Original Article

Fournier's gangrene and diabetes mellitus: Our experience with 50 patients

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Abstract

Introduction: Fournier's gangrene is a rare, rapidly progressive, necrotizing fasciitis of the external genitalia and perineum. In this study we aimed to share our experience as association of diabetes mellitus as most important and independent risk factor for development of Fournier's gangrene and its direct relation to mortality. **Methods:** This is a retrospective study of the patient admitted in RCSMGMC CPR Hospital from January 2015 to June 2016, of 50 patients with Fournier's gangrene and diabetes mellitus to analyze association of diabetes mellitus for development of Fournier's gangrene and as a prognostic indicator of mortality. **Results:** All the 50 patients were male. The mean age was 48 years (range 30– 75 years). Average length of treatment was 25.8 days (from 14 to 36 days). The most common predisposing factor was diabetes mellitus (100%). E. coli was the most frequent bacterial organisms cultured. Etiology of FG was perianal infection in 36 patients (72 %), Urogenital infection in 11 patients (22 %), and skin infection in 3 patients (6 %). All patients were treated with a common approach of resuscitation, broad-spectrum antibiotics, and wide surgical excision. The mortality rate was 24%. The advanced age, renal failure on admission, extension of infection to the abdominal wall, occurrence of septic shock and need for postoperative mechanical ventilation are the main prognostic factors of mortality. Dm was not determined as a risk factor for mortality. **Conclusions:** Fournier's gangrene is still a very severe disease with high mortality rates. Early recognition of infection associated with invasive and aggressive treatment is essential to reduce these prognostic indices. Our hypothesis is that the key of the successful treatment is to treat as soon as symptoms onset, early and aggressive necrosectomy under broad antibiotic coverage. Dm was not determined as a risk factor for mortality.

Keywords: Fournier's gangrene, Mortality, diabetes mellitus, Outcome analysis.

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Received Date: 05/07/2016 Revised Date: 13/08/2016 Accepted Date: 03/09/2016

Access this article online

Quick Response Code:

Website: www.statperson.com

DOI: 12 September 2016

INTRODUCTION

Fournier's gangrene (FG) is a rare, rapidly progressive, fulminant form of necrotizing fasciitis of the genital, perianal and perineal regions, which may extend up to the abdominal wall between the fascial planes[1]. The scrotum readily develops dermal gangrene because it has virtually no subcutaneous fat between the epidermis and dartos muscle. These infections are typically polymicrobial, with both aerobic and anaerobic organisms present in the majority of cases.[2,3,4] The cause of infection is identifiable in 95% of cases, mainly arising from anorectal, genito-urinary and cutaneous sources.[5] Predisposing factors such as diabetes and Immunosuppression lead to vascular disease and suppressed immunity that increase susceptibility to polymicrobial Infection. Common predisposing conditions include lower socioeconomic status, state of uncleanliness and poor personal hygiene, generalised debilitating diseases, alcoholism, steroid use, cancer chemotherapy or presence of diabetes[6]. Diagnosis is based on clinical signs and physical examination. Radiological methods may help to delineate the extent of the disease. Its treatment is unique for all cases including emergency removal of the devitalized tissues, adequate resuscitation, and intravenous (iv) administration of wide-

How to site this article: Shivprasad Hirugade, Harish N Patil, Shilpa S Hirugade. Fournier's gangrene and diabetes mellitus: Our experience with 50 patients. *International Journal of Recent Trends in Science and Technology*. September 2016; 20(2): 209-213. http://www.statperson.com (accessed 15 September 2016).

spectrum antibiotics.[3,7] Fournier's Gangrene Severity Index (FGSI) has become a standard index and being routinely used as a good predicting tool[8,9]. Acute Physiology and Chronic Health Evaluation (APACHE) II scoring system is a commonly used method for predicting outcomes of critically ill patients with necrotizing soft tissue infection (NSTI).[10] The mortality rate for FG is still very high, at 20–50% in most of the studies[11,12]. Fortunately, it is a rare condition, with a reported incidence of 1.6/100,000 males with peak incidence in the 5th and 6th decades. However, the incidence is rising, most likely due to increased numbers of patients on immunosuppressive therapy or suffering from human immunodeficiency virus (HIV) infection[13,14]. Fournier's gangrene may occur in both sexes but is less reported in females.[11,15] A similar infection can occur in women with necrotising infection of the vulva or perineum, and sometimes may be secondary to bartholian cyst or abscess[16]. Vulvar phacomycosis occurs in diabetics and mimics necrotising fascitis[17]. Worldwide DM is the most common medical comorbidity condition in Fournier's gangrene.[18] Early diagnosis, aggressive resuscitation of the patient, administration of broad-spectrum antibiotics and aggressive radical surgical debridement(s), are the key of successful treatment. In this study, we aimed to investigate patients with Fournier's Gangrene and association of diabetes mellitus as risk factors that affect mortality.

MATERIALS AND METHODS

This is a retrospective study of the patient admitted in RCSMGMC CPR Hospital from January 2015 to June 2016, of 50 patients with Fournier's gangrene and diabetes mellitus. The inclusion criteria included diabetic patients undergoing wide surgical excision of scrotal and/or perineal skin with a diagnosis of Fournier's gangrene. All patients underwent at least one radical debridement of affected devitalized tissues within 12 hours after admission. Iv. third-generation cephalosporin antibiotic therapy was started at the emergency room and continued. Empiric antibiotic therapy was changed according to culture and sensitivity report. Wound dressings were changed daily. Repeated debridements were performed until healthy granulation tissue was formed in the wound. Skin defects were closed with staged tertiary closure with testicular repositioning in the thighs. Statistical analysis was performed using Statistical Package for Social Sciences (SPSS II). The correlation of prognostic variables and mortality were studied by univariate analysis using chi-squared test and Fisher's exact probability test. P values less than 0.05 were considered as statistically significant.

RESULTS

Of the 50 patients studied, 12 died and 38 survived; the overall mortality rate was 24%. Most common cause of death was the multi-organ failure due to septic shock. All patients were male with a mean age of 48 years (range 30– 75 years). The survivors (mean age 44 years) were significantly younger than the non-survivors (mean age 57 years) ($p < 0.001$). The source of infection was identified in all patients. The commonest source of sepsis was the anorectum (Table 1).

Table 1: Etiology in 50 patients with Fournier's gangrene

Etiology	Patients	%
Anal Abscess	31	62
Urogenital diseases	11	22
Thrombosed hemorrhoids	5	10
Skin infection	3	6
Total	**50**	**100**

Diabetes mellitus (DM) was the most common comorbidity associated with Fournier's gangrene and was present in all patients at the time of admission. The most common symptoms at the time of admission were deterioration of the generally state (44%), perineal necrosis (92%), fever (60%), perineal or genital pain (76%), septic shock (22%). The average time of symptoms prior to referral to treatment was 11 days, ranging from 4 to 25 days. Mortality rate was higher among patients with symptom duration longer than 10 days. Regarding the investigations performed on admission, complete blood count showed the presence of a hyperleukocytosis (> 10.000/mm3) in 39 patients (78%). 9 patients required blood transfusion. The mortality of the patients presented with renal failure (blood urea >50 mg / dl) on admission was significantly higher than the patient without renal failure. Fournier's gangrene was confined to the perineal area in 5 patients (10%), scrotum in 35 (70%) individuals and extending to the abdominal wall in 10 patients (20%). It was found that the extension of the infection to the abdominal wall was a predictor of mortality ($p < 0.003$) (55% in the non survivors compared to 7% in the survivors). The most frequent bacterial organisms cultured from the wound sites were Escherichia coli (85.6%) and Klebsiella (40.5%). *Enterococci, Streptococci, Staphylococci, Pseudomonas* and *Proteus* were other microorganisms isolated in wound cultures, consecutively. Anaerobic culture could not be performed in our hospital because of technical difficulties. Before surgery, all patients underwent aggressive fluid resuscitation and were treated with third-generation cephalosporin and received hemodynamic support when required. Mechanical ventilation, continuous monitoring, and inotropic support were applied when necessary in patients with

cardiopulmonary failure due to sepsis. Majority of the debridement's were performed under spinal anesthesia; however, seven patients (14 %) required general anesthesia. All patients underwent radical surgical debridement, ranging from 1 to 10 procedures, with an average of 2.5. Debridement consisted of excision of all necrotic tissue, cleansing with hydrogen peroxide, then saline and drainage. Orchidectomy was carried out unilaterally for gangrenous testes in one patient (2%). Wounds of all patients were suitable for staged tertiary closure with testicular repositioning in the thigh. Fecal diversion with a temporary colostomy was not required in any patient. Of 50 patients, 11 patient required mechanical ventilation. Patients had a median hospital stay of 21 (range, 4–66) days. The significant predictors of mortality were the advanced age, presence of diabetes, and extension of the infection to the abdominal wall, renal failure and need of Mechanical ventilation (Table 2).

Table 2: Comparison of the patients' characteristics between survivors and non-survivors

Patient characteristics	Survivors n= 38	Non-survivors n = 12	p
Age (years, mean ± SD)	44	57	<0.001
Extension of the infection to the abdominal wall	7%	55%	<0.003
Renal failure	18	82	<0.001
Need of Mechanical ventilation	0%	91.6%	<0.0001

DISCUSSION

Fournier's gangrene, caused by synergistic aerobic and anaerobic organisms, is a life-threatening disorder in which infection of the perineum and scrotum spreads along fascial planes, leading to soft-tissue necrosis. In spite of the developing medical technology and experience, FG is still a fatal disease. There are several methods of mortality prediction including APACHE II score and FGSI which are commonly used traditional scoring systems. This infectious was initially described by Baurienne in 1764[19]. Before in 1883 Jean Alfred Fournier, French dermatologist described a syndrome of unexplained sudden onset and rapidly progressing gangrene in the penis and scrotum of 5 young men with no other pathology basis of sudden onset and rapid progression[20]. In its early reports Fournier's gangrene was described as an idiopathic entity, but in most cases a perianal infection, urinary tract and local trauma or skin condition at that level can be identified[13]. The mortality rate for FG is still high, (20–50%) in most of the studies[11,12], despite an increased knowledge of the etiology, diagnosis and treatment, and intensive-care techniques. The high mortality reflects both the aggressive nature of the infection and the destructive effects of accompanying predisposing factors. Several factors affecting the mortality were studied such as increasing age, primary anorectal infections, existence of diabetes, delay in treatment, evidence of systemic sepsis at presentation, extent and depth of involvement, a low haematocrit, a high leukocytosis and blood urea, a low serum albumin, and many others[9,11-14,21]. FGSI is a scoring system first described by Laor *et al*. in 1995.[22] It is a physiological and metabolic status based scoring system. It has been validated in several reported studies[9,12]. Early diagnosis was reported to be associated with better outcomes in FG.[23-26] Early surgical treatment within two days after admission reduces mortality of FG.[25] Also, the interval time between the onset of symptoms and initial debridement has been reported to be a major predictor of mortality.[26] The average age of the patients was 47.5 years, in most published series from 40.9 to 61.7 years[11,13]. In a population based study of 1641 patients, Sorensen *et al*. found that an increasing patient age was the strongest independent predictor of mortality (p <0.0001)[13]. Numerous factors have been implicated at the onset of FG, in particular, those involving the immune system[21]. Diabetes mellitus was the most reported co-morbid disease associated with this pathology. Some authors estimate the prevalence of DM among FG patients between 50 and 70 percent[27]. There are other several studies showing DM as a risk factor for patients with FG.[3,7,11,23] Nevertheless, there are also some studies where DM has been reported as one of the most frequent comorbidities but not determined as a risk factor for mortality (p=0.429).[13,24] It is also suggested that renal failure on admission might be a noticeable factor for the prediction of the mortality rate[23]. Among many laboratory parameters studied in FG, Clayton *et al*., reported that only a level of blood urea > 50mg/ dl on admission was statistically significant for mortality[29]. In our study we also found that renal failure on admission is significantly higher in non survivors. Few articles have highlighted the poor prognosis of FG in patients with a delay between time of presentation and treatment. This factor has been reported in a study by Jeong *et al*., as a predictor of mortality[30]. The most common origin of the FG was anorectal diseases (72%) in our study, followed by urogenital diseases (22%) and skin infections (6%). There are two previous studies reporting perianal abscess as the most common etiological factor.[24,28] Extent to abdominal wall has been reported to be directly related to mortality[31], which was confirmed in our series. Ultimately, occurrence of septic shock and need for postoperative mechanical ventilation, have been demonstrated as a powerful (even late) factors of mortality[9]. Furthermore, Yanar *et al*. found that the

presence of sepsis was as the only significant independent risk factor for mortality in FG[3]. Role of cystostomy and colostomy, are controversial as a treatement protocol and it should be applicated in accordance to individual patient condition[32,33]. Since mortality is the major problem for this devastating disease, extra attention is required for the management of the patients in high-risk group.

CONCLUSIONS

Fournier's gangrene is still a very severe disease with a high mortality rate. The advanced age, renal failure on admission, extension of infection to the abdominal wall, occurrence of septic shock and need for postoperative mechanical ventilation are the main prognostic factors of mortality. Early recognition of infection associated with invasive and aggressive treatment is essential for attempting to reduce these prognostic indices. Diabetes mellitus was the most reported co-morbid disease associated with this pathology. Although it was the most common co-morbidity among all patients, DM was not determined as a risk factor for mortality.

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Source of Support: None Declared
Conflict of Interest: None Declared