is predictive of a 78% probability of survival. The score is based on nine parameters which are each

scored from 0 to 4 and include body temperature, heart rate, respiratory rate, serum level of sodium, potassium, creatinine, bicarbonate, as well as hematocrit and leukocyte count.

Imaging

Radiographic studies can be useful to aid diagnosis when the diagnosis of Fournier's gangrene is uncertain; however, treatment should not be delayed by unnecessarily obtaining radiographic studies. Computed tomography (CT) can be utilized to aid confirmation of Fournier's gangrene in the setting of an ambiguous case, as it has been shown to have a greater specificity than radiography or ultrasound.[30] CT findings associated with Fournier's gangrene are soft-tissue thickening and inflammation. Fascial thickening, abscesses, and subcutaneous gas secondary to gas-forming bacterial can also be seen on CT (Figure 4).

Magnetic resonance imaging with gadolinium is an excellent radiographic modality to examine soft tissues; however, the test can be costly, require a stable patient and can impair valuable time that should be devoted to treatment. While it has been shown to have a high sensitivity and specificity to diagnose necrotizing fasciitis, magnetic resonance imaging only has a limited role for select patients that are clinically stable and cooperative[25].

Thickened scrotal tissue due to inflammation and edema is a typical ultrasound finding associated with Fournier's gangrene[30]. Acoustic shadowing from soft tissue gas

secondary to bacteria can result in a “snow globe” appearance due to hyperechoic foci. Testicular blood supply is commonly preserved with Fournier’s gangrene due to a retroperitoneal blood supply from the aorta; however, the testicles can be negatively affected with a retroperitoneal or abdominal source of infection. In such circumstances, testicular viability can be assessed with Doppler ultrasound.

Standard radiography is less useful given other advanced imaging modalities that are now available. For example, gas on plain radiographs is not a reliable findings, as it has been reported to be present in only 57% of cases[31].

Operative Findings

Surgical debridement can serve as an aid in the diagnosis of Fournier’s gangrene. Early surgical intervention remains the standard of care, which can be life saving. Lack of bleeding secondary to thrombosis of blood vessels, foul odor, grey discoloration of soft tissue due to necrosis, “dirty dishwater” fluid, pus and lack of tissue resistance during finger dissection along tissue planes are operative findings highly associated with Fournier’s gangrene. These markers can serve as indicators of Fournier’s gangrene and provide visual confirmation that additional debridement is necessary.

SUMMARY

Fournier’s gangrene is a life-threatening diagnosis that requires early diagnosis to reduce morbidity and mortality. Knowledge of anatomy, risk factors and etiology can be helpful when these rare cases are suspected. While clinical diagnosis is the most

common method to diagnose Fournier's gangrene followed by expeditious surgical debridement, laboratory and radiography services can serve as useful adjuncts.

1. Fournier JA. Gangrene foudroyante de la verge [over-whelming gangrene]. *Semin Med.* 1883;3:345-347.
2. Baurienne H. Sur une plaie contuse qui s'est terminee par le sphacele de la scrotum. *J Med Chir Pharm.* 1764;20:251-256.
3. Wilson B. Necrotizing fasciitis. *Am Surg.* 1952;18(4):416-431.
4. Jones J. *Investigation upon Nature, Causes and Treatment of Hospital Gangrene as It Prevailed in the Confederate Armies 1861-1865.* New York: US Sanitary Commission; 1871.
5. Eke N. Fournier's gangrene: a review of 1726 cases. *Br J Surg.* 2000;87(6):718-728.
6. Sorensen MD, Krieger JN, Rivara FP, et al. Fournier's Gangrene: population based epidemiology and outcomes. *The Journal of urology.* 2009;181(5):2120-2126.
7. Osbun N, Hampson LA, Holt SK, et al. Low-Volume vs High-Volume Centers and Management of Fournier's Gangrene in Washington State. *J Am Coll Surg.* 2017;224(3):270-275 e271.
8. Misiakos EP, Bagias G, Patapis P, et al. Current concepts in the management of necrotizing fasciitis. *Front Surg.* 2014;1:36.
9. Kim SY, Dupree JM, Le BV, et al. A contemporary analysis of Fournier gangrene using the National Surgical Quality Improvement Program. *Urology.* 2015;85(5):1052-1056.
10. Tang LM, Su YJ, and Lai YC. The evaluation of microbiology and prognosis of fournier's gangrene in past five years. *SpringerPlus.* 2015;4:14.
11. Aridogan IA, Izol V, Abat D, et al. Epidemiological characteristics of Fournier's gangrene: a report of 71 patients. *Urol Int.* 2012;89(4):457-461.
12. Malik AM, Sheikh S, Pathan R, et al. The spectrum of presentation and management of Fournier's gangrene--an experience of 73 cases. *J Pak Med Assoc.* 2010;60(8):617-619.
13. Martinschek A, Evers B, Lampl L, et al. Prognostic aspects, survival rate, and predisposing risk factors in patients with Fournier's gangrene and necrotizing soft tissue infections: evaluation of clinical outcome of 55 patients. *Urol Int.* 2012;89(2):173-179.
14. Ayan F, Sunamak O, Paksoy SM, et al. Fournier's gangrene: a retrospective clinical study on forty-one patients. *ANZ J Surg.* 2005;75(12):1055-1058.
15. Czymek R, Hildebrand P, Kleemann M, et al. New insights into the epidemiology and etiology of Fournier's gangrene: a review of 33 patients. *Infection.* 2009;37(4):306-312.
16. Ulug M, Gedik E, Girgin S, et al. The evaluation of microbiology and Fournier's gangrene severity index in 27 patients. *Int J Infect Dis.* 2009;13(6):e424-430.
17. Backhaus M, Citak M, Tilkorn DJ, et al. Pressure sores significantly increase the risk of developing a Fournier's gangrene in patients with spinal cord injury. *Spinal cord.* 2011;49(11):1143-1146.
18. Wroblewska M, Kuzaka B, Borkowski T, et al. Fournier's gangrene--current concepts. *Pol J Microbiol.* 2014;63(3):267-273.
19. Morris MW, Jr., Aru M, Gaugler A, et al. Necrotizing fasciitis of the perineum associated with a bartholin abscess. *Surg Infect (Larchmt).* 2014;15(2):131-133.

20. Lin WT, Chao CM, Lin HL, et al. Emergence of antibiotic-resistant bacteria in patients with Fournier gangrene. *Surg Infect (Larchmt).* 2015;16(2):165-168.
21. Giuliano A, Lewis F, Jr., Hadley K, et al. Bacteriology of necrotizing fasciitis. *Am J Surg.* 1977;134(1):52-57.
22. Hakkarainen TW, Kopari NM, Pham TN, et al. Necrotizing soft tissue infections: review and current concepts in treatment, systems of care, and outcomes. *Curr Probl Surg.* 2014;51(8):344-362.
23. Jain D, Kumar Y, Vasishta RK, et al. Zygomycotic necrotizing fasciitis in immunocompetent patients: a series of 18 cases. *Mod Pathol.* 2006;19(9):1221-1226.
24. Goh T, Goh LG, Ang CH, et al. Early diagnosis of necrotizing fasciitis. *Br J Surg.* 2014;101(1):e119-125.
25. Kaufmann JA and Ramponi D. Recognition of risk factors and prognostic indicators in Fournier's gangrene. *Crit Care Nurs Q.* 2015;38(2):143-153.
26. Wong CH, Khin LW, et al. The LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) score: a tool for distinguishing necrotizing fasciitis from other soft tissue infections. *Crit Care Med.* 2004;32(7):1535-1541.
27. Schuster L and Nunez DE. Using clinical pathways to aid in the diagnosis of necrotizing soft tissue infections synthesis of evidence. *Worldviews Evid Based Nurs.* 2012;9(2):88-99.
28. Bozkurt O, Sen V, Demir O, et al. Evaluation of the utility of different scoring systems (FGSI, LRINEC and NLR) in the management of Fournier's gangrene. *Int Urol Nephrol.* 2015;47(2):243-248.
29. Laor E, Palmer LS, Tolia BM, et al. Outcome prediction in patients with Fournier's gangrene. *J Urol.* 1995;154(1):89-92.
30. Levenson RB, Singh AK, and Novelline RA. Fournier gangrene: role of imaging. *Radiographics.* 2008;28(2):519-528.
31. Anaya DA, Dellinger EP. Necrotizing soft-tissue infection: diagnosis and management. *Clin Infect Dis.* 2007;44(5):705-710.

Figure Legends:

Figure 1. Care pathway for Fournier's gangrene (adapted from Guidelines on Urological Infections, European Association of Urology; https://uroweb.org/wp-content/uploads/18_Urological-infections_LR.pdf)

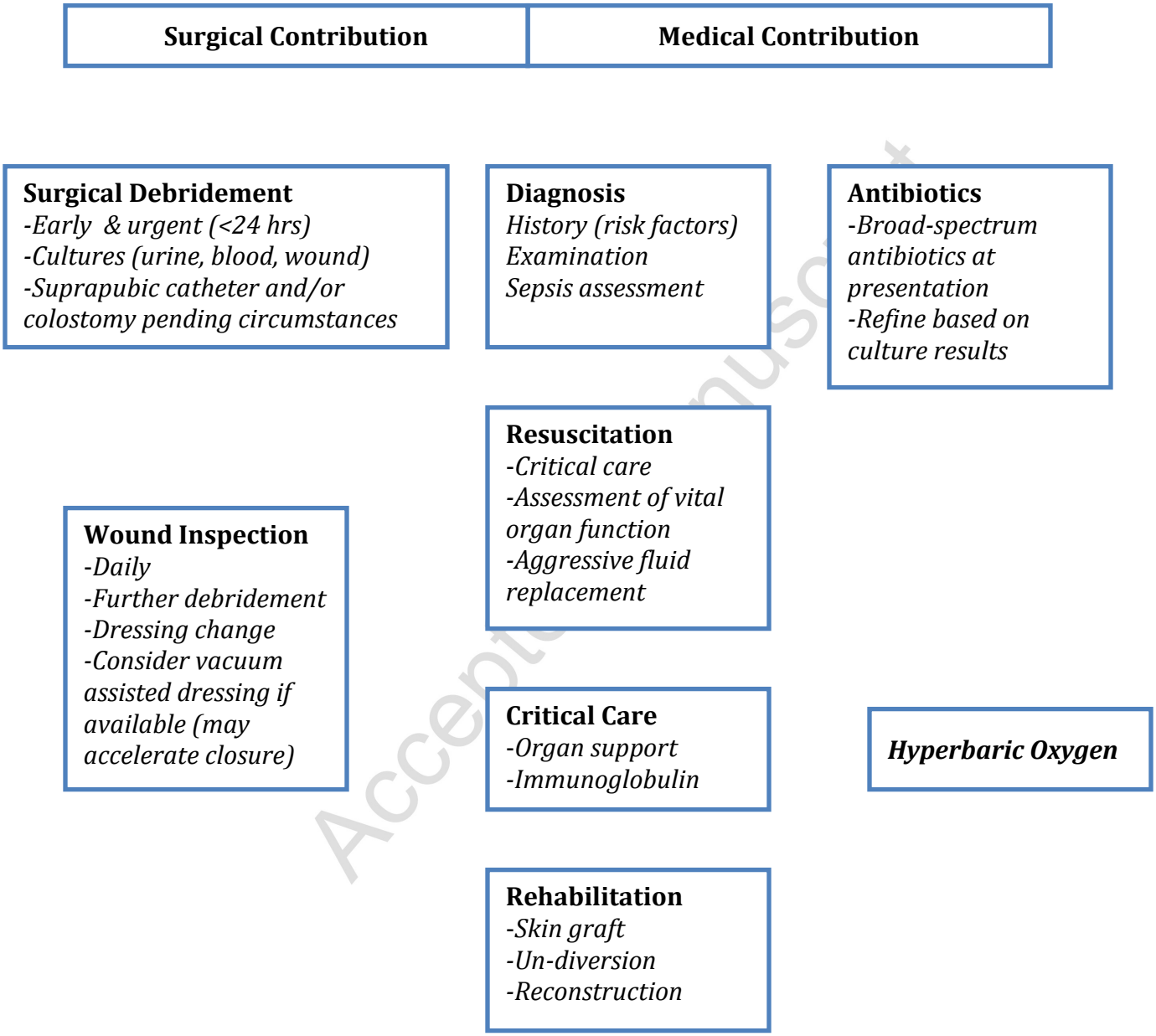

Figure 2. Visible scrotal edema and erythema with ill-defined margins tracking up the left inguinal area (arrow).

Figure 3: Intra-operative picture after surgical skin preparation with betadine, showing extensive scrotal edema and erythema with skin necrosis on the right hemi-scrotum.

Figure 4. Coronal image of CT abdomen and pelvis in a patient with suspected Fournier's gangrene. Diffuse soft tissue gas (arrow) can be seen in the left hemi-scrotum tracking to the penile shaft on the left side with associated inflammatory changes (arrow).