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Fournier's Gangrene: Diagnostic and Therapeutic Considerations

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1. Introduction

Fournier's gangrene is a necrotising fasciitis of the genitalia. Jean Alfred Fournier (1832-1914) was the first French syphilologist, the first professor of cutaneous and syphilitic diseases at the Paris Faculty of Medicine, and the most prominent European venereologist of the second half of the 19th century. He first described idiopathic, rapidly progressive necrotizing gangrene of the male genitalia in 1883 and emphasised three characteristics; abrupt onset of scrotal pain and swelling in a healthy young man, rapid progression to gangrene, and the absence of a definitive cause (Fournier, 1883). Fournier's original description included five otherwise healthy young males with scrotal gangrene and emphasised the sudden onset and rapid progression of the disease. Over the years several terms have been applied to Fournier's gangrene including 'streptococcus gangrene', 'necrotising fasciitis', 'periurethral phlegmon', 'phagedena' and 'synergistic necrotising cellulitis' (Eke, 2000). Although originally described in healthy young men Fournier's gangrene is frequently seen in elderly patients as well as children (Woodside, 1980) and women (Lowthian and Gillard Jr, 1980).

2. Pathophysiology

Initially described as an idiopathic entity, a source of infection can now be identified in the majority of cases. Perineal and genital skin infections comprise most of the sources identified but anorectal or urogenital trauma, diverticular disease, pelvic and perineal injury and pelvic interventions are other causes of Fournier's gangrene (Thwaini et al., 2006). In a large case series by Eke the distribution of the source of sepsis was 24% dermatological, 21% colorectal, 19% urological and unknown in 34% of patients (Eke, 2000). Whilst this condition does continue to affect healthy young men, the mean age of patients is between 50-65 years of age. Most patients have associated co-morbidities such as diabetes, alcoholism or HIV infection (Kuo et al., 2007). Diabetes is reported to be present in 20%-70% of patients with Fournier's gangrene (Morpurgo, 2002) and chronic alcoholism in 25%-50% of cases (Clayton et al., 1990).

The disease is believed to be an obliterative end-arteritis caused by the spread of micro-organisms. Inflammation and oedema from infection results in an impaired local blood supply, leading to vascular thrombosis in the cutaneous and subcutaneous tissues. Perifascial dissection with subsequent spread of bacteria and progression to gangrene of the

overlying tissues ensues (Levenson et al., 2008). The rate of fascial necrosis has been estimated to be as high as 3 cm per hour making early diagnosis crucial (Safioleas et al., 2006). The subcutaneous infection with oedema and inflammation in an enclosed space impairs the blood supply and the resulting hypoxia permits the growth of facultative and obligatory anaerobes. These anaerobic micro-organisms produce hydrogen and nitrogen that accumulate in subcutaneous tissues resulting in crepitus (Hejase et al., 1996). The presence of subcutaneous emphysema signifies anaerobic conditions in the affected area (Wolach et al., 1989). Deeper infection that extends below the facial layers to involve myonecrosis not generally thought to be a feature of classical Fournier's gangrene, although it has been described (Rye et al., 1987).

Testicular involvement is rare in Fournier's gangrene because of the separate blood supply to the testes (Gupta et al., 2007). In a retrospective review of 29 patients over a 13-year period Baskin et al. reported that only three patients underwent orchidectomy due to testicular gangrene (Baskin et al., 1990). Ayan et al reviewed 41 cases of Fournier's gangrene and found that a bilateral orchidectomy was performed in 4 patients and a unilateral orchidectomy was performed in 5 patients (Ayan et al., 2005). In his large review of 1726 patients Eke suggested that when testicular involvement does occur it indicates a retroperitoneal or intra-abdominal source of infection (Eke, 2000). Penis involvement is also rare and the corpora are usually spared while the skin sloughs off. Thrombosis of the corpus spongiosum and cavernosum has, however, been reported (Campos and Martos, 1990).

3. Bacteriology

There have been many types of bacteriological culture encountered in Fournier's gangrene, both single strain and polymicrobial culture. In their experience of 38 patients Hejase et al found that 90% of the patients grew polymicrobial flora, including gram-positive and gram-negative rods and gram-positive cocci. The main strains grown were *Staphylococcus aureus*, β -hemolytic *Streptococcus*, *Pseudomonas* sp., *E. coli* and *Klebsiella* sp. (Hejase et al., 1996). In 5% of their cases no growth was reported. Korkut et al had a 64% positive culture rate of the 36 patients in their case series who had cultures sent during their initial debridement, and the leading micro-organism was *Escherichia coli* (Korkut et al., 2003). In their review of 70 patients with Fournier's gangrene Ersay et al found that the most frequent bacterial organisms cultured from the wounds were *Escherichia coli* (40.0%), *Bacteroides* spp. (38.6%), *Streptococcus* spp. (37.1%), *Enterococcus* spp. (27.1%), *Staphylococcus* spp. (25.7%), *Pseudomonas* spp. (24.3%), *Klebsiella pneumoniae* (20.0%), and *Proteus* spp. (18.6%). The bacterial organisms cultured from wound however were not independent predictors of outcome (Ersay et al., 2007). Kuo et al cultured a variety of organisms in their series of 44 patients in northern Taiwan (Kuo et al., 2007). These were cultured from necrotic tissue or pus during surgery or at the bedside. Only 1 organism was identified in 13 patients whilst culture results in 28 patients demonstrated polymicrobial infection. In 3 patients wound cultures were negative. The most commonly isolated organisms from wound were *Escherichia coli* in 26 patients, *Bacteroides fragilis* in 17 patients, *Klebsiella pneumoniae* in 16 patients, *Enterococcus* spp. in 14 patients and *Proteus mirabilis* in 10 patients. Similar to the case series by Ersay et al, mortality was not related to the specific isolated organism. In their review of 43 reconstructive patients Ferreira et al had a positive culture from 35 of the 43 patients, with 29 (82.9%) of these being polymicrobial (Ferreira et al., 2007). The most

common organisms isolated were *Staphylococcus aureus* (21 patients), *Escherichia coli* and *Pseudomonas aeruginosa* (11).

In their review article on Fournier's gangrene Thwaini et al state that "cultures from the wounds commonly show polymicrobial infections by aerobes and anaerobes, which include coliforms, klebsiella, streptococci, staphylococci, Clostridia, Bacteroides and *Corynebacteria*. On average, at least three organisms are cultured from each diagnosed patient" (Thwaini et al., 2006). Along with the above organisms mentioned there have been cases reported of Fournier's gangrene caused by unusual organisms such as *Clostridium perfringens* (Korhonen et al., 1998) and *Clostridium tetani* (Omotoso, 1990).

4. Clinical

The clinical features of Fournier's gangrene include sudden pain in the scrotum, prostration, pallor and pyrexia. At first only the scrotum is involved, but if unchecked, the cellulitis spreads until the entire scrotal coverings slough, leaving the testes exposed but healthy (Russell et al., 2000). The presentation may also be insidious as opposed to the classical sudden onset presentation. One overwhelming feature of the presentation is the strong 'repulsive, fetid odour' that is associated with the condition (Randall, 1920). Patients can present with varying signs and symptoms including fever greater than 38°C, scrotal swelling and erythema, purulence or wound discharge, crepitation or fluctulance (Ozden Yenyol et al., 2004). In their case series Ferreira et al found that the most common presentations were scrotal swelling, fever and pain. The mean interval between initial symptoms and arrival at the hospital was 5.1 ± 3.1 days. Scrotal involvement was found in 93.3% of cases, the penis was involved in 46.5% of cases, and the perineum or peri-anal region was involved in 37.2% of cases (Ferreira et al., 2007). Ersay et al found that the most common presentation was peri-anal/scrotal pain (78.6%) followed by tachycardia (61.4%), purulent discharge from the perineum (60%), crepitus (54.3%) and fever (41.4%) (Ersay et al., 2007). Crepitus of the inflamed tissue is a common feature of the disease due to the presence of gas forming organisms. As the subcutaneous inflammation worsens, necrotic patches start appearing over the overlying skin and progress to extensive necrosis (Laucks 2nd, 1994). The spread of infection is along the fascial planes and is usually limited by the attachment of the Colles' fascia in the perineum (Thwaini et al., 2006). Infection can spread to involve the scrotum, penis and can spread up the anterior abdominal wall, up to the clavicle (Saijo et al., 1990). As mentioned previously testicular involvement is rare in Fournier's gangrene because of the separate blood supply to the testes, although it can occur and result in unilateral or bilateral orchidectomy.

5. Differential diagnosis

Although the diagnosis of Fournier's gangrene is usually obvious due to the gangrene, patients may present at an earlier stage with an acutely swollen tender scrotum. Differential diagnoses in this scenario include intra-testicular injuries such as fracture and haematoma, extra-testicular injuries including haematomas or hematoceles, torsion of the spermatic cord, haemorrhage and necrosis of a testicular tumour, strangulated scrotal hernia, and inflammatory disease (Begley et al., 1988). Aside from the rare abscess or granulomatous infection the majority of inflammatory diseases affecting the scrotum are epididymitis and epididymo-orchitis.

6. Investigations

The diagnosis of Fournier's gangrene is primarily clinical. Imaging modalities may be helpful in those where the presentation is atypical or when there is concern regarding the true extent of the disease (Thwaini et al., 2006). Ultrasound has been shown to be effective in demonstrating specific features of Fournier's gangrene, although CT has greater specificity for evaluating the disease. Unlike other conditions that cause acute scrotal pain, in Fournier's gangrene the scrotal contents- the testes and epididymides- are normal, and no masses or other abnormal structures are present. Instead the ultrasound characteristics of Fournier's gangrene include marked thickening of scrotal skin and, most significantly, air in the subcutaneous tissues. If the patient has more advanced disease, the skin thickening and subcutaneous air can be traced from the scrotum with ultrasound to demonstrate its full extent (Begley et al., 1988). Because the majority of cases of Fournier's gangrene are not primary and are secondary to other conditions described earlier (e.g. diverticulitis), CT plays an important role in the diagnosis as well as the evaluation of disease extent for appropriate surgical treatment. In their review of the role of imaging in Fournier's gangrene, Levenson et al describe the CT features seen in the disease: "The CT features on Fournier's gangrene include soft-tissue thickening and inflammation. CT can demonstrate asymmetric fascial thickening, any co-existing fluid collection or abscess, fat stranding around involved structures, and subcutaneous emphysema secondary to gas-forming bacteria. The subcutaneous emphysema in Fournier's gangrene dissects along fascial planes and can extend from the scrotum and perineum to the inguinal regions, thighs, abdominal wall, and retroperitoneum. The underlying cause of Fournier's gangrene, such as perianal abscess, a fistulous tract, or an intra-abdominal or retroperitoneal infection process may also be demonstrated on CT. In cases caused by colonic perforation, not only does CT demonstrate extraluminal foci of air, but extravasation of enteric contrast material may also be seen" (Levenson et al., 2008). Features of Fournier's gangrene can also be seen on plain radiography with hyperlucencies representing soft-tissue gas seen overlying the scrotum or perineum. Subcutaneous emphysema may also be seen within the soft tissues. Deep fascial gas is rarely seen at plain film radiography, which represents a significant weakness of this modality in the diagnosis and evaluation of Fournier's gangrene (Wysoki et al., 1997).

Routine blood investigations should be sent including a FBC, urea & electrolytes, C-Reactive Protein (CRP), glucose, and Arterial Blood Gas (ABG). The LRINEC (Laboratory Risk Indicator for Necrotizing Fasciitis) is a robust laboratory measurement score capable of determining even clinically early cases of necrotizing fasciitis (Wong et al., 2004). Using logistic regression analysis of independent variables from 89 cases of necrotizing fasciitis 6 factors were identified to be independent predictors. A summary table of these variables is shown below in Table 1.

Of the cohort of 89 patients only 13 (14.6%) patients had a diagnosis or suspicion of necrotizing fasciitis on admission. A majority were therefore missed, resulting in delayed operative debridement. In contrast, 80 (89.9%) of these patients had a LRINEC score of ≥ 6 . According to Wong et al the biochemical and hematologic changes in necrotizing fasciitis develop early in the evolution of the disease and the LRINEC score can stratify patients into high and moderate risk categories even when the clinical picture is still equivocal.

Laor et al determined outcome prediction on 30 patients with Fournier's gangrene and proposed a Fournier's gangrene severity index (Laor et al., 1995). Admission laboratory parameters that were statistically related to outcome included hematocrit, blood urea

Variable, Units	Score
C-Reactive Protein, mg/L	
<150	0
≥150	4
Total white cell count, per mm ³	
<15	0
15-25	1
>25	2
Haemoglobin, g/dL	
>13.5	0
11-13.5	1
<11	2
Sodium, mmol/L	
≥135	0
<135	2
Creatanine, µmol/L	
≤141	0
>141	2
Glucose, mmol/L	
≤10	0
>10	1

Table 1. Summary of the Laboratory Risk Indicator for Necrotizing Fasciitis (LRINEC) score. A LRINEC score of ≥6 should raise the suspicion of necrotizing fasciitis among patients with severe soft tissue infections, and a score ≥8 is strongly predictive of this disease (Wong et al., 2004).

nitrogen, calcium, albumin, alkaline phospatase and cholesterol levels. White blood count, platelets, potassium, bicarbonate, blood urea nitrogen, total protein, albumen and lactic dehydrogenise levels one week following hospitalization were also associated with outcome. These levels combined with the acute physiology and chronic health evaluation II severity score was used to create the Fournier's gangrene severity index. The authors found that using a threshold of 9 on the severity index there was a 75% probability of death with a score greater than 9, while a score less than 9 was associated with a 78% probability of survival (p=0.008).

7. Treatment

The cornerstones of treatment of Fournier's gangrene are urgent surgical debridement of all necrotic tissue as well as high doses of broad-spectrum antibiotics. Urgent resuscitation with fluids as well as blood transfusions may be needed. Empirical broad spectrum antibiotics should be initiated regardless of the Gram-stain and culture results, and the antibiotics chosen should cover streptococci, staphylococci, gram-negative Coliforms, Pseudomonas, Bacteroides and Clostridia (Laucks II, 1994). Early surgical debridement is the primary aim of treatment and if delayed will have a negative impact on prognosis (Elliott et al., 2000).

The goal of surgery is to excise all non-viable tissue until well-perfused viable tissue is reached. The subcutaneous disease may be more extensive than the cutaneous involvement and more radial debridement may need to be undertaken than originally planned pre-operatively. Care must be taken not to open up deeper fascial planes that were not originally involved. Depending on the original foci of the disease, urinary or faecal diversion may be necessary. Multiple debridements of necrotic tissue are the rule rather than the exception. As mentioned previously, orchidectomy is a rare but sometimes necessary eventuality of extensive Fournier's gangrene.

Once the infection has subsided the scrotum has traditionally been left to heal by secondary intention as it has been noted to possess a remarkable ability to regenerate and heal (Thomas, 1956). The use of skin grafts and flaps are common to provide coverings of debrided tissue. In their review of 43 reconstructive cases Ferreira et al performed surgical debridement of scrotal, penile, and perineal necrosis along with other involved areas in all patients, including seven patients who required debridement twice, and one patient who required debridement three times (Ferreira et al., 2007). All patients received delayed surgical reconstruction after the appearance of healthy granulation tissue at the base of the wound. The mean time between the last debridement performed and the first reconstruction was 37.4 days. In total, 61 reconstructive procedures were performed in the 43 patients with up to four operations being performed on each patient. The superomedial thigh flap was performed for scrotum reconstruction in 26 patients. Split-thickness skin grafts were the major solution for covering penile skin losses. In four patients with urethral stricture, tubed urethroplasty was performed using free full-thickness skin grafts. Mean hospital stay was 73.6 ± 42.5 days.

Along with the increased use of skin flaps & grafts to cover bare areas after surgical debridement, the use of vacuum-assisted closure (VAC) has increased in popularity and aided the healing process in patients with Fournier's gangrene. In their case series of 35 patients with Fournier's gangrene who received surgical debridement of necrotic areas, Czymek et al compared patients who were treated with conventional dressings to those who received VAC dressings over an 11 year period (Czymek et al., 2009). In the conventional dressings group, patients had their dressings changed once per day until the wounds were clean and healthy and local wounds could be closed with meshed grafts or flaps. In the VAC therapy group the VAC dressing was initiated 3-5 days after primary debridement. Continuous negative pressure of 75 mmHg was applied to the wounds and the VAC was changed every 48 hours. Similar to the conventional dressing group, the VAC therapy was continued until the wounds were healthy and clean and could be closed with meshed grafts or advancement flaps. Although the VAC therapy group was associated with significantly longer hospitalization it was also associated with lower mortality. Although the authors state that their study does not demonstrate that VAC dressings are superior to conventional dressings in terms of length of stay or clinical outcome, they state that "experience has shown that vacuum dressings are clinically effective and successfully used in the management of large wounds". It is important to note that although this study did compare two groups it was not randomized, although the authors do address this point by correctly stating that it would be practically impossible to perform a randomized controlled trial on this group of patients because of the rarity of Fournier's gangrene.

8. Complications

The complications of Fournier's gangrene can include single or multi-organ failure, as well as large scrotal, peri-anal, penile and abdominal wall skin defects. As mentioned previously, Fournier's gangrene may involve the testes, and single or bilateral orchidectomy may need to be performed. The penis may need to be partially or completely amputated in cases of severe gangrene (Schneider et al., 1986). Fournier's gangrene may be the presenting feature of diabetes mellitus, and may be associated with keto-acidosis (Slater et al., 1982). Long-term pain is not uncommon in Fournier's gangrene and 50% of patients can be expected to be free of pain. The sexual function may be impaired by penile deviation or penile torsion as well as loss of sensitivity to the penile skin or pain during erection (Ferreira et al., 2007). Infertility is rare after Fournier's gangrene, but has been reported (Baskin et al., 1990).

9. Conclusion

Fournier's gangrene is a rare necrotising fasciitis of the genitalia originally described in healthy young men. Recent evidence has shown that a cause for the condition can be identified in most patients and today's cohort are unlikely to be healthy young men but elderly patients with co-morbid conditions such as diabetes, immunosuppression or alcoholism. The most common sources of infection are perineal and genital skin infections, although other factors have been implicated in the aetiology of the disease such as pelvic or perineal injury, pelvic interventions and colorectal diseases such as neoplasia or diverticulitis. As outlined above, Fournier's gangrene demonstrates a wide variety of clinical presentations from slow insidious progression of scrotal swelling and pain over weeks to a rapid and fulminant onset within hours. Patients with full-blown Fournier's gangrene usually have pronounced systemic signs such as tachycardia, tachypnoea, fever and possibly altered mental state. Although a wide variety of bacteria have been implicated in the disease (and the disease is frequently polymicrobial) the most common organisms isolated are *Staphylococcus aureus*, β -haemolytic *Streptococcus*, *Pseudomonas* sp., *E. coli*, *Enterococcus* and *Bacteroides*. The spread of infection is along fascial planes and is usually rapid so prompt medical and surgical therapy is mandatory. The mainstay of treatment is early recognition of the disease, prompt resuscitation with intravenous fluids and oxygen therapy, broad-spectrum high dose intravenous antibiotics, and urgent surgical debridement of affected areas. If there is any doubt about the diagnosis of the condition, radiology may be helpful in identifying gas forming organisms or areas of necrosis, and CT has been shown to be particularly helpful in this regard, as well as demonstrating accurately the extent of the disease, and the underlying cause. Due to their separate blood supply the testes are usually spared in Fournier's gangrene and wide areas of skin necrosis may involve debridement of the scrotum, penis, thighs and anterior abdominal wall. Frequently more than one surgical debridement is necessary as a 'second look' at 24-48 hours reveals further areas of necrosis. Once the patient has been stabilised and there is evidence of granulation tissue forming in the debrided areas further treatment can now be instigated. Skin grafting, local and free flaps have all been used with success in covering areas of debridement after Fournier's gangrene. Recently, VAC (Vaccum Assisted Closure) therapy has been used with promising results in Fournier's gangrene after debridement.

Although early series reported high mortality rates for Fournier's gangrene at around 80% (Stephens et al., 1993) more recent studies have shown an improvement with lower rates of mortality of generally less than 40% (Morpurgo, 2002, Thwaini et al., 2006). Long-term complications of this disease are not uncommon. Pain, sexual dysfunction, incontinence, scarring, and infertility have all been reported.

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Gangrene - Current Concepts and Management Options

Edited by Dr. Alexander Vitin

ISBN 978-953-307-386-6

Hard cover, 178 pages

Publisher InTech

Published online 29, August, 2011

Published in print edition August, 2011

Gangrene is the term used to describe the necrosis or death of soft tissue due to obstructed circulation, usually followed by decomposition and putrefaction, a serious, potentially fatal complication. The presented book discusses different aspects of this condition, such as etiology, predisposing factors, demography, pathologic anatomy and mechanisms of development, molecular biology, immunology, microbiology and more. A variety of management strategies, including pharmacological treatment options, surgical and non-surgical solutions and auxiliary methods, are also extensively discussed in the book's chapters. The purpose of the book is not only to provide a reader with an updated information on the discussed problem, but also to give an opportunity for expert opinions exchange and experience sharing. The book contains a collection of 13 articles, contributed by experts, who have conducted a research in the selected area, and also possesses a vast experience in practical management of gangrene and necrosis of different locations.

How to reference

In order to correctly reference this scholarly work, feel free to copy and paste the following:

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