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Fournier gangrene. A retrospective study of 41 cases☆

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A B S T R A C T

Introduction: Fournier's gangrene is a rapidly progressing necrotizing fascitis that affects the perineal and genital area. Mortality still remains high. The aim of this study was to evaluate the epidemiological progression and morbidity-mortality of Fournier's gangrene at our centre over the past 10 years.

Methods: Retrospective study of 41 patients treated for Fournier's gangrene between 1998 and 2007. Variables studied included, demographic variables, aetiology, microbiology, surgical and antibiotic treatment, morbidity, and mortality.

Results: The mean age of the patients was 60, and 93% were male. The most common co-morbidity was diabetes (49%), followed by alcoholism (46%) and immunosuppression or neoplasia (34%). The origin was perianal in 66% of cases, followed by a urological origin (32%). The median time from the onset of symptoms to diagnosis was 3 days. Several surgical debridements were required in 49% of the patients, and the mortality rate was 29%. Most cases had positive cultures (93%), and in 76% more than one microorganism was isolated (enterobacteriaceae and anaerobic flora). In the bivariate analysis, antimicrobial treatment with carbapenems and the absence of systemic complications were associated with lower mortality.

Conclusions: Fournier's gangrene continues to be a severe surgical emergency, with a high mortality rate. Early diagnosis and aggressive surgical and antibiotic therapy are necessary for adequate management.

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Gangrena de Fournier: Estudio retrospectivo de 41 casos

Palabras clave:
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RESUMEN

Introducción: La gangrena de Fournier es una fascitis necrotizante con diseminación rápidamente progresiva que afecta la región perineal y genital. A pesar de los avances terapéuticos, puede relacionarse a un alto índice de mortalidad. El objetivo de este estudio es analizar la epidemiología y la morbimortalidad de la gangrena de Fournier en nuestro centro en los últimos años.

Material y métodos: Estudio retrospectivo de 41 pacientes con diagnóstico de gangrena de Fournier tratados entre los años 1998–2007. Se analizaron datos correspondientes a edad, sexo, comorbilidad, origen, extensión, evolución, estudio microbiológico, aspectos quirúrgicos, tratamiento antibiótico y mortalidad.

Resultados: De los 41 pacientes tratados en este periodo, el 93% fueron hombres, con edad media de 60 años. La diabetes fue el antecedente patológico más común (49%) seguido del alcoholismo (46%) y la inmunosupresión o neoplasia (34%). El origen fue perianal en el 66% de los casos, seguido del urológico (32%). El tiempo de evolución antes del diagnóstico fue 3 días (mediana). El 49% precisaron varias revisiones quirúrgicas, y la mortalidad fue del 29%. La mayoría (93%) de los cultivos fueron positivos, y en el 76% de los casos se aisló más de un microorganismo (los más frecuentemente aislados fueron enterobacterias y anaerobios). En el análisis univariado, el tratamiento antibiótico con carbapenémicos y la ausencia de complicaciones sistémicas se asociaron a menor mortalidad.

Conclusiones: La gangrena de Fournier sigue siendo una patología grave con una mortalidad elevada. El diagnóstico precoz y tratamiento quirúrgico y antibioterápico agresivos son necesarios para su adecuado tratamiento.

Introduction

Fournier's gangrene (FG) is a necrotising fasciitis of infectious aetiology that produces a rapidly progressive necrotising gangrene of the genito-perineum. The first author who described this disease was Baurienne in 1764.[1-4] However, it was not until 1883 when the French venereologist Jean Alfred Fournier described the clinical features of the disease following examination of a personal series of 5 cases.[5] Fournier attributed the gangrenous process to an idiopathic aetiology, although today is considered the result of a polymicrobial infection involving aerobic and anaerobic pathogens. The process mainly affects males, and although it has a broad age range, mainly affects patients over the age of 50.[6]

Risk factors include diabetes mellitus (DM), chronic alcoholism, malignant neoplasms and HIV.[7] It originates in the genitourinary and anorectal areas and frequently spreads to the anterior abdominal wall. This progression is a result of vascular thrombosis secondary to endarteritis obliterans, which allows the normal microbial flora to penetrate by fascial dissection into previously sterile spaces. The conditions of low oxygen pressure, limited vascular supply and bacterial overgrowth lead to the production of hydrogen and nitrogen by anaerobic microorganisms that accumulate in the subcutaneous tissue, clinically resulting in crepitus of the affected territories.[8]

This translates clinically in the vast majority of cases in severe sepsis. Despite the therapeutic advances in recent years, mortality is between 3%-67%, according to published series.[9]

The aim of this study was to analyze the clinical and epidemiological characteristics of the patients with FG and compare our results with previously published series. A secondary objective was to determine the factors associated with mortality in these patients.

Materials and methods

The present study included retrospectively all patients with FG treated in the University Hospital of Bellvitge, a tertiary care adult's centre, by the Departments of General and Digestive Surgery and the Department of Urology between 1998–2007.

The diagnosis of FG was made from anamnesis, physical examination, imaging and intraoperative findings, based on the following criteria, modified from Kuo et al[10]: 1) soft tissue infections with involvement of the scrotum, perineum or perianal areas 2) presence of air infiltrating the subcutaneous tissue, demonstrated by physical examination or radiological findings, 3) surgical findings of gangrenous and necrotic tissue, 4) histologically proven necrotising fasciitis.

Data were collected for age, sex, comorbidities, origin, extent, evolution, microbiological studies, surgical aspects, antibiotic therapy, postoperative morbidity and mortality during hospitalisation.

The descriptive data analysis is shown as mean or median (continuous variables) or percentage (categorical variable). Given the sample size, for the comparison of variables potentially related to mortality between the two groups (alive and dead) nonparametric tests (Mann-Whitney U for continuous variables and Fisher for categorical) were used. Multivariate analysis was performed using statistically significant variables in the bivariate analysis, and then adjusted for age, sex and underlying disease, using a stepwise regression method. All tests were performed using the software SPSS, version 15.0. Statistical significance was set at $P<.05$ for all analyses.

Results

A total of 41 patients were diagnosed and treated at the University Hospital of Bellvitge by the Departments of General and Digestive Surgery or Urology during the years 1998–2007. Thirty-eight (93%) of the 41 patients were male. The median age was 60 years (range: 19-78).

A total of 20 patients were diabetic (49%), being the most common antecedent in this series, followed by active alcoholism (46%). Demographic data and comorbidities are shown in Table 1.

The origin of the infection was: perianal in 27 cases (66%), urological in 13 (32%) and gynaecological in 1 (2%).

In 8 patients (20%) radiological examinations were performed to delineate the extent of the process. Six patients underwent CT and 2 ultrasound imaging.

The mean evolution time was 3 days (1–15 days). In 14 patients (34%) there was a diagnostic delay (defined as a previous visit to an emergency department). Data from physical examination and laboratory are shown in Table 2.

The mean length of stay was 18 days (range 1–64 days). A total of 26 patients (68%) required admission to the intensive care unit for a period longer than 24 h, with a mean stay in the unit of 5.5 days (2–62 days).

All patients in this study were treated with extensive surgical debridement, broad-spectrum antibiotics and topical wound care during admission (Figure 1). Twenty patients (49%) required reoperation, mainly in the first 96 hours (50%). Five patients (12%) required a third surgery. Completion of intestinal stoma was required in 37% of cases. In a total of 15 colostomies, FG aetiology was perianal in 12 patients (80%) and urological in 3 cases (20%). Three patients with colostomy died in the postoperative period.

Suprapubic cystostomy was also performed in 22% of patients, orchiectomy in 5% and penectomy 2%.

In 38 of the 41 cases the cultures of the samples harvested during surgery were positive and in most of these cases (76%) 2 or more microorganisms were isolated. By groups, the most frequently isolated organisms were anaerobic of any type (63%), followed by Enterobacteriaceae (32%) and polymicrobial cultures without predominance of any particular microorganism (29%). Except for the anaerobes, the most frequently isolated species was E. coli. Potentially resistant organisms such as *Acinetobacter* spp., *methicillin-resistant S.*

Table 1 – Demographics and comorbidities (No.=41)

Predisposing factor/risk	n	%
Sex male	38	93
DM	20	49
HIV	0	0
Chronic alcoholism	19	46
Psychiatric illness	6	15
Pharmacological immunosuppression	5	12
Active neoplasm	9	22
Metastatic	5	12
Urologic or colorectal neoplasm	6	14
Obesity	5	12
Vasculopathy	1	2
CVH	1	2
Bladder outlet obstruction syndrome	2	5
Previous urological manipulation	3	7

DM indicates diabetes mellitus.

Table 2 – Physical examination and laboratory (No.=41)

Physical examination	
Temperature, °C	37.3 (1.1)
Heart rate,* bpm	97 (78–150)
Laboratory	
Na, mmol/l	134 (5.4)
K, mEq/l	3.9 (0.7)
Cr,* µmol/l	114 (57–631)
Urea,* mmol/l	9.4 (2.1–27.7)
Blood glucose,* mmol/l	9.1 (4.4–31.5)
Bicarbonate, mmol/l	25.7 (4.5)
Fibrinogen, g/	8.5 (1.9)
Haematocrit,* l/l	37.7 (13.3–45.9)
Hb,* g/l	12,7 (6,5–15,6)
WBC, /µl	18,353 (8,352)
Neutrophils* (%)	85.9 (68–92)
Lymphocytes (%)	7.1 (3.3)
Platelets,* /µl	240,268 (58.000–788,000)

All values are expressed as mean (SD) except the variables marked with * that are expressed in median (range).

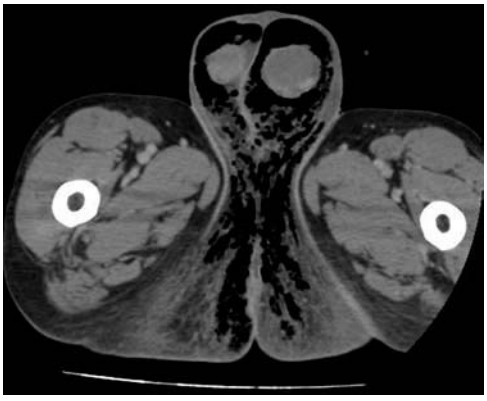

Figure 1 – Abdominal CT.

Table 3 – Microbiology (No.=41)

Aerobics	n (30)	%	Anaerobics	n (36)	%
Enterobacteriaceae	13	43.3	Peptostreptococcus	12	33.3
E. Coli	10		Bacteroides	7	19.4
Proteus	2		*Bacteroides fragilis*	4	
Morganella morganii	1		*Bacteriodes distasonis*	1	
Streptococcus	12	40	*Bacteroides caccae*	1	
Streptococcus intermedius	6		Prevotella	5	13.9
Streptococcus anginosus	1		*Prevotella sp*	2	
Streptococcus agalactiae	1		*Prevotella bivia*	2	
Streptococcus bovis	1		*Prevotella intermedia*	1	
Streptococcus viridans	1		Eubacterium	4	11.1
Streptococcus pyogenes	1		*Eubacterium aerofagens*	1	
Streptococcus sanguis	1		*Eubacterium lentum*	1	
Staphylococcus	3	10	Clostridium	3	8.3
Staphylococcus aureus	2		*Clostridium perfringens*	1	
Staphylococcus lugdunensis	1		Lactobacillus	3	8.3
Enterococcus	1	3.3	Porphyromonas	2	5.6
Enterococcus faecalis	1		*Porphyromonas asaccharolyticus*	2	
Acinetobacter	1	3.3			
Acinetobacter baumanii	1				

Table 4 – Postoperative complications

Complications	n	%
Renal failure	9	39
Acute respiratory distress syndrome	6	26
Heart failure	8	35
Cardiac arrhythmias	2	9
Septic metastasis	1	4
Other complications	5	22

aureus and *Enterococcus* spp. were isolated infrequently (Table 3). Most patients received empirical antibiotic monotherapy with broad-spectrum agents, being carbapenems the most frequent choice (61%), followed by beta-lactams associated with beta-lactamase inhibitors (22%).

Postoperative complications occurred in 56% of patients (Table 4). Despite aggressive surgical and antibiotic treatment, 29% of the patients died during hospitalisation. When comparing the group of survivors (n=29) with the group of patients who died (n=12), by bivariate analysis the only variables associated with significantly higher mortality were the presence of complications (38% vs 75%, *P*=.03), treatment with carbapenems (72% vs 33%, *P*=.03), haematocrit (mean 38 versus mean 32, *P*=.006) and temperature (mean = 37.5 ºC compared to 36.8 ºC, *P*=.041). The need for stoma was not significantly associated with mortality. The logistic regression analysis did not identify any factor independently associated with mortality in patients with FG.

Discussion

A number of underlying systemic disorders have been identified frequently in the FG and, in some series, have been associated with mortality.[9,11,12] In all cases, there was a decrease in the host cellular immunity that determined the development of the infection. Among them, DM (20%–70%) is worth to mention. Most authors consider DM as a risk factor although there is some disagreement on whether it is associated with increased mortality. According to Nisbet, diabetes is a risk factor for the occurrence of FG, but does not affect the prognosis.[11] In contrast, Yanar found no increased mortality among diabetic patients.[12] In our series, diabetes is listed as underlying pathology in 49% of patients, data that agrees with the literature, but has not been found significantly related to mortality.

Chronic alcoholism has been described as a risk factor for FG with a frequency of 4–66% and has been associated with worse prognosis, especially in those patients with DM.[13] Also, in our series, we detected a high percentage of chronic alcoholism (46%).

Other associated factors include organ transplantation,[14,15] antineoplastic treatments,[16-18] HIV[19,20] and gastrointestinal disease.[7]

Laor et al[21] established a prognostic index, the FGSI (Fournier's Gangrene Severity Index) to determine the severity and prognosis of the disease in their patients. This index was subsequently validated by Yeniyol and Tuncer.[22,23] The parameters used in the FGSI are: temperature, heart rate,

respiratory rate, serum sodium, serum potassium, serum creatinine, serum bicarbonate, haematocrit and white blood cell count. In our series only temperature and haematocrit have been related with mortality.

In doubtful cases the implementation of imaging techniques can be very useful. Plain abdominal x-rays may reveal the presence of gas in the subcutaneous tissue, although soft tissue ultrasonography and CT have high sensitivity for the detection of this phenomenon.[24] Soft tissue ultrasonography is very useful in the initial stages of the disease, and can detect thickening of the scrotal wall and the presence of subcutaneous gas. However, this technique has a high false negative rate (10–21%).[25-27]

CT and MRI are also useful in the early diagnosis of FG aiming the presence of gas in the subcutaneous tissue, thickening of the scrotal wall and indemnity of testes and epididymides (Figure 2). These techniques can also report on the cause and are useful for delineating the extent of the process.[28,29] In this series, the use of these tests was not considered necessary in most cases because the clinical history and physical findings were compatible enough to make the diagnosis of FG and indicate the surgical treatment.

Nowadays, FG is considered usually a polymicrobial infection[6,7], involving synergistic aerobic and anaerobic bacteria. Most bacteria isolated from cultures are often part of normal flora, but, in combination with local and systemic factors, they can acquire high virulence. The role of anaerobes in the FG is sometimes manifested by a characteristic odour, which is considered pathognomonic of its participation.[6] However, in many cases it cannot be proved by the cultures (the inadequate processing of samples and more strict nutritional requirements are common causes of this).[30] Unlike most published series, in our series anaerobic involvement has been identified in most cases.

Key parts of FG treatment are general supportive measures. Rapid haemodynamic stabilisation, correction of distributive shock, correction of electrolytic abnormalities and energy intake that confers an adequate nutritional status throughout the process are necessary.[31]

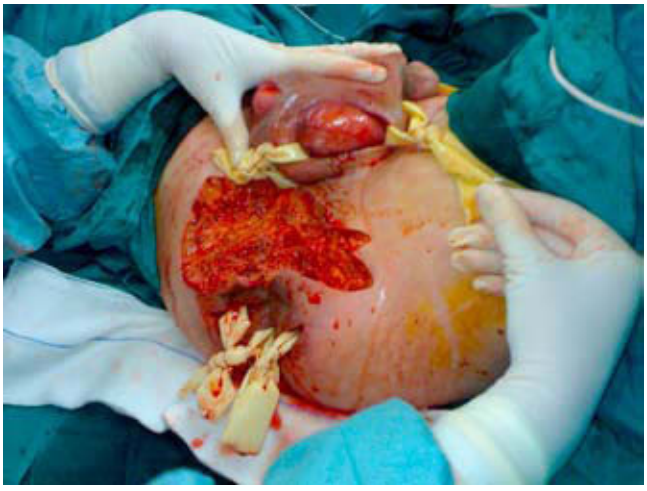

Figure 2 – Surgical debridement.

Given the severity of the symptoms and the rapid progression of this disease, surgical exploration should be done quickly, with radical debridement of all necrotic areas. Large incisions through the skin and subcutaneous tissues should be made, which must overpass affected areas until normal fascia are found.[8,13,32] Abundant washes of the debrided area are performed and the wound is left open. If after 24–48 hours there is persistence of areas affected by necrosis, a second surgical procedure, similar to that observed in our series, should be indicated.

In selected cases, intestinal or urinary tract derivations will also be required. If it is suspected that the cause is urethral trauma or extravasation of urine, a suprapubic cystostomy should be done, in order to prevent retrograde bladder catheterisation.[32] The performance of a colostomy is reserved for cases in which during surgery has been demonstrated rectal or colonic perforation or anal sphincter involvement.[8,13,32,33] Although there are discrepancies, intestinal bypass can be considered in order to prevent faecal contamination of the wound.[34] In our centre, this indication depends on the surgeon's indication. In all patients with colostomy, the reason for performing the procedure was proctitis or anal sphincter necrosis.

The indication of penectomy or orchiectomy is rare because the penis and testicles have their own blood supply independent of the compromised circulation of the fascia and skin of the scrotum.[34] Despite this, 2 of our patients required orchiectomy, and one patient penectomy.

Other adjuvant therapies such as local application of honey, VAC therapy, and hyperbaric oxygen therapy have been described for infections caused by Clostridium, in some series associated with stoma in selected cases, with promising results.[34,36] In our centre these forms of therapy were not available during the study period.

Antibiotic intravenous therapy should be carried out empirically with broad-spectrum antibiotics covering gram-positive cocci, gram-negative bacilli and anaerobes. A classic pattern is the use of the triple treatment with: 1) third-generation cephalosporins or aminoglycosides for gram-negative coverage, 2) benzathine benzylpenicillin or amoxicillin for streptococcus species, 3) metronidazole or clindamycin for anerobics.[35] Recent studies advise the administration of third-generation cephalosporins and metronidazole, and gentamicin could be added.[23,36] Monotherapy with carbapenems (imipenem, meropenem, ertapenem) or broad-spectrum beta-lactams of ureidopenicillins (piperacillin-tazobactam) is equally effective, and simpler to administer.[31]

In our hospital, taking into account the microorganisms isolated later, empiric antibiotic treatment was appropriate in 86% of cases. The inadequacy of empirical antibiotic therapy was triggered by the presence of multiresistant pathogens such as methicillin-resistant *Staphylococcus aureus* and *Acinetobacter baumannii*. Although we observed a lower mortality associated with carbapenem treatment, this fact has not been confirmed as a factor independently associated with mortality.

Conclusions

In our centre, in the past 10 years, FG has been presented as a severe disease with a high mortality. For its proper treatment a high diagnostic suspicion and early recognition, surgical treatment and aggressive antibiotic therapy are still necessary.

Conflict of interest

The authors affirm that they have no conflicts of interest.

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