Original Research Article

Risk factors, microbiological findings and outcomes of necrotizing fasciitis at a tertiary care centre

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ABSTRACT

Background: Necrotizing fasciitis (NF) is a uncommon and serious infection involving the skin and subcutaneous tissues of lower and upper limbs, perineal area (Fournier’s gangrene), and the abdominal wall with high morbidity and mortality. Early diagnosis and aggressive treatment can reduce the mortality rate of NF. The objectives of this study are to study the etiopathological, microbiological factors determining the outcome of necrotizing fasciitis.

Methods: It is prospective study and was conducted in JSS Medical College and Hospital in October 2008 to October 2010. Total 50 patients diagnosed with necrotizing fasciitis were admitted to JSS Medical College and Hospital. Demographic data, type of co morbidities, site of infection, clinical features with microbiology and laboratory results, and outcomes of patients were analyzed.

Results: Out of 50 patients there were 42 males and 8 females. Highest number of cases was found in the age group of 65-74 years among males, 55-64 years among females. The commonest site in the present study is lower limbs (74%). Diabetes mellitus was the commonest (76%) co morbidity. Beta hemolytic streptococci 22 (44%) was the highest to be isolated. In type I and Coagulase positive staphylococci 18 (36%) was the commonest organism isolated in type II necrotizing fasciitis. The significant risk factors were gender, comorbidities, hospital length of stay, and albumin level, leucocytosis, anemia, hypoalbumenemia, low serum ferritin levels increase blood sugar levels. The mortality was 12% (8 patients).

Conclusions: Patients with advance age, co-morbid conditions like diabetes mellitus, hypertension, peripheral vascular disease, osteomyelitis had high unexplained susceptibility to the disease and with a higher incidence in males. Thus, early recognition with a high index of clinical suspicion would definitely reduce both morbidity and mortality. It has gross morbidity and mortality if not treated in its early stages. Leucocytosis, anemia, hypoalbumenemia, low serum ferritin levels, increase blood sugar levels were consistent findings seen in majority of the patients which resulted in increased morbidity.

Keywords: Dishwater, Fasciitis, Fournier’s gangrene, Necrotizing fasciitis

INTRODUCTION

Necrotizing fasciitis is a severe, fulminant, life threatening infection affecting the deep fascia with secondary necrosis of the subcutaneous tissue spreading unrecognized along the facial planes beneath seemingly normal skin. It is commonly known as flesh-eating disease.1

It is a rapidly progressing process, which is characterized by supportive fasciitis following by vascular thrombosis and cutaneous, gangrene and is often accompanied by
severe systemic toxicity, seen as septic shock and progressive multi organ failure.\textsuperscript{2,3}

The mortality is quite high and is related to late presentation or late diagnosis, co-morbidities like diabetes and advanced age, alcoholics, chronic liver disease, malnutrition, though it can occur in young and healthy individuals.\textsuperscript{4,5}

In Most cases the infection process starts with Blunt or penetrating trauma to the skin surface with seeding of bacteria, operation site infection, burn, ulcers, abscess, child birth, acupuncture and tattooing. Infection starts in the deep tissue planes, and the epidermis might not be initially affected.\textsuperscript{4,5,9}

NF has been classified as type 1 (polymicrobial) or type 2 (monomicrobial).\textsuperscript{10} Frequently the disease is polymicrobial. The usual cause is a mixture of aerobic and anaerobic organisms, although group A streptococcus alone or Streptococcus pyogenes or group A streptococci, Staphylococcus aureus, Escherichia coli, Clostridium and Bacteroides species. Rarely, group B, C, and G streptococci, Haemophilus influenzae type b, Pseudomonas aeruginosa, Vibrio vulnificus, and fungi are responsible.\textsuperscript{11}

NF can occur anywhere in the body but extremities, perineum, abdominal wall are the commonly affected sites. Meleney’s gangrene (Meleney’s synergistic hospital gangrene) is necrotizing fasciitis associated with infections of the abdominal wall. Another variant is Fournier’s gangrene, after necrotizing infection of the perineum was described by FOURNIERS in 1824.\textsuperscript{12}

The precise mechanism resulting in the fascial necrosis is not known. Bacterial enzymes, like lipases and hyaluronidase, which degrade fat and fascia, are thought to be the cause. Through a triggering mechanism, infection results, leading to activation of interleukins, tumor necrosis factor alpha, and gamma-interferon. Which results in capillary thrombosis with necrosis of the fascia, cutis, and sub cutis.\textsuperscript{13,14}

NF symptoms and signs includes pain, swelling, pyrexia, skin discoloration, blistering, haemorrhagic bullae, discharge of “dishwater” fluid, crepitus, tachycardia, sepsis or systemic inflammatory response syndrome or multiorgan failure.

NF has high morbidity and mortality mainly due to acute renal failure, shock, multi-organ dysfunction, coagulopathy, arrhythmia, and myocardial infarction and which consumes a large amount of health-care resources. Its management requires urgent surgical debridement and intravenous antibiotics and intensive care unit (ICU) admission. Large numbers of patients who survive require multiple admissions, skin grafting and reconstructive surgery.\textsuperscript{15}

Only early diagnosis and aggressive surgical treatment can reduce mortality and morbidity.\textsuperscript{16}

\textbf{METHODS}

Total 50 patients diagnosed with necrotizing fasciitis were admitted to JSS Medical College and Hospital. The data is collected from clinical history, general physical examination relevant investigations and imaging modalities and follow up of patients which is spread over the study period of Oct 2008 to Oct 2010

Statistical methods applied: To study the association between outcome and characteristics, Chi square test for qualitative data and T-test/ANOVA in case of quantitative variables will be applied at 5\% level of significance. All the statistical methods were carried out through the SPSS for Windows (version 16.0).

\textbf{RESULTS}

The results of clinical study of 50 cases of necrotizing fasciitis studied at JSS Hospital, Mysore.

\textbf{Table 1: Age distribution.}

| Ages (years) | Male | Female |
|--------------|------|--------|
| 24-34        | 4    | 0      |
| 35-44        | 8    | 2      |
| 45-54        | 7    | 1      |
| 55-64        | 7    | 4      |
| 65-74        | 15   | 1      |
| 75+          | 1    | 0      |
| Total        | 42   | 8      |

Chi-square = 16.9; P-value = 0.005

Age distribution is shown in Table 1. The youngest patient was 26 years and the eldest was 86 years. Highest numbers of cases were found in the age group of 65-74 years among males, 55-64 years among females. Out of 50 cases studied, there were 42 males and 8 females.

\textbf{Table 2: Site of NF.}

| Site                      | No. of cases | (%) |
|---------------------------|--------------|-----|
| Scrotum                   | 3            | 6   |
| Lower limb                | 37           | 74  |
| Scrotum and perineum      | 8            | 16  |
| Scrotum and abdomen       | 2            | 4   |

Chi-square = 65.68; P-value=0.000

Out of 50 cases study in 37 (74\%) patients’ lower limbs were involved and next common site was scrotum and perineum (Table 2).

Out of 50 patients studied 15 (30\%) patients presented with septicemia at the time of admission (Chi-square = 8.00, P value = 0.005). 38 (76\%) patients had diabetes, 19 patients had 2 or more co-morbid conditions (Table 3).
Table 3: Co-morbid conditions.

| Co-morbid conditions                      | No. of patients | % |
|-------------------------------------------|-----------------|---|
| DM (Diabetes Mellitus)                    | 13              | 26|
| HTN (Hypertension)                        | 6               | 12|
| DM, HTN                                   | 8               | 16|
| DM, PVD (Peripheral vascular disease)     | 2               | 4 |
| DM, HTN, IHD (Ischemic heart disease)     | 3               | 6 |
| DM, HTN, CKD (Chronic kidney disease)     | 3               | 6 |
| DM, HTN, PVD                              | 2               | 4 |
| DM, PVD, Osteomyelitis                    | 1               | 2 |
| None                                      | 12              | 24|
| Total                                     | 50              | 100|

Chi-square: 29.2; P-value: 0.000

Table 4: Organism isolated.

| Organism isolated                      | No. of cases | % | Chi-square | P-value |
|----------------------------------------|--------------|---|------------|---------|
| Beta Hemolytic streptococci            | 22           | 44| 3.92       | 0.048   |
| E. coli                                | 18           | 36| 0.72       | 0.396   |
| Coagulase negative staphylococci       | 4            | 8 | 35.28      | 0.000   |
| Providencia                            | 1            | 2 | 46.08      | 0.000   |
| Coagulase positive staphylococci       | 18           | 36| 3.92       | 0.48    |
| Klebsiella                             | 9            | 18| 20.48      | 0.00    |
| Pseudomonas                            | 13           | 26| 11.52      | 0.0001  |
| Proteus                                | 4            | 8 | 35.28      | 0.000   |
| Citrobacter                            | 4            | 8 | 35.28      | 0.000   |
| MRSA                                   | 2            | 4 | 42.30      | 0.000   |

Type of Necrotizing Fasciitis, 36 (72%) out of 50 patients had type I NF (polymicrobial) and 14 (28%) patients had type II NF (monomicrobial). Organism isolated were (Table 4) beta hemolytic streptococci was the highest in type I and Coagulase positive staphylococci was the commonest in type II necrotizing fasciitis.

Table 5: Total count at the time of presentation.

| Total count (Cumm) | No. of patients | % |
|--------------------|-----------------|---|
| >14000             | 36              | 72|
| <14000             | 14              | 28|
| Total              | 50              | 100|

Chi-square = 9.68; P-value = 0.002

Table 6: Serum ferritin levels.

| Serum ferritin levels (ng/dl) | No. of patients | (%) |
|-------------------------------|-----------------|-----|
| Low                           | 35              | 70  |
| Normal                        | 15              | 30  |
| Total                         | 50              | 100 |

Chi-square: 8.00; P-value: 0.005

Table 7: Serum albumin levels.

| Serum albumin levels (gm/dl) | No. of patient | % |
|------------------------------|----------------|---|
| Hypo albuminemia             | 32             | 64 |
| Normal                       | 18             | 36 |
| Total                        | 50             | 100|

Chi-square: 10.24; P-value: 0.006

Table 8: Serum electrolytes.

| Serum electrolytes | Serum levels (mmol/L) | No. of patients | Chi-square | P-value |
|--------------------|------------------------|-----------------|------------|---------|
| Sodium             | <128                   | 20              | 13.5       | 0.00    |
|                    | >128                   | 30              |            |         |
| Potassium          | <5                     | 39              | 15.6       | 0.00    |
|                    | >5                     | 11              |            |         |
| Chloride           | <95                    | 6               | 28.8       | 0.00    |
|                    | >95                    | 44              |            |         |

Table 9: Types of surgery.

| Surgery            | No. of cases | % |
|--------------------|--------------|---|
| Debridement        | 31           | 62|
| Debridement and fasciotomy | 20 | 40 |
| Split skin grafting| 37           | 74|
| Secondary suturing | 11           | 22|
| Amputation         | 5            | 10|
| Disarticulation    | 2            | 4 |

Chi-square: 11.5; P-value: 0.001 for split skin grafting

Table 7: Serum albumin levels.

- Out of 50 patients, 36 patients had haemoglobin level less than normal. Total count at the time of presentation; 36 (72%) patients out of 50 patients have a total count >14000 at the time of presentation (Table 5).

- Serum ferritin levels are shown in Table 6. 35 (70%) patients out of 50 had serum ferritin levels less than normal compared to their age and sex.

- Serum albumin levels Table 7, 32 (64%) patients out of 50 had hypo albuminemia levels at the time of presentation.

- Serum electrolytes are shown in Table 8. 20 out of 50 patients had sodium levels less than 128 and 11 patients had hyperkalemia. Types of surgery is shown in Table 9. All 50 patients underwent debridement. 31 patients underwent debridement alone, 20 patients underwent debridement and fasciotomy, 37 patients had to undergo split skin grafting.

Number of surgeries is shown in Table 10. 30 patients out of 50 had to undergo 2 operations and 45 out of 50 required two or more operations.
Table 10: Number of surgeries.

| No. of Surgeries | No. of cases | %  |
|------------------|-------------|----|
| One              | 5           | 10 |
| Two              | 30          | 60 |
| Three            | 11          | 22 |
| Four             | 2           | 4  |
| Five             | 2           | 4  |

Chi-square: 55.40; P-value: 0.000

Duration of hospital stay, 44 patients out of 50 had a hospital stay for more than 2 weeks.

Table 11: Mortality.

| Mortality | No. of cases | %  |
|-----------|--------------|----|
| No        | 44           | 88 |
| Yes       | 6            | 12 |

Mortality is shown in Table 11. Overall mortality rate noted in this study is 12%. All these cases were having low hemoglobin, albumin, ferritin, hyponatremia and leucocytosis with comorbid conditions.

DISCUSSION

NF is causes rapid destruction of tissue, systemic toxicity, with high morbidity and mortality. Necrotizing soft tissue infection was first described as hospital gangrene by Jones in 1871. In 1950, it was named as necrotizing fasciitis by Wilson.17 Synonyms for NF are Flesh eating disease, gangrenous erysipelas, hospital gangrene, acute cutaneous gangrene, non-clostridial crepitant cellulitis, streptococcal gangrene, synergistic necrotizing cellulitis, Meleney’s cellulitis. Based on microbiological cause NF has been classified into two types either type 1 (polymicrobial) or type 2 (monomicrobial).18 Type I infections are more common, caused by a mixture of aerobic and anaerobic organisms, which is common in immunocompromised individuals, such as patients with diabetes mellitus or chronic renal failure.19 Type II infections are less, typically occur in the limbs and afflict healthy patients with no comorbidities.

In most of the cases, there will be history of trivial trauma to the skin surface with seeding of bacteria. Infection starts in the deep tissue planes and infective organisms spread through the deep fascial tissue planes. The epidermis may not be initially affected. Bacteria load increases within viable tissue, and infection will spread to blood vessels leading to venous thrombosis of dermal papilla, resulting in ischemia and gangrene of subcutaneous fat and dermis. Infection of lymphatic channels leads to edema.20

At initial presentation there might be minimal epidermal involvement, make it difficult to differentiate from cellulitis. When the fascia breaches, myositis can occur. Clostridium species can cause gas gangrene. Toxin-producing bacteria (S aureus and S pyogenes) infection can lead to a toxic shock–like syndrome – septic shock/multiorgan dysfunction syndrome.

There are multiple predisposing factors like Diabetes, Renal failure, old age, malnutrition, obesity, PVD, intravenous drug abuse, Immunosuppressive drugs (eg-prednisolone). In a Singapore study, 70.3% of patients with NF had diabetes mellitus and in present study it is 74%.21

Extremities are the most common sites of infection. As in present study it was 74%. As per the study conducted by Golger A et al, common sites of infection are lower extremities (28%), upper extremities (27%), perineum (21%), trunk (18%), and the head and neck (5%).22

Patients with NF can also present with symptoms of sepsis like fever, altered mental state, diabetic ketoacidosis alone or with features of skin inflammation. Patients with NF typically presents with pain out of proportion to the degree of skin inflammation. Patients presenting with features of sepsis should include thorough examination of all parts of the body including perineum and oral cavity, which can be easily missed.23 The pain may be out of proportion to the degree of skin involvement.24 The progression is identified by tense swelling, vesicles, bullae (Hemorrhagic bullae and crepitus fascia and muscle involvement), cutaneous gangrene, creptis (in around 18% cases) with grayish-brown discharge. Lymphangitis and lymphadenopathy are usually absent in necrotizing infections.25 Creptit and blistering are the most specific signs of NF but they are not sensitive.

NF can present with hyperacute or a subacute course. In hyperacute course there will be sepsis with rapid progression to multiorgan failure. In subacute course there will be slow indolent course, without systemic disturbance. There will be gradual cutaneous changes with tissue necrosis, antibiotic resistant later sudden deterioration.26

It must be emphasized that diagnosis of NF is clinical, findings include gray necrotic tissue, thrombosed vessels, “dishwater” pus, noncontracting muscle, and a positive “finger test” result, which is characterized by lack of resistance to finger dissection in normally adherent tissues.27

Neutrophilic leukocytosis, acidosis, altered coagulation profile, impaired renal function, raised creatinine kinase levels, and raised C-reactive protein levels, are all helpful with clinical correlation.

Plain X-ray films can demonstrate subcutaneous gas, but this is a specific not a sensitive.28 Computed tomography (CT) and magnetic resonance imaging (MRI) shows asymmetrical fascial thickening, fat stranding, and gas tracking along fascial planes. These modalities can be
used in wherever their diagnosis is in doubt. Early and repeated wound debridement with broad spectrum antibiotic is the mainstay of the treatment. 29

Mortality rate in present study was 12%. In the recent data the mortality is 16.4% for community-acquired necrotizing soft tissue infections and 36.3% for post procedural necrotizing infections. 30, 31 NF is having considerable postoperative morbidity due loss of neurovascular bundles, muscle, amputation and needs period of rehabilitation. Few patients will have scarring and disfigurement.

CONCLUSION

Patients with advanced age, co-morbid conditions like diabetes mellitus, hypertension, peripheral vascular disease, and osteomyelitis had high susceptibility to the disease and with a higher incidence in males. Patients presenting with pain out of proportion, fever, skin discoloration, cellulitis, edema, local cutaneous anesthesia, crepitations should be viewed with high clinical suspicion to be diagnosed as NF. Leukocytosis, anaemia, hypoleukemia, low serum ferritin levels increase blood sugar levels were consistent findings seen in majority of the patients which resulted in increased morbidity.

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