Institutional experience encompassing 2008-2015 in the management of Fournier’s gangrene and a literature review


Division of Urology, Hospital General «Dr. Manuel Gea González», Secretaría de Salud, México, Mexico City, Mexico

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Abstract
Background: Fournier’s gangrene is characterized by necrosis and gangrene of the subcutaneous tissue, superficial and deep fascia, and muscles in the perineum and genitals. The risk factors are: alcoholism, diabetes, malnutrition, advanced age, and immunosuppression. Treatment is based on broad-spectrum antibiotics and radical surgical debridement.

Aim: To report our institutional experience in the treatment of Fournier’s gangrene.

Methods: A retrospective, analytic study was conducted that included 46 patients attended to within the time frame of 2008-2015.

Results: Low socioeconomic level was the most frequent factor (61.4%), followed by diabetes (52.3%). Multiple surgeries were required in 79.5% of the cases and the mortality rate was 6.8%. A total of 68.3% of the cases had a urologic origin, followed by soft tissue involvement (27.3%), and the most frequent microorganism was Escherichia coli (61.4%).

Discussion: Treatment included broad-spectrum antibiotics (carbapenems) and radical surgical treatment; vacuum-assisted closure was recommended. Once a negative culture was obtained, rehabilitation and reconstruction were carried out to optimize the functional capacity of the patients. In our population, economic limitations and treatment abandonment limited the described management.

Conclusions: Fournier’s gangrene presents with a critical mortality rate. Initial aggressive antibiotic and surgical treatment improves survival and later rehabilitation and reconstruction improve functional capacity.

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Introduction

Fournier’s gangrene is a progressive and potentially fatal infection of the perineum and genitals. In infection at the level of the genital region, its etiology is due to mixed flora that includes Gram-positive, Gram-negative, and anaerobic infections.¹

In 1764, Baurienne was the first author to describe this disease and in 1883, the venereologist Fournier described this gangrene as a sudden onset disease with rapid progression to gangrene with no identifiable cause, resulting in the name, Fournier’s gangrene.

Today, Fournier’s gangrene tends to affect both sexes of all ages, with a predominance for the male sex (man:woman ratio, 10:1) and in men older than 50 years of age. Despite aggressive modern management, there is a 16-67% mortality rate with an incidence of 1:7,500 to 1:750,000.

The use of scoring systems, such as the severity index for Fournier’s gangrene, has been evaluated, where a sum of nine points or less is associated with a mortality rate of 46%, whereas a sum of nine points or more is associated with a mortality rate of 6.8%. El origen urológico representó el 68.3%, seguido de la afección a tejidos blandos (27.3%).

The infection process is generally conditioned by three or more organisms, the most common of which are Escherichia coli (E. coli), Proteus, Enterococcus and anaerobes (Bacteroides fragilis).²

Fournier’s gangrene is characterized by a polymicrobial synergist infection that produces necrotizing fasciitis initiating with a rupture of the skin barrier, creating an entrance point for microorganisms due to the decompensation of the cutaneous defense mechanisms. Local ischemia secondary to tussular hypoxemia due to obliterating endarteritis of the subcutaneous arteries results in gangrene of the subcutaneous tissue and the adjacent skin, promoting the extension of the infectious process through the deep tissues, producing purulent necrotizing fasciitis. The anaerobic microorganisms that accumulate in the subcutaneous tissue produce nitrogen and hydrogen. This action is fomented by the conditions of hypoxemia, limited blood irrigation, and bacterial overgrowth, clinically resulting in the presence of crepitation in the affected areas and the characteristic odor of Fournier’s gangrene, which is a pathognomonic trait of its participation.³

It gradually progresses within 2-7 days, and is characterized by the presence of discomfort, local hypersensitivity, fever, crepitation, erythema, hardening of the affected zone, areas that progress to ecchymosis and necrosis, accompanied by the drainage of purulent matter, and gangrene of the genitals, anemia, hyderolelectrolytic alterations, hyperglycemia, leukocytosis, and sometimes clear signs of septic shock.

If the anorectal area is the entrance site, presentation is perianaal pain and hypersensitivity in the zone, whereas in cases of genitourinary origin, symptoms are characterized by acute urine retention and testicular and/or scrotal pain.

Antecedentes: La gangrena de Fournier se caracteriza por necrosis y gangrena de tejido subcutáneo, fascias superficiales-profundas, músculos, en perine y genitales. Los factores de riesgo son: alcoholismo, diabetes, desnutrición, edad avanzada e inmunosupresión. El tratamiento se basa en antibióticos de amplio espectro y debridación quirúrgica radical.

Objetivo: Reportar la experiencia en el tratamiento de la gangrena de Fournier en nuestra institución.


Resultados: Un nivel socioeconómico bajo fue el antecedente más frecuente (61.4%), seguido de diabetes (52.3%). El 79.5% requirió múltiples cirugías, con una mortalidad del 6.8%. El origen urológico representó el 68.3%, seguido de la afección a tejidos blandos (27.3%).

Discusión: El tratamiento incluye antibióticos de amplio espectro (carbapenémicos), manejo quirúrgico radical y se recomienda el uso de sistemas de asistencia para el cierre al vacío. Obtenido un cultivo negativo, se realiza rehabilitación y reconstrucción, para optimizar la capacidad funcional de los pacientes. En nuestra población las limitaciones económicas y el abandono del tratamiento, limitan el manejo descrito.

Conclusiones: La gangrena de Fournier posee una mortalidad grave, el tratamiento antibióticoquirúrgico agresivo inicial mejora la sobrevida, posteriormente la rehabilitación-reconstrucción mejora la capacidad funcional.

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The testes and spermatic cords are generally spared from the infectious process due to an independent blood supply (scrotal irrigation arises from the branches of the pudendal artery, whereas testicular circulation arises from the gonadal arteries and branches of the aorta), but 21% of the patients will need orchiectomy on the affected side when there is a non-viable testis. 4

Horta et al. described the following four characteristic phases of Fournier’s gangrene: 5

First phase (nonspecific): nonspecific symptoms associated with hardening, pruritus, edema, and erythema of the affected tissues.

Second phase (invasive): short phase with local and regional inflammatory manifestations.

Third phase (necrotic): progressive general state of health deterioration involving septic shock in 50% of the cases. The necrosis can sometimes extend to the anterior abdominal wall, the axillas, and thighs.

Fourth phase (spontaneous restoration): cicatrization with deep granulation followed by epithelization (for several months) and progressive reestablishment of general state of health.

The pathognomonic anatomic data are the presence of necrosis and gangrene of the subcutaneous tissue, fat, arteries, veins, superficial fascia, muscle, and deep fascia accompanied by fat necrosis, focal bleeding, and inflammation of the dermis and subcutaneous fat. The reticular dermis and subcutaneous tissue present with edema and abundant polymorphonuclear infiltrate. This disease has rapid progression of the gangrenous area (reported at 2-3 cm/h). 6

Diagnosis demands emergency surgery due to the rapid progression of the disease. This entity should be ruled out during any evaluation of soft tissue infection at the level of the genitals and where pain that is out of proportion to lesion extension is suspected, as well as when there is a grayish skin coloration and a characteristic fetid odor (not detected in cases of uncomplicated cellulitis). Wrinkle loss at the level of the scrotum is highly suggestive of necrosis.

Laboratory results are nonspecific, sometimes detecting anemia (due to the lack of activity of the erythropoietic line secondary to the presence of thrombosis and sepsis), leukocytosis, thrombocytopenia, hydroelectrolytic abnormalities (hypotension, hypokalemia, hypocalcemia), hyperglycemia, increased serum creatinine levels, azotemia, and hypalbuminemia.

Kuo et al. 7 suggest that Fournier’s gangrene diagnosis should be based on: soft tissue infection with involvement of the scrotum, perineum, and perianal region, presence of subcutaneous emphysema (demonstrated upon physical examination and radiologic findings), surgical findings of necrotic tissue, and histopathologic findings that confirm the presence of necrotizing fasciitis.

In regard to diagnosis with the aid of imaging studies, characteristic ultrasound findings are the presence of thickening, tumefaction, and edema of the scrotal wall (sometimes with involvement of the penis). Peritesticular fluid can also be detected. In general, the testes and epididymides are spared.

Tomography plays a primary role in the diagnosis, revealing the underlying cause and evaluating the degree of extension so that a more adequate surgical treatment can be planned. The findings include: asymmetric thickening of the fasciae, fluid collections, abscess formation, subcutaneous emphysema, origin, and the degree of extension. It has a high sensitivity and specificity for detecting the presence of abnormal collections of gas. 8

Follow-up with tomographic studies after treatment are beneficial for observing disease improvement or deterioration and they provide useful information for making decisions in relation to treatments and/or additional surgical treatments. 9

A study by Sorensen et al. 10 conducted on 1,641 men with Fournier’s gangrene (treated at 593 hospitals) reported an increase in mortality associated with advanced age, four specific comorbidities (high blood pressure, congestive heart disease, renal insufficiency, and coagulopathies), certain procedures carried out during hospitalization (colostomy, phallectomy, mechanical ventilation, and dialysis), and prolonged hospital stay. Every surgical procedure increases the relative risk for mortality to 27% (reflecting the most severe grades of Fournier’s gangrene). In contrast, orchiectomy is associated with a 70% decrease in the risk for mortality.

Despite the fact that hyperglycemia has been associated with adherence alterations, chemotaxis and macrophage bactericide activity, as well as the development of damaging effects in cellular immunity, no increase in mortality was found when diabetic and non-diabetic patients were compared. 11

Treatment is based on the combination of broad-spectrum antibiotics (including a third generation cephalosporin, an aminoglycoside, and metronidazole and/or carbapenems) and radical and extensive surgical debridement of the tissue until healthy tissue margins are achieved (total scrotectomy). Once tissue cultures have been carried out, antibiotic management can target the developed microorganisms (specific antibiotic treatment).

This type of patient usually requires a second evaluation procedure at 24-48 h to exclude progression. In some cases, multiple explorations and surgical debridement procedures are needed.

After surgical debridement, adequate nutrition must be administered, starting with enteral feeding, which is crucial for better cicatrization. If the source of infection is anorectal or the lesion is contaminated, colostomy to divert bowel transit should be considered. Likewise, urinary diversion through cystostomy should also be considered in cases with a urinary source of infection, thus preventing necrotizing fasciitis exacerbation.

Once the patient is under treatment and the necrotic tissue has been excised, secondary closure of the wounds can be carried out. Very extensive lesions generally require graft application (such as the use of fasciocutaneous grafts of the thigh), which can be used with good cosmetic results. Wound closure should be performed as soon as there is a negative culture and absence of necrotic tissue, and enough healthy tissue is observed to enable re-approximation or graft application. In those patients with less than 50% involvement of the scrotal skin, primary closure can usually be performed without much difficulty. The testes can be placed at the level of the thighs and wrapped by skin, until definitive reconstruction is achieved in cases of extensive scrotal skin loss.

The use of negative pressure wound therapy can be potentially beneficial. This type of system has been used in...
cases of complex lesions after wide surgical excision and debridement with good long-term results.

Aims

Primary:
To report on the experience at our institution in the treatment of Fournier’s disease.

Secondary:

a) To report on the most frequently associated etiology.
b) To report on the most frequently isolated microorganism(s) through secretion culture.
c) To report on the most frequently observed comorbidities observed in our population.

Materials and methods

A retrospective analysis of 49 patients was carried out. Five cases were excluded due to clearing out of case records after patient death. Included in the study were 44 men with a mean age of 55.07 ± 17.60 years, diagnosed with Fournier’s gangrene with urologic involvement within the timeframe of January 2007 to December 2014, treated at the Urology Department of the Hospital Dr. Manuel Gea González. Before the surgical procedure, the evaluation protocol consisted of complete blood count, blood chemistry, coagulation tests, urinalysis, and urine culture. Among the imaging studies carried out to assess the degree of extension of the infectious process were soft tissue ultrasound and non-contrast and contrast-enhanced abdominal tomography scans. Radiologic studies were obtained using the Synapse® image processing software.

The diagnosis of Fournier’s gangrene was made based on the medical history, physical examination, imaging tests, and intraoperative findings using the following criteria modified by Kuo et al.: 1) soft tissue infection with scrotal-perineal zone or perianal involvement, 2) the presence of air infiltrated into the subcutaneous tissue demonstrated through physical examination or as a radiologic finding, 3) surgical findings of tissue presenting with gangrene or necrosis, and 4) necrotizing fasciitis with histopathologic confirmation.

The data corresponding to age, sex, comorbidities, origin, extension, progression, microbiologic study, surgical aspects, antibiotic treatment, and mortality during hospitalization were collected.

The SPSS version 21.0 (SPSS Inc, Chicago, Illinois, USA) statistical software was employed. Descriptive statistics of measures of central tendency, mean, median (minimum-maximum) for the metric variable and frequency (percentage) for the categorical variables were carried out. The chi-square test was used to compare the association between risk factors and death. Statistical significance for all the analyses was set at a p < 0.05.

Results

The present study included the analysis of 44 cases. The mean age of the patients was 55.07 ± 17.60 years (range: 14-92). A total of 31 patients had a past history of chronic alcoholism (70.50%), followed by 52.30% with type 2 diabetes mellitus. Table 1 shows the demographic data and comorbidities.

The main involvement of the disease was urologic in 30 cases, corresponding to 68.30% of the total, followed by soft tissue involvement in 27.30% of the cases, and finally 4.50% of the cases had coloproctologic etiology.

A total of 63.60% of the cases had initial radiologic evaluation and control follow-up with non-contrast and contrast-enhanced abdominal tomography scans. The remaining 36.40% of the cases had soft tissue ultrasound studies. Tables 2 and 3 show the initial patient vital signs and laboratory tests.

The Fournier’s gangrene severity index was calculated in a retrospective analysis with a median of 5 points and a score of 7.50 ± 3.95 in the Acute Physiology and Chronic Health Evaluation (APACHE II). There was no correlation in our study between those indices in relation to mortality (p = 0.717).

All patients in the present study were treated with radical surgical debridement, broad-spectrum antibiotic therapy, and wound management with dressings at the time of their evaluation up to the patient’s release from the hospital. Thirty-five of the cases (79.50%) required surgical reintervention, mainly within the first 72 h (57%). Nine of the patients (20.40%) needed more than 3 surgical interventions to adequately control the infectious process, and bowel transit diversion through colostomy was performed on 9 (20.50%) patients.

Likewise, among the urologic procedures required during patient management were urinary diversion through suprapubic cystostomy (29.50%), simple orchectomy (6.80%), and phallectomy (6.8%).

Mean hospital stay was 14.41 ± 8.77 days (range: 3-36). A total of 9.10% of the patients had to be admitted to the intensive care unit for longer than 24 h, with a mean stay in that unit of 5.5 ± 7.14 days (range: 1-15).

Of the cases reviewed, intraoperative cultures were done on different secretions of all the patients and E. coli (61.40%) was developed in 27 of the cases, followed by Pseudomonas aeruginosa (11.40%); 76.70% of the cultures had growth of more than one microorganism (table 4). Broad-spectrum beta-lactamase-producing microorganisms were shown in the antibiogram results of 12 cases (E. coli in 83.33% and Klebsiella pneumonia in the remaining 16.66%).
In twenty-seven of the cases (61.40%), double-regimen empirical broad-spectrum antibiotic treatment was begun and the most frequently used combination was third generation cephalosporin with metronidazole in 14 cases (31.80%), followed by the combination of third generation cephalosporin with aminoglycoside in 9 cases (20.50%). The use of carbapenems as monotherapy in the empirical broad-spectrum antibiotic treatment was registered in seven patients (13.60%), and the most frequently used combination was third generation cephalosporin with metronidazole in 14 cases (31.80%), followed by the combination of third generation cephalosporin with aminoglycoside in 9 cases (20.50%).

In one case (2.27%), a histopathologic diagnosis of squamous cell carcinoma of the penis was reported that was managed with radical phallectomy. In another case (2.27%), the patient presented with a late complication of colovesical fistula that was managed through diverted colostomy by the general surgery department.

Despite radical surgical treatment and the use of broad-spectrum antibiotics, there was a mortality rate of 6.81%. Of the patient total studied, 18.18% abandoned their outpatient follow-up.

Upon continuing outpatient follow-up, only 31 patients remained under surveillance at one year from their initial evaluation. Of those patients, 35.50% presented with some type of urethral involvement that required management through direct vision urethrotomy or urinary diversion by suprapubic or perineal meatus cystostomy. Anal sphincter involvement that required diversion through colostomy was observed in 12.90% of the cases. In regard to surgical wound management, 83.90% had second intention closure, whereas some type of reconstruction was performed in only 16.10% of the patients.

### Discussion

The majority of studies reported in the literature are retrospective ones that mention institutional experience. For example, in 2010, Torremade et al. conducted a retrospective study of 41 Fournier’s gangrene cases to analyze their etiology and morbidity and mortality. The data assessed were age, sex, comorbidity, origin, extension, progression, microbiologic study, surgical aspects, antibiotic treatment, and mortality. In their results, they state that 93% of the patients were men with a mean age of 60 years. Diabetes was the most frequent pathologic past history (49%), followed by alcoholism (46%) and immunosuppression or neoplasias (34%). Disease origin was perianal in 66% of the cases, followed by urologic etiology (32%). Progression time before diagnosis was 3 days (median) and 49% of the patients underwent several surgical revisions. Mortality was reported at 29%. More than one microorganism was isolated in 76% of the cases (the most frequently isolated were enterobacteriaceae and anaerobic bacteria). In the univariate analysis, antibiotic treatment with carbapenems and the absence of systemic complications were associated with lower mortality. It can be concluded from that study that Fournier’s gangrene is a critically fatal disease and that initial antibiotic and aggressive surgical treatment improve survival.12
In our study, the majority of patients evaluated were above 55 years of age and they were associated with the cases of mortality (p = 0.061). In 2014, Jong-Ming et al. analyzed the clinical characteristics of older patients (above 65 years of age) compared with younger patients (below 65 years of age). It was a retrospective study that included 73 patients, 24 of whom were older adults (32.87%). The most frequent initial presentation in the older adult patient was the state of shock, requiring reanimation measures for its management and a longer stay in the intensive care unit. The mortality rate was higher in that group, but with no statistical significance (16.21% of all the patients died). Of the patient total, those with a higher Fournier's gangrene severity score and a longer time in intensive care were associated with a higher mortality rate, compared with patients that survived (p ≤ 0.001, p = 0.030, respectively). Their study concluded that the clinical characteristics of the older adult patient with Fournier's gangrene were not different from those of younger patients and that older adults did not characteristically present with more advanced grades of the disease. Thus, they recommended strict monitoring of the vital signs and adequate cardiovascular support, especially in the elderly.13

Different factors should be considered during the initial evaluation of the patient with Fournier's gangrene to determine the degree of extension of the infectious process, but certain predictive factors for mortality should also be taken into account to be aware of the prognosis of the patients we treat. In 2015, Garcia-Marin et al. conducted a study that attempted to assess the predictive factors for mortality in cases diagnosed with Fournier's gangrene, and based on their results, they proposed a new predictive model for mortality. Their retrospective study included 59 patients, 44 of which survived [S] (74%) and 15 died [D] (26%). The independent predictive factors were peripheral vasculopathy, serum potassium, and severe sepsis criteria. The model was created with an ROC area under the curve of 0.850 (0.760-0.973), higher than the Fournier's gangrene severity index (0.746 [0.601-0.981]) and the Uludag Fournier's gangrene severity index (0.760 [0.617-0.904]). Among their conclusions, they state that Fournier's gangrene showed a high mortality rate and that the independent predictive factors observed were peripheral vasculopathy, serum potassium, and severe sepsis criteria.14

Considering the prognosis of our patients, once the initial evaluation is completed and radical surgery and broad-spectrum antibiotic therapy have been carried out (measures that have been shown to improve survival rates), the use of vacuum-assisted closure (VAC) systems are recommended. Obtaining a negative culture of the lesion, rehabilitation and reconstruction are performed to optimize the functional capacity of the patients. In 2013, Czymek et al. published a study that assessed the treatment, results, and quality of life after suffering Fournier's gangrene. The retrospective, multicenter study included 86 patients. The survivors were invited to form part of a follow-up and to fill out a quality of life questionnaire and a disease-specific questionnaire with special interest in physical examination. Their results showed that 83.7% of the affected patients were men, hospital stay was 52 ± 54 days (range: 1-329), 82.5% of the patients had a polymicrobial infection, and mortality was 16%. The SF-36 physical function questionnaires (p = 0.01), and the physical functioning (p = 0.008), general health (p = 0.01), and overall physical health (p = 0.006) items were significantly lower than those of the general population. Sexual function deterioration was reported in 65% of the cases. With these results, they concluded that patients with Fournier's gangrene experience physical and mental health problems for a long period of time after their first hospitalization and they recommend that these patients receive varied long-term specialized care. If this is not done, there is a resulting increase of morbidity and a reduced quality of life.15

In our study it was not possible to evaluate the use of negative pressure assisted closure systems or reconstructions and their results after treatment, given that this type of management is not often performed in our population due to economic limitations and treatment abandonment.

Conclusions

Fournier's gangrene is an entity that has a critical mortality rate associated with its rapid progression and devastating effects on patient functional capacity. Initial broad-spectrum antibiotic (with carbapenems) and aggressive surgical treatments have been shown to conclusively improve survival. Different factors at the initial evaluation can represent prognostic factors and in our population the most frequently associated factor was a low socioeconomic level followed by diabetes mellitus. After adequate treatment, rehabilitation and reconstruction should be considered for improving both the physical and mental functioning capacity of our patients.

Ethical responsibilities

Protection of persons and animals. The authors declare that no experiments were performed on humans or animals for this study.

Data confidentiality. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Financial disclosure

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Conflict of interest

Dr. Carlos Martinez-Arroyo belongs to the consulting group on behalf of the BAARD brand. None of the other above-mentioned authors have any conflict of interest.

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Bibliografía