

Full Length Research Paper

What changed in necrotizing fasciitis in twenty-five years?

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Necrotizing fasciitis (NF) is a deadly soft tissue infection characterized by necrosis of subcutaneous tissues. In this study, our aim was to identify variables affecting patient outcome and mortality in necrotizing fasciitis and their temporal changes. We reviewed records of 45 patients treated at our institution between 1979 and 2004. Data about gender, age, etiology, site of involvement, bacteriology, type of surgery, supportive treatment, accompanying diseases, mortality were collected. Factors contributing to mortality were sepsis, renal failure, liver failure, multi organ failure, disseminated intravascular coagulopathy and long term intubation. Mortalities accumulated in first 23 patients. There was not difference in microbiology, demographics, etiology, site of involvement, debridement technics between first patients and recent patients of the institution. Mortality in necrotizing fasciitis is mostly because of sepsis and associated disorders. Adequate control of the microbiological agent and preventing further contamination of the wound is cardinal part of treatment in NF.

Key words: Necrotizing fasciitis, bacteriology, mortality, sepsis, Fournier's gangrene.

INTRODUCTION

Necrotizing fasciitis (NF) is deeply located infection of subcutaneous tissue resulting in progressive destruction. Its histological patterns are large necrosis of the fascia, subcutaneous fat and skin with thrombosis of the microvasculature and sparing of the underlying muscles and the skin (Wilson, 1952; Giuliano et al., 1977; Misago et al., 1996).

NF can be divided into two groups depending on the causative organism. In type I, at least one anaerobic species is isolated in combination with facultative anaerobic species and members of *Enterobacteriaceae*. In type II, *group A streptococci* or *Staphylococcus aureus* are isolated (Levine and Manders, 2005).

There are a number of predisposing factors to NF such as diabetes mellitus (DM) (Salcido, 2007) immunocompromised state, corticosteroid use, intravenous drug abuse, trauma, malnutrition, burns and atherosclerosis (Thompson et al., 1993). Early diagnosis and prompt

treatment consisting of surgery and antibiotics are key to improved patient outcome in NF.

Depending on the depth of invasion, necrotizing soft tissue infections can cause extensive local tissue destruction, tissue necrosis, systemic toxicity and even death. Mortality rates for necrotizing soft tissue infections range from 6% to as high as 76% despite advances in management (Brandt et al., 2000; Singh et al., 2002; Bilton et al., 1998).

In this study, our aim was to identify the temporal changes in incidence, etiology, bacteriology, management and outcome in NF at our institution to help define better strategies in treatment for this challenging condition.

MATERIALS AND METHODS

After ethics committee approval was obtained, inpatient records of patients treated for necrotizing fasciitis between 1979 and 2004 in our university hospital general surgery department were retrospectively reviewed. Patients were identified from hospital archives and data was collected from hospital records and electronic database. There were 29 men and 16 women whose ages ranged between 16 and 88 years. We reviewed the charts of the patients

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and recorded sex, age, predisposing factors, duration between the onset of symptoms and the first surgical debridement, bacteria isolated, duration of hospital stay, reconstructive procedures, and clinical outcome. Plastic and Reconstructive Surgery at our hospital was consulted for patients who needed reconstructive procedures after initial debridement was performed in General Surgery Department. Broad spectrum antibiotics were given initially and specific antibiotics were advised after confirmation of the organism isolated from the wound tissue. Patients with minor skin and soft-tissue loss or wound healing with secondary intention were referred for wound evaluation and wound care. The scrotal advancement flap, pudendal thigh fasciocutaneous flap, gracilis muscle/myocutaneous flap, or split-thickness skin graft was used as the reconstructive procedure to correct the defects arising from failure of secondary intention or primary closure. The statistical analysis was carried out with SPSS software (SPSS, Chicago, Illinois) using Chi-Square test. A *P*-value < 0.05 was considered significant.

RESULTS

There were totally 45 patients. The median age of the patients was 50 (minimum 16, maximum 88). Sixteen patients (35.6%) were female and 29 (64.4%) were male. The diagnoses of NF were established based on clinical symptoms and findings including combinations of fever, pain, swelling, erythematous change of the involved skin and purulent discharge.

The most common etiology was perianal abscess (*n*=17, 37.8%) followed by surgical site infection (*n*=9, 20%) and others (perineal shaving, decubitus ulcer, strangulating inguinal hernia, vulvar trauma, intramuscular injection, pilonidal abscess, colocutaneous fistula, diabetic foot, gun shot wound, enterocutaneous fistula). It was seen that majority of cases were actually Fournier's gangrene. This was supported by the analysis of the site of involvement as perianal area, scrotum/vulva with highest frequency (*n*=16), followed by combinations of localizations including scrotum, vulva, gluteus and inguinal region.

Twenty-two percent of patients in our study had comorbidities while thirteen patients (28.9%) did not have any accompanying disease. The most common associated disease was DM (17.8%) followed by malignancies (8.9%), coronary artery disease (6.7%) and combinations of DM, hypertension, ulcerative colitis, paraplegia, chronic obstructive airway disease. During management 46.7% of patients had sepsis and 11.1% had multiorgan failure.

Polymicrobial bacterial strains were isolated from tissue and pus cultures. In 9 patients there was not any growth in bacterial cultures. The rest of isolated bacteria are listed in Table 1.

Antimicrobial agents, surgery and nutritional support were the mainstay of treatment for patients with NF. Antibiotic therapy was started empirically and continued based on the microbiology of the wounds. In 3 patients antifungal medication was added to antibiotics. Median duration of antimicrobial therapy was 17 days (minimum 3 – maximum 55).

Surgery was performed as soon as the diagnosis of NF was suspected. There was delay in 18 patients between diagnosis and surgical intervention. Median time of delay was 1.5 days. Debridement under local anesthesia was performed only to 4.4% of the patients and 95.6% of the patients had debridement under general anesthesia. Of those who had debridement under general anesthesia, 27 (60%) had only one debridement while 9 (20%) had twice and 4 (8.9%) had three times. Overall, colostomy was performed to 22.2% of patients and to 90% of the patients with Fournier's gangrene.

Twenty-six patients (48.8%) required reconstruction. Primary closure was performed in 15 (57.6%) patients whereas 4 (15.3%) patients had split-thickness skin grafting and 3 (11.3%) had flap reconstruction.

Nutritional support was given to 17 patients. Of these, six patients received total parenteral nutrition whereas 8 had enteral nutrition.

The longest hospital stay was 92 days while the shortest stay was 9 days (median: 35.5). The overall mortality was 22.2% (*n*=10). Twenty-five percent of women and 20% of men died. Comparison of survivors and non-survivors are given in Table 2. Statistically significant factors contributing to mortality were sepsis (*p*=0.001), multiorgan failure (*p*<0.001) and intubation longer than one day (*p*<0.001). When first 23 patients and last 22 patients were compared there was not any mortality in the latter group (Table 3).

DISCUSSION

Although rare, NF remains to be a deadly condition. There is no gender predilection (Elliott, 1996). and the etiology is not identified in most cases as in our series. Any insult to the integumentary system might cause NF but it can also originate from a hematogenous source. In our series perineal infection and surgical site infections were the most common etiologies.

Despite 28.9% of our patients did not have any accompanying disease DM, malignancy and coronary artery disease were the most common comorbidities which are also cited in other publications (Salcido, 2007).

In our series, we had a higher proportion of Fournier's gangrene and lower proportion of extremity NF than other series (Anaya and Dellinger, 2007). This explains mixed species in bacterial cultures we retrieved from tissues.

Surgical debridement is the main treatment in NF and should be done as soon as the diagnosis is established. Delaying surgery more than 12 h after admission is shown to increase amputation and mortality rates (Fulda et al., 2003). Median delay time of non-survivors in our cases was higher than survivors but this was not a statistically significant factor in mortality in further statistical analysis.

In NF, colostomy should be performed in patients with sphincter damage to prevent contamination of the

Table 1. Combinations of bacteriologic strains isolated from tissues in chronological order starting from 1979 to 2004.

Case	Year	Microorganisms
1	1979	<i>Enterobacteriaceae</i> spp.
2	1979	<i>Escherichia coli</i> , <i>Clostridium tetani</i>
3	1980	Coagulase positive <i>Staphylococcus aureus</i> (SCP)
4	1983	No growth
5	1983	<i>Escherichia coli</i> , <i>Proteus</i> , SCP, Diphtheroids
6	1985	<i>Escherichia coli</i> , Diphtheroids
7	1986	<i>Escherichia coli</i> , SCP, <i>Pseudomonas aeruginosa</i>
8	1988	SCP, <i>Acinetobacter</i>
9	1991	<i>Klebsiella pneumonia</i> , <i>Pseudomonas aeruginosa</i>
10	1993	<i>Streptococcus pneumonia</i> , SCP
11	1993	No growth
12	1994	No growth
13	1994	<i>Pseudomonas aeruginosa</i>
14	1994	No growth
15	1995	<i>Enterobacteriaceae</i> species
16	1995	No growth
17	1995	<i>Proteus vulgaris</i>
18	1996	<i>Klebsiella oxytoca</i> , <i>Escherichia coli</i>
19	1996	<i>Escherichia coli</i> , <i>Streptococcus viridens</i>
20	1997	<i>Escherichia coli</i>
21	1997	<i>Enterococcus faecalis</i> , <i>Pseudomonas aeruginosa</i> , <i>Klebsiella Oxytoca</i>
22	1997	<i>Escherichia coli</i> , <i>Streptococcus viridens</i>
23	1997	<i>Escherichia coli</i> , <i>Klebsiella pneumonia</i> , Coagulase positive <i>Staphylococcus aureus</i>
24	1998	<i>Escherichia coli</i> , <i>Staphylococcus aureus</i>
25	1998	<i>Morganella morgagni</i> , <i>Pseudomonas aeruginosa</i>
26	1998	<i>Enterobacteriaceae</i> spp.
27	1998	No growth
28	1998	<i>Streptococcus pneumonia</i> , SCP
29	1998	<i>Staphylococcus aureus</i>
30	1998	<i>Escherichia coli</i> , <i>Klebsiella pneumonia</i>
31	1998	No growth
32	1999	<i>Staphylococcus aureus</i> , <i>Serratia marcescens</i>
33	2000	<i>Escherichia coli</i> , <i>Klebsiella pneumonia</i> , <i>Staphylococcus aureus</i>
34	2001	<i>Escherichia coli</i> , <i>Streptococcus agalactiae</i>
35	2001	<i>Escherichia coli</i> , <i>Pseudomonas aeruginosa</i>
36	2002	No growth
37	2002	<i>Acinetobacter</i> , <i>Staphylococcus epidermidis</i>
38	2003	<i>Acinetobacter</i> , <i>Escherichia coli</i>
39	2003	<i>Staphylococcus epidermidis</i>
40	2003	<i>Morganella morgagni</i>
41	2003	Methicillin resistant <i>Staphylococcus aureus</i> , <i>Escherichia coli</i> , <i>Acinetobacter</i>
42	2003	No growth
43	2003	<i>Escherichia coli</i> , <i>Staphylococcus aureus</i>
44	2003	<i>Streptococcus agalactiae</i>
45	2004	<i>Escherichia coli</i> , <i>Enterococcus faecalis</i> , <i>Proteus mirabilis</i>

debrided area (Villanueva-Sáenz et al., 2002). Colostomy rate of survivors and non-survivors was similar in our study while there was an increase in tendency to perform colostomy in the second half of the study group.

The defects after surgical debridement in NF can be managed with primary closure, grafting or flap reconstruction (Baharestani, 2008). Our center had a propensity towards primary closure whenever possible

Table 2. Comparison of survivors and non-survivors.

Variable	Non survivors	Survivors
Age (years)	59.7±16.9	45.6±12.6
Gender	6 Males, 4 Females	23 Males, 12 Females
Etiology	Predominantly SSI with peritonitis	Predominantly perianal abscess
Duration of symptoms (days)	8±4.24	7.71±4.36
Delay in surgery (days)	2.66±2.05	1.66±1.54
Co-morbidity present	60%	60.7%
Site of involvement	Predominantly ABW	Predominantly perianal area
Number of debridements	1.4±0.51	1.34±0.787
Colostomy	20%	22.9%
Intubation	60%	8.6%
Duration of Intubation (days)	3.66±3.2	0.087±0.288
Red packed cell transfusion (Units)	4.5±1	1.7±2.2
Antibiotic therapy (days)	14.8±10.56	23.18±14.1
TPN administration	20%	20%
Enteral nutrition	10%	20%
Leukocyte count at admission (/uL)	21650±12834	16537±6943
Neutropenia	1 patient	1 patient
Renal failure	70%	34.3%
Liver failure	50%	11.4%
Sepsis	100%	31.4%

SSI:Surgical site infection; ABW:Anterior abdominal wall; TPN: Total parenteral nutrition.

Table 3. Characteristics of first 23 and last 22 cases.

Variable	First 23 patients (1979-1996)	Last 22 patients (1997-2004)
Age (years)	49.56±16.5	47.90±12.95
Gender	65.2% Male	63.6% Male
Etiology	Predominantly SSI with peritonitis and perianal abscess	Predominantly perianal abscess
Site of involvement	Predominantly perianal area	Predominantly perianal area
Number of debridements	1.42±0.676	1.28±0.78
Colostomy	15%	33.3%
Mortality	28.6%	None

SSI: Surgical site infection.

and all reconstructions were done between 1997 and 2004.

Empirical antibiotic prophylaxis should be started in NF until the responsible pathogen is identified in cultures. In our study, when compared with respect to years, recent regimens started to contain piperacillin-tazobactam, teikoplanin and imipenem. Of note, 3 patients with sepsis in the second half of study received fluconazole along with antibiotics.

Published mortality rates due to NF vary widely. Brandt et al. (2000) and Lille et al. (1996) from USA reported 24% (Brandt et al., 2000) and 25% (Lille et al., 1996) respectively while Rietveld et al (1995) from New Zealand reported 43% (Rietveld et al., 1995). We found approximately the same result (22.2%) as those reported

from USA.

In our study, factors predicting mortality were mainly the end results of sepsis and multi-organ failure. In contrary to what we found, a study from Canada cited that the contributing factors for mortality were advanced age, immunocompromised state and presence of streptococcal toxic shock syndrome (Golger et al., 2007).

In this study, we tried to reflect our 25 years of experience in NF between 1979 and 2004. Due to change in institutional policy our department stopped admitting and following NF patients after 2004.

The first thing in analysis of cases was better mortality rate in more recent cases when compared to the earlier days of the institution. In this regard, when we look at the variables it seems that microbiology, demographics,

etiology, site of involvement, debridement technics are similar but frequency of colostomy procedure, type of antibiotics, utilization of antifungals seem to accumulate in the second chronological half of the series. The main outcome of our study is the fact that adequate control of the microbiological agent and preventing further contamination of the wound is the cardinal part of the treatment in NF and particularly in Fournier's gangrene.

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