Fournier gangrene

Approaches to diagnosis and treatment

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ABSTRACT

Objectives: To investigate the factors associated with patients with Fournier's gangrene, and to clarify the effect of diabetes mellitus (DM) as a comorbid disease on morbidity and mortality of patients with Fournier's gangrene.

Methods: Twenty-six Fournier's gangrene patients who were admitted to the Emergency Department of Ankara Numune Teaching and Research Hospital, Ankara, Turkey from 1997 to 2003 were examined retrospectively.

Results: The mean age of the patients was 52.8 years. There were 8 female (30.8%) and 18 male (69.2%) patients. The etiological causes were as follows: diseases of the perianal region, history of operations, trauma and injections. Major comorbid disease states were diabetes mellitus (DM) and hypertension. The lesions in Fournier's gangrene were most commonly located in the perineum and genital region. Female patients with diabetes mellitus had significantly unusual extensive involvement, especially abdominal wall involvement. The most frequently isolated pathogen was *Escherichia coli*, while staphylococcal infection was most commonly seen in the presence of DM. Colostomy was performed on 53.8% of the patients, and cystostomy on 7.6% of the patients. Average time of staying at the hospital was 25 days with a mortality rate of 34.6%. Patients with DM had high mortality rates and stayed longer at the hospital than the non-diabetic patients.

Conclusion: In addition to early diagnosis, early and aggressive debridement and administration of multiple wide spectrum antibiotics chosen for the causative agent are the golden standard for decreasing the mortality and morbidity. Diabetes mellitus has been found to be an important factor to increase mortality rates of patients with Fournier's gangrene.

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Fournier's gangrene (FG) has been first reported in 1764; in 1883, a French dermatologist and venereologist, Jean Alfred Fournier, made the first definition in the literature, and in 1920, the first surgical intervention was proposed.[1] After this date, this clinical entity has been described by different terminological alternatives such as; "streptococcal gangrene", "necrotizing fasciitis", "suppurative fasciitis", "acute dermal gangrene" and "progressive dermal gangrene".[2] Today, FG is known as the "progressive necrotizing fasciitis" of the perineum and genital region.[3] Fasciitis is usually of superficial nature affecting colles fascia; it extends throughout dartos fascia in scrotum, penis and to Scarpa fascia at a superior

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level. However, due to the high vascularizations of the penis and the scrotum, it is usually thought to be localized to the perineum.[4] It usually presents itself as a synergistic microbiological entity caused by aerobic and anaerobic organisms together.[1,4-6] Most commonly encountered pathogens are; *Escherichia coli (E. coli)*, *Staphylococci*, *Streptococci* and *Proteus*.[1,3,4,6,7] Although several studies have been reported regarding the etiopathogenesis, progression and treatment strategies for the disease, its mortality continues to be very high (0-67%).[1,4,8] The main predisposing factors contributing to the occurrence of the disease are: diabetes mellitus (DM), alcohol uses, immunosuppression, liver and kidney disease.[1-7] Generally, in the presence of such predisposing factors, especially DM, a pathogen of low virulence found in the rectum or perianal flora gets aggressive and triggers the disease; the process can have a fatal course by sepsis that might ensue. Until today, the most important approaches in reducing mortality were early diagnosis, early surgical debridement and administration of multiple aggressive antibiotic therapies.[1,4,9]

We aimed to evaluate the factors associated with FG. Treatment approaches used in these patients were analyzed in an attempt to discuss our own experience with regard to this aggressive clinical entity.

Methods. Twenty-six patients who were diagnosed with FG from 1997 to 2003 at the Emergency Department of Ankara Numune Teaching and Research Hospital, Ankara, Turkey were retrospectively evaluated. Factors playing a role in the etiology, existence of predisposing disease states, clinical and laboratory characteristics of the patients and the influences of all such factors on mortality and morbidity were investigated. Furthermore, the surgical procedures employed in these groups of patients, the need for colostomy and cystostomy, the methodology employed for choosing the medical treatment alternatives were all examined in an attempt to reflect our own clinical experience.

The Statistical Package for Social Sciences for Windows version 10 program was used for the statistical analyses. The comparisons between the groups were realized using chi-square and t-tests, where appropriate. A *p*-value of lesser than 0.05 was accepted as having statistical significance.

Results. There were 18 male (69.2%) and 8 female patients (30.8%). The mean age was 52.8 (19-90) years. The average period of staying at the hospital was 25 days, ranging from 4-75 days. The mortality rate was 34% (n=9). The age and gender difference

did not have any effect on mortality (*p*>0.05), but FG was significantly higher in female patients with DM (*p*=0.011).

With regard to the etiological focus of the disease, 11 patients (42.3%) had diseases of the perianal region (perianal abscess, hemorrhoids, fistulas) (**Figure 1**), 4 patients (15.4%) had history of operations (transurethral resection, ureteroplasty, urethral stenosis, vascular graft resection for by-pass operation), 4 patients (15.4%) had trauma in their history (traffic accidents, application of a vascular graft to the left leg due to a stab wound), 1 patient (3.8%) had a history of an injection. In 6 patients (23.1%) no factor that could be named as foci was identified. History of perianal region diseases and past history of operation had a greater role in etiology of FG diseases in diabetic patients (**Table 1**).

Fifty-three percent (n=14) of wound cultures had growth of multiple microorganisms, while 47% had a single microorganism. *Escherichia coli* was isolated in 61.5% of patients. The other organisms were *Staphylococcus aureus* and *Streptococcus*, *Klebsiella*, *Pseudomonas*, *Acinetobacter* and *Enterobacteria* (**Table 1**). *Escherichia coli* was the most commonly observed pathogen in both group, but *Staphylococcal* infection was seen to be 53.8% in diabetic patients, while 15.4% in non-diabetic patients. There was no correlation between mortality, and having single or multiple organisms growing in the culture or the type of the microorganism identified (*p*>0.05). However, multiple microorganisms were seen to be higher in diabetic patients than non-diabetic patients (77.4-30.6%). After being admitted to the hospital, 69.2% of the patients received empirical dual anti-biotherapy, 23% had 3 antibiotics and 7.6% had an anti-biotherapy with a single agent. Treatment was further adjusted depending on the results of the culture-antibiograms. All patients were isolated during the acute period, 6 patients (23.1%) needed to be followed-up in the intensive care unit in the early course of their disease.

As to the localization, 69.2% of the patients had multiple lesions in the perineum, genital region, inguinal region, anterior abdominal wall and the extremities; while the remaining 42.3% of the patients had lesions only localized in the genital region. Patients with DM had an extensive involvement (*p*=0.001). Patients with DM had abdominal involvement (61.2%), but non-diabetic patients had no abdominal involvement. Patients with abdominal wall involvement had higher mortality rate than the others (50-27%). There were no significant relations between the involved region and mortality (*p*>0.05). Predisposing principal factors were identified in 18 (69.3%) of patients. Most

Table 1 - The parameters affecting diabetic and non-diabetic FG patients

Parameters	No. of patients (%)				P-value
	Diabetic		**Non-diabetic**		
Gender					
Male	6	(46.2)	12	(92.3)	
Female	7	(53.8)	1	(7.7)	0.011
Etiology					
Perianal region disease	7	(53.8)	4	(30.6)	
Operation	3	(23.1)	1	(7.6)	
Trauma	0	0	4	(30.6)	
Injection	0	0	1	(7.6)	
Idiopathic	3	(23.1)	3	(23.1)	
Microorganism					
Single	4	(30.6)	8	(61.2)	
Multiple	10	(77.4)	4	(30.6)	
Escherichia coli	9	(69.2)	7	(53.4)	
Staphylococci	7	(53.8)	2	(15.4)	
Streptococci	4	(30.6)	4	(30.6)	
Klebsiella	2	(15.4)	4	(30.6)	
Acidomonas	1	(7.6)	1	(7.6)	
Acinetobacter	1	(7.6)	0	0	
Enterobacteria	0	0	1	(7.6)	0.078
Having Colostomy	7	(53.8)	7	(53.8)	1
Abdominal wall involvement	8	(61.2)	0	0	0.001
Average hospital stay	37.67 ± 22		24.09 ± 12		0.076
Mortality rate	7	(53.8)	2	(15.4)	0.039

frequent comorbidity was DM, which was observed in 13 (50.0%) patients. Four patients (15.3%) had hypertension, 3 had atherosclerotic cardiac diseases, 3 had medication and 3 patients used to smoke as a predisposing factor. Eight patients (30.7%) did not have any comorbidity while 6 patients (23.1%) had more than one disease states. The mortality rates were significantly higher in patients with comorbid disease states (0-50%) (*p*=0.013). Mortality rate was 53.8% in the patients with DM, but 4.4% in the non-diabetic Fournier gangrene patients (*p*=0.039, **Table 1**). Diabetic patients stayed in the hospital for 37.67 ± 22 days, but it was 24.09 ± 12 days for non-diabetic patients (*p*=0.076).

All necrotic tissues including skin, subcutaneous tissues, fascia and muscle were débrided until the appearance of well-vascularized tissue (**Figure 2**). Aggressive debridement was performed for 2-3 times in 11 patients (44%), 4 or more times in 5 patients (20%). Although it was not statistically significant, number of operations performed was higher in diabetic patients. Fifty-three percent of diabetic patients had 2 or more operation, while only 30.8% in non-diabetic patients. Eighty percent of DM patients and 20% of non-diabetic patients had operation more than 4 times. The patients who had good progression of the wound

site, whose wounds were clean and had granulation tissue received grafts (**Figures 3 & 4**). Colostomy was generally preferred in patients who had involvement of the perineum and genital region together with the damage of the sphincter. Fifty-three percent of the patients (n=14) had required colostomies. Two patients (7.69%) had undergone cystostomy to be protected from urinary contamination and for the repair of the urethral perforation. The mortality rate was higher in patients with colostomies (50%) than patients who did not require colostomies (16.7%) (*p*=0.075). There were no correlations between the presence of DM and having colostomies or cystostomies.

Discussion. In contrast with the initial definition, FG can be observed in both gender at all ages, and men still have a higher incidence of the disease than women. In a series by Eke et al[1] with 1726 patients, male to female ratio was stated as 10:1. The reason behind was the fact that women had better drainage of perineal secretions.[1,4] In our study, 30.8% of the patients were women and 69.2% were men. Fournier's gangrene can be seen in all ages; furthermore, the incidence might increase together with the increase in the age, and being 60 or above might also influence the mortality.[1,4,10] However, in a study by Asci et

Figure 1 - Perianal abscess was detected as an etiologic factor in female patient.

Figure 2 - Necrosis rapidly invaded tissues including skin, subcutaneous tissues and camper fascia in same patient.
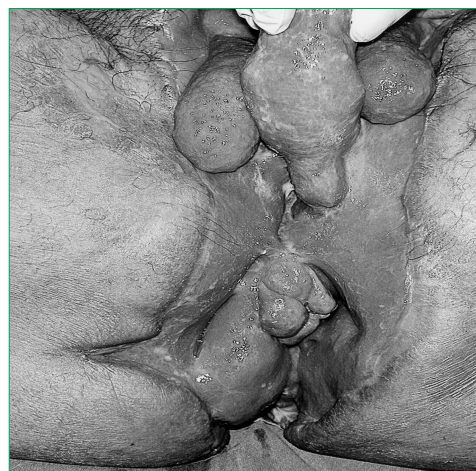

Figure 3 - Aggressive perineal necrosis of a patient. Clean and granulation tissues had been achieved after the multiple and wide surgical debridement. The patient had urethral necrosis as a result of involvement of urethra. Cystostomy was applied to this patient due to of urethral perforation.

Figure 4 - Appearance of patients with perineal and scrotal necrosis after the receiving graft.

al[11] mortality was not influenced by age. In our study, the mean age of the patients was 52.8 years and a correlation could not be found between age and mortality. The fact that the disease is more frequently seen at advanced age might be the result of the increase in life expectancy.

The source of the infection is thought to be a pathogen of colorectal or urological origin being imposed on local skin lesion thereby gaining high virulence. The evolving pathogens exert synergistic effects on each other and resulting in local thrombosis and ischemia, which spread to the fascial planes.[1,4,6,9] Different etiological sources have been quoted at different rates in various studies, yet the most common origin of infection is related to colorectal sources.[4] Hollabaugh et al[12] reported 19% as related with colorectal sources; however, Benizri et al[13] reported 58% to be such cases. Most of these figures are generated by perirectal and perianal infections.[1,6] Other possible sources of colorectal origin are perforated appendicitis, carcinoma of the colon, diverticulitis, perforation of the rectum and Crohn's disease.[14-18] Most commonly encountered urological causes are urethral stenosis, renal abscesses, renal stones and urethral traumas.[1,6] In 70-100% of FG cases, etiological factors can be identified; however, sometimes it might not be possible to identify any etiological factor.[7,12,19] In our series, we identified the etiological cause in 20 of 26 patients (76.9%); 42.3% of these were diseases of the perianal region. In the remaining patients in whom the source could not be identified, we think that a subtle and superficial skin lesion was complicated with comorbid disease states resulting in this clinical presentation.

There are studies claiming the fact that FG might be related to several diseases and these might be influential on the prognosis of the disease. Diabetes mellitus is the most commonly encountered comorbid disease state. According to Eke et al,[1] DM is seen in 20% of FG cases, while Yaghan et al[20] state this as 70%. It is still controversial whether the prognosis is hindered or not, when the DM was comorbidity in FG patients.[13,21] In our study the prevalence of DM was 50%. Mortality rates were significantly found to be higher in FG patients with comorbid conditions. Especially in patients with DM, mortality rate was higher; they stayed longer at the hospital and had higher abdominal wall involvement. It is very well known that in diabetic patients, chemotaxis, phagocytosis and intracellular digestion functions have all deteriorated and in circulation, which is impaired due to diabetic angiopathy, predisposes the individual to an infection. Furthermore, diabetic patients develop neuropathy, which delays their referral to the hospital as well as wound healing. According to Rajbhandari et al,[22] diabetic patients carry more numerous pathogens with a tendency for skin infections and are less resistant to such infections. In the present study, number of pathogens was high in diabetic patients and these patients had higher incidence of perianal history. This situation was supported by the theory that was explained above. In addition, we demonstrated that presence of DM in FG caused higher incidence of *Staphylococcal* infection as a hospital opportunistic infection. Immunosuppression, alcoholism, hypertension, smoking, histories of drug use and trauma are other comorbid factors accompanying the disease. In many studies these factors have been identified at different frequencies in FG cases.[1,4,6,9] Berg et al[23] and Martinelli et al[24] found higher mortality rates especially in immunosuppressed patients. In a study by Norton et al,[9] no correlation was found between mortality and DM, hypertension, alcoholism or smoking.

There is no specific microorganism for FG. In different studies, despite the fact that similar organisms have been identified, they were identified at different frequencies. Most commonly observed microorganisms were *E. coli*, *Staphylococci*, *Streptococci*, *Proteus*, *Klebsiella*, *Pseudomonas*, *Clostridium*, *Bacteroides* and *Enterobacter* group, and these were generally observed in combination.[1,2,4,6,7,9] However, the microorganism could not be identified in cultures.[13,25] In our study group, 53% of the patients had growth of more than one pathogen in their cultures. Most commonly identified microorganism was *E. coli* with a frequency of 61.5%, and bacteriological reports for our patients were not different from other studies.

Furthermore, in our study there was no correlation between mortality and the type of microorganism or its being single or multiple. This might make us consider the fact that rather than the presence of single or multiple organisms, the virulence of the microorganism and host related factors were to be taken into account.

Early and aggressive surgical management is the most important aspect of the treatment of this disease. We applied debridement in all of our cases. Debridement was repeated more than 4 times in 20% of the cases, and at least 2 times in 44% of the patients. The patients who had good progression of the wound site received grafts. Other surgical options for FG patients are colonic and urinary diversions. Colostomy and cystostomy attempts have been recommended at different rates in different studies in cases with the involvement of the pararectal region in the necrosis and the presence of sphincteric damage, and also in cases with the involvement of the urethra in the necrosis together with urinary contamination. This rate changes between 0-57% for colostomies and between 0-32% for urinary diversions.[4,6] In our study these figures were 53.8% for colostomy and 7.7% for cystostomy. Another conclusion that we arrived from our study was that in patients undergoing colostomy operations, mortality was higher and very close to the limit of being significant (p=0.075). Similarly in a study by Saenz et al,[6] 10 out of 28 patients who had fatal courses, all patients were identified to have undergone colostomy or cystostomy. This is due to the fact that the patients chosen for colostomy have more widespread lesions together with the possibility of pathogens of colonic origin showing more rapid progression.

The initiation of broad-spectrum antibiotic treatment as early as possible without waiting for the results of gram stains or cultures should be the second main principal in the treatment of FG. In the beginning, the antibiotic treatment should be directed at gram positive, gram negative and anaerobic microorganisms.[1,2-4,6,13] We have to be alert for *Staphylococcal* infection in diabetic FG patients. In addition to medical treatment enteral or parenteral nutritional support should be provided for positive nitrogen balance.[2,3] Enteral nutrition was recommended due to the intolerable adverse effects of parenteral nutrition.[21,26] Fifty-four percent of our patients received nutritional support. Certain studies claim that beneficial effects are obtained by the addition of hyperbaric oxygen (HBO) to the medical treatment.[8,12,27] However, there are others claiming that HBO did not reduce the mortality to a significant extent.[28] As we did not have a HBO system

in our hospital, we could not find the opportunity to investigate the efficacy of this treatment option.

Mortality rate changes between 0-67% in different studies. This rate might be effected by age, immunosuppression, primarily by DM and other comorbid disease states and factors such as renal and hepatic failure.[13,15,24,27] The duration of stay at the hospital for FG ranged between 2-278 days.[29,30] In our study, the mortality rate was 34.6%, and the mean duration of staying at the hospital was 25 days (ranged from 4-75 days).

In conclusion, despite the developments in intensive care conditions and broad spectrum antibiotics, FG still carries a high rate of mortality and morbidity. The cornerstone of treatment is the sufficient and timely surgical intervention. In addition to surgery, we should refrain from single type approaches and try providing aggressive antibiotic treatment and struggle with predisposing factors. We believe that a multidisciplinary approach will help to save patients with FG.

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