FOURNIER'S GANGRENE: A MICROBIOLOGICAL OVERVIEW

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ABSTRACT

Fournier's gangrene (FG) is a rare, rapidly progressive, fulminant form of necrotizing fasciitis of the genital, perianal and perineal region and is usually secondary to polymicrobial infection.

OBJECTIVES

Presently, the literature regarding the spectrum of pathogens causing FG is limited. Hence, this study was undertaken to get a better understanding of (a) Microbial pathogens causing FG and (b) The clinical outcome.

METHODS

The present study is a retrospective cohort study of the microbial pathogens isolated from FG patients admitted in a tertiary care centre. Data was collected from the hospital records of patients admitted with FG during June 2012 to November 2015.

RESULTS

A total of 55 male patients with FG were included in this study. The mean age of patient was 49.36 years. Out of 55 samples, 47- showed evidence of microbial growth, 12 samples showed mono-microbial and 35 samples showed poly-microbial growth. Among the cases included in the present study, anaerobic culture was requested for only 10 samples; 3 out of the 10 samples subjected to anaerobic culture yielded *Bacteroides fragilis* (*B. fragilis*). *Klebsiella pneumoniae* was the most common pathogen isolated (*K. pneumoniae*) (29/47, 61.70%), followed by *Enterococcus faecalis* (*E. faecalis*) (15/47, 31.91%), *B. fragilis* (3/10, 30%) and *Escherichia coli* (*E. coli*) (13/47, 27.65%). Gram negative organisms were highly susceptible to levofloxacin and piperacillin-tazobactam. Gram positive organisms were highly susceptible to linezolid (92%), vancomycin (84%) and tetracycline (68%). Major risk factors associated with FG were diabetes (43.6%) and obesity (40%). The mortality rate was 5.45%.

CONCLUSION

FG is a rapidly progressive fulminant life threatening condition. Early diagnosis, aggressive surgical intervention and appropriate antimicrobial therapy may help to reduce the mortality rate.

KEYWORDS

Fournier's Gangrene, *Klebsiella Pneumoniae*, Polymicrobial.

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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] It is secondary to polymicrobial infection by aerobic and anaerobic bacteria with a synergistic action.^[2-4] The cause of infection mainly arising from anorectal, genitourinary and cutaneous sources.^[5] Predisposing factors such as diabetes, obesity and immunosuppression lead to vascular disease, which in turn increases susceptibility to polymicrobial infection.^[6]

The overall (reported) incidence of FG increased dramatically in the 20th century. From 1764 to 1978 there were 386 reported cases and from 1950 to 1999, 1726 cases.^[7]

The incidence is rising due to factors like increase in the mean survival age of the population, increase in the number of patients with co-morbidities and widespread use of immunosuppressive therapy.^[8,9] A study by Sorensen et al. showed an overall incidence is 1.6/100000 males, i.e. (<0.02% of hospital admissions).^[8] Since it is a rare clinical condition, there is no clear data available about its prevalence in India. The real incidence could be underestimated because most cases with grave prognosis are not published.

FG is commonly seen in males especially from 40 to 70 years of age. Besides diabetes, chronic alcoholism, renal failure and obesity are also other risk factors of FG. The median time from the onset of symptoms to the gangrenous changes of the skin is 6 days.^[10] The most common symptoms of FG are perineal pain and fever, accompanied by swelling, reddening of perineum or genital area and the gangrenous change of overlying skin.^[11] Early diagnosis and aggressive management is required for better patient outcome. In this study, clinically suspected cases of FG were analysed to determine the microbiological spectra of organisms and their antibiotic susceptibility pattern.

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METHODS

Source of Specimens

This study was conducted in the department of microbiology of a tertiary care centre in Bangalore. Fifty-five pus culture samples received from FG patients between June 2012 and November 2015 were included in the analysis.

LABORATORY METHODS

Culture of Specimens

All samples were transported to our laboratory within 1 hour of collection. Immediately after receiving the sample, the material was subjected to microscopic examination. After Gram staining, it was streaked on Blood agar and MacConkey agar plates and incubated at 37°C for 24 - 48 hours. Along with aerobic culture method, specimens requested for anaerobic culture (10 samples) were streaked on *Brucella* blood agar and incubated at 37°C in anaerobic jar with Gaspak.^[12] The colonies obtained were subjected to Gram's stain and to biochemical tests for preliminary identification of the organisms.

Antibiotic Susceptibility Testing

All bacterial isolates obtained by aerobic culture were subjected for antibiotic susceptibility testing on Mueller Hinton agar medium and on blood agar for *E. faecalis* and Group A *Streptococci* by the Kirby Bauer disc diffusion method as per CLSI guidelines.^[13] Antibiotic susceptibility testing for anaerobes was not done as CLSI recommends minimum inhibitory concentration measurement for susceptibility breakpoints.

RESULTS

The population included in this study comprised of 55 male patients belonging to the age group of 30-80 years. The mean age of the study population was 49.36 years. Three patients succumbed to the infection while rest of them responded to the treatment and were discharged. The overall mortality rate was 5.45%. Diabetes Mellitus (DM) was the most common co-morbid condition associated with FG and was present in 24 (43.6%) patients. The other co-morbid conditions commonly associated with FG were obesity (22/55, 40%) with the body mass indices (BMI) of > 30, hypertension (20/55, 36.4%), heart disease (19/55, 34.5%), and alcoholism (16/55, 29.1%). (Figure 1).

Sample from more than half of the patients (35/55, 63.6%) showed *polymicrobial* growth. The most commonly found spectrum was a combination of *K. pneumoniae*, *E. coli* and *E. faecalis*. The other pathogens like *Acinetobacter baumannii* (*A. baumannii*), *Staphylococcus aureus* (*S. aureus*), *Pseudomonas aeruginosa* (*P. aeruginosa*), Group A *Streptococci*, *Candida albicans* (*C. albicans*) were also isolated. *B. Fragilis* was isolated from 3/10 (30%) samples sent for anaerobic culture. *B. Fragilis* was identified based on Gram stain (Pleomorphic gram negative rods with rounded ends), colony morphology on Brucella blood agar (2-4mm in diameter, convex, non-hemolytic, gray, entire edge and opaque with concentric whorls or ring like structures inside the colonies), biochemical reactions (catalase producer, esculin hydrolysis positive, ferment glucose and lactose), resistant to penicillin 2-U disk, kanamycin 1-µg disk, vancomycin 5-µg disk and susceptible to rifampin 15-µg disk.^[12] Polymicrobial growth of *B. fragilis* was seen along with *S. aureus*, *E. coli* + *E. faecalis* and *K. pneumoniae* respectively from the three anaerobic culture positive samples (Figure 2).

Antimicrobial Susceptibility Pattern

The antimicrobial susceptibility was carried out by using the disc diffusion technique as per CLSI guidelines.^[13] Gram positive bacterial pathogens were highly susceptible to linezolid, vancomycin followed by tetracycline (Figure 3).

Gram negative bacterial pathogens were highly susceptible to levofloxacin, piperacillin-tazobactam followed by amikacin, gentamicin and imipenem (Figure 4).

Most of the isolates were resistant to amoxicillin-clavulanic acid combination.

DISCUSSION

FG is a rare emergent condition that affects the perineum and urogenital region. Data from multiple sources have shown that FG is commonly associated with risk factors like diabetes mellitus, obesity, hypertension, heart disease, smoking, long-term steroid therapy, alcoholism or alcohol abuse, hot and humid climate, and renal failure.^[14-19] Out of all risk factors, diabetes mellitus was found to be the most common risk factor (43.6%) in the present study. Obesity was another frequent association, wherein 40 % of FG patients in the present study had BMIs of higher than 30, similar to the data published by Czymek et al. and Mehl et al.^[16,17]

Suppurative bacterial infections result in microthrombosis of the small subcutaneous vessels leading to the development of gangrene of the overlying skin. When managing FG patients, this gangrenous tissue requires extensive and repeated debridement.^[15] The most common microbiological cause involved in FG in the present study was polymicrobial infection (63.6%) similar to other studies.^[16,17,20] and the most commonly found pathogen was *K. pneumoniae* (62%). Other contributing pathogens were *E. faecalis*, *E. coli*, Group A *Streptococci*, *A. Baumannii*, *S. aureus*, *P. aeruginosa*, *C. albicans* and *B. fragilis*. Rarely *C. Albicans* have been reported earlier. In the present study, *C. albicans* has been isolated in 5% patients. Most of these organisms isolated are normal commensals of the perineum and genitalia, which become virulent due to impaired host immunity and act synergistically to cause extensive tissue damage.

The synergistic activity of microbes lead to the production of various exotoxins and enzymes like collagenases, heparinases, hyaluronidases, streptokinases and streptodornases which aid in tissue destruction and spread of infection.^[21]

The treatment of FG is immediate extensive debridement and a combination of antibiotics along with treatment of the predisposing conditions. After surgical resection, daily wound care needs to be carried out to fight local infection. A combination of antibiotics targeting all three of the main bacterial groups must be used. Many studies have suggested the use of penicillin against *Streptococci*, metronidazole for anaerobes and third-generation cephalosporins against *Staphylococci* and *Enterobacteriaceae*.^[22-24] In our study, Gram positive cocci like *E. faecalis* and *S. aureus* have shown highest susceptibility to linezolid and vancomycin. *Enterobacteriaceae* were highly susceptible to levofloxacin and piperacillin-tazobactam. Hence, an empirical antimicrobial therapy against gram positive cocci, gram negative bacilli and anaerobic bacteria in combination should be started until the culture and sensitivity reports are available.

CONCLUSION

FG is a rapidly progressive fulminant life threatening condition with high mortality rate which can be prevented by early diagnosis, aggressive surgical intervention and the use of broad spectrum antibiotics. Broad-spectrum antibiotic treatment is suggested to adequately cover poly-microbial pathogens, and careful patient monitoring is required to avoid fungal or hospital acquired infection.^[24] Proactive

management of the diabetic and immunosuppressed patients with perineal infections is of extreme importance to prevent the development of FG. Weight reduction and avoidance of alcohol consumption and tobacco use may be helpful in reducing the possible risk of FG. Early recognition of infection associated with invasive and aggressive treatment is essential for the superior therapeutic consequences of patients with FG.

Fig. 1: Percentage distribution of associated risk factors

Fig. 2: Percentage distribution of Commonly found pathogens

Fig. 3: Susceptibility pattern of Gram Positive Cocci

Fig. 4: Susceptibility pattern of Gram Negative Organisms

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