

Bacterial Isolates From Necrotizing Fasciitis: A Clinico-pathological Perspective

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Abstract

Background: Necrotizing fasciitis (NF) is a progressive, polymicrobial, potentially fatal soft tissue infection that can affect both sexes, all age groups and any anatomical region of the body. Identification of the offending microorganisms is important, since the eventual outcome of treatment is dependent on aggressive surgical, chemotherapeutic and supportive therapy.

Aim: To determine the spectrum of aerobic bacterial organisms responsible for NF in Sokoto, Northwestern Nigeria, and to establish a baseline for which further studies can be conducted.

Patients and Methods: A 5-year prospective study of aerobic bacteria isolated from all consecutive patients with NF seen at the Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria from January 2001 to December 2005. All necessary information from each patient was fed into the computer for analysis.

Results: There were 62 patients, of which 33 (53.2%) were males while the remaining 29 (46.8%) were females. The ages ranged from six days to 70 years (mean = 21.4 years). One or more precipitating factors were identified in 32 (51.6%) patients, while 40 (64.5%) patients had identifiable pre-morbid pathology. The body surface area (BSA) involved ranged from 1–31% (mean = 5.2%). The commonest anatomical region involved was the trunk in 23 (37.1%) patients; this was followed by the lower limbs, upper limbs, head and neck, perineum and buttocks in that order. From the 62 patients, 176 aerobic cultures were carried out. Of this, 147 cultures (83.5%) were positive, while the remaining 29 (16.5%) grew no organisms after 48 hours of incubation. The commonest offending organisms were *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Infection was polymicrobial in 64% of patients. Cephalosporins, quinolones and aminoglycosides were the most sensitive antibiotics. Multiple wound debridements were required in nearly half of the patients. The duration of hospital stay ranged from 3–132 days (mean = 39 days). The overall mortality was 14.5%.

Conclusion: NF is essentially polymicrobial, deriving significant contributions from both gram-negative and

gram-positive bacteria. The cultural characteristics of the disease, and sensitivity to antibiotics, require periodic assessments.

Keywords: Necrotizing fasciitis, aerobic bacteria, antibiotics.

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Introduction

Diffuse necrotizing infections are the most treacherous soft tissue infections, because they may masquerade as simple cellulitis, thereby delaying diagnosis and treatment¹. The term necrotizing fasciitis (NF) is now used in a generic sense to include all diffuse soft tissue infections except gas gangrene¹, although it was originally coined by Wilson² to refer to infections characterized by necrosis of the superficial fascia with sparing of the deep fascia and muscle. Initially attributable mainly to streptococcal infections, it is now known to be a clinical entity caused by a combination of various synergistically acting organisms without any specific combination³⁻⁶.

Both gram-positive and gram-negative organisms have been implicated in the aetiopathogenesis of the disease. The primary pathogens are usually the aerobic partners, which contribute the destructive enzymes that create an anaerobic environment for invasion by the anaerobic organisms⁷. It has been suggested that tissue necrosis occurs either directly by the action of microbial enzymes or indirectly through thrombosis of nutrient blood vessels serving the area^{1,8}. Usually, both processes occur simultaneously. Recently, various studies⁹ reported the increasing incidence of gram-negative organisms in the causation of NF. It has further been observed, as in other infections, that bacterial flora from surface swabs may well be contaminants and different from what is obtained from deeper structures¹⁰. Identification of the infective organisms and determination of their sensitivity pattern is central to the management of this disease condition. Treatment must be prompt and radical. This study was undertaken to determine the spectrum of aerobic bacterial organisms responsible for NF in the Sokoto environment, and to establish a baseline for further studies.

Patients and Methods

This 5-year prospective study was conducted between January 2001 and December 2004 at the Usmanu Danfodiyo University Teaching Hospital, Sokoto, Nigeria. Approval for the study was obtained from the hospital's ethical committee on research. Permission to include all patients in the study was sought from each patient or their parents, and 100% participation was obtained from all the patients who presented within the study period. The study included all patients with diffuse necrotizing soft tissue infections, according to the known standards of classification of soft tissue infections¹. Patients with cancrum oris (noma) or Fournier's gangrene were excluded. This is because patients with the former are being managed in a specialized hospital built for that purpose in the same city, while those with the later are being managed mainly by the Urologists in our center. All the patients were admitted and resuscitated. Each patient was thoroughly evaluated at initial assessment to determine the exact nature of the infection and ascertain the involvement or otherwise of other systems. This included a detailed clinical evaluation, clinical photography, and relevant microbiological, haematological, immunological, chemical, radiological and histological investigation. Blood samples, surface swabs, tissues and/or tissue fluids were taken and subjected to aerobic bacterial cultures only. This was because only facilities for aerobic bacterial cultures were in regular supply in the hospital during the period of study. The samples were taken on admission, during and after debridements, and any other time considered necessary, depending on the nature of the wound, and the patient's response to treatment.

Wound care measures were instituted after prompt and radical surgical debridement. Nutritional, physical and other forms of rehabilitation were instituted when necessary. Major surgical debridements were carried out in the main theatre under general anaesthesia and subsequently repeated where and when necessary. Tetanus toxoid, broad-spectrum antibiotics and analgesics were given routinely. The antibiotics were commenced after the initial specimen(s) for culture and sensitivity were appropriately taken. Subsequent antibiotic therapy was based strictly on the result(s) obtained from the culture(s). Final wound resurfacing was either by secondary intention, direct closure, skin graft or flap reconstruction, depending on the state of the wound and other variables that each patient presented with. All patients were followed-up after discharge from hospital at the surgical out patient unit. Each patient's information was entered into the computer for analysis.

Results

Over the 5-year period, 62 patients were treated for necrotizing fasciitis (NF), 56 of which have been reported earlier¹¹. There were 33 (53.2%) males and 29 (46.8%) females, giving a male: female ratio of 1.1: 1. The ages ranged from six days to 70 years (mean = 21.4 days). The ages of the patients ranged from 6 days to 70 years (mean = 18.3 years). More than half of the patients (54.8%) were children aged 15 years and below. One or more precipitating factors were identified in 32 (51.6%) patients, including pustules in 17 (27.4%), various degrees of trauma in 13 (21.0%) and injection in the remaining 10 (16.1%) patients. A child had it after colostomy for a high ano-rectal anomaly, while a middle-aged woman had it following radiotherapy for cervical carcinoma. Pre-morbid conditions were noted in 27 (43.5%) patients, including malnutrition in 17 (27.4%), diabetes mellitus in 5 (8.1%) and lymphoedema of the legs in 3 (4.8%); two patients (3.2%) were retroviral positive. The duration of symptoms ranged from 3 to 45 days (mean = 11 days) while the body surface area (BSA) involved ranged from 1-31% (mean = 5.2%). The commonest anatomical region involved was the trunk, as this was noted in 23 (37.1%) patients; this was followed by the lower limbs (30.1%), head and neck (17.7%), upper limb (17.7%), perineum (8.1%) and the buttocks (8.1%). Multiple debridements were required in over 35% of patients. A total of 176 aerobic cultures were carried out in 62 patients. Of these, 147 cultures (83.5%) were positive, while the remaining 29 (16.5%) grew no organisms after 48 hours of incubation. Multiple cultures were obtained in all the patients. The commonest offending organisms were *Staphylococcus aureus* and *Pseudomonas aeruginosa*. Infection was polymicrobial in 64% of patients. Table I shows the cultural characteristics of the offending organisms. Cephalosporins, quinolones and aminoglycosides were the most sensitive antibiotics in that order. The *in vitro* antibiotic sensitivity pattern of the cultured organisms is shown in table II. A mortality rate of 14.5% (9 patients) was recorded during the study.

Discussion

Necrotizing fasciitis (NF) is a fatal soft tissue infection that requires radical surgical, antibiotic and supportive therapy. Because the infection may start as cellulitis before the onset of necrosis, many patients indulge in consumption of self-prescribed antibiotics before hospital consultations. This antibiotics abuse may partly be responsible for the sensitivity pattern and the 16.5% negative cultures encountered in this study. The

presence of pre-morbid conditions in 27 (43.5%) patients may have predisposed them to NF. The results in this study are a confirmation that no sex, age group or anatomical region of the body is exempt in this condition. It has been observed that surface swab cultures may remain negative while organisms continue to invade the

deeper tissues¹⁰. This understanding necessitated the use of tissues and/or tissue fluid, in addition to surface swabs for culture in our patients. The progressive nature of the disease did not only account for multiple debridements (Figure 1), but also multiple cultures in all the patients.

Table 1: Cultural characteristics of isolated organisms.

Organism	Number of positive Cultures	Percentage
<i>Staphylococcus aureus</i>	103	70.1
<i>Pseudomonas aeruginosa</i>	97	66.0
<i>Klebsiella species</i>	76	51.7
<i>Streptococcus pyogenes</i>	71	48.3
<i>Eshcherichia coli</i>	59	40.1

Note: 29 (16.5%) of the 176 cultures grew no organisms after 48 hours of incubation.

Table 2: Antibiotic sensitivity pattern

Organism	Percentage sensitivity to antibiotics						
	Ceph	Quin	Gent	Clox	Eryt	Amp	Tcn
<i>Staphylococcus aureus</i>	93	91	86	48	62	46	31
<i>Pseudomonas aeruginosa</i>	97	92	89	31	66	27	24
<i>Klebsiella species</i>	96	88	87	36	71	21	27
<i>Streptococcus pyogenes</i>	92	92	89	42	58	26	32
<i>Eshcherichia coli</i>	96	87	66	27	63	24	21

Key: Ceph Cephalosporins (Cephalexin, Cefuroxime, Ceftriaxone, Ceftazidime, Cefotaxime)
 Quin - Quinolones (Ciprofloxacin, Pefloxacin, Ofloxacin)
 Gent Gentamycin
 Clox Cloxacillin
 Eryt Erythromycin
 Amp Ampicillin
 Tcn - Tetracycline



Figure 1: Necrotizing fasciitis affecting the posterior trunk in a young Nigerian boy, after two major debridements. Note the exposed trapezius muscles, apparently not involved.

The polymicrobial culture in 64% of our patients is in consonance with previous reports^{1,2,7-9,12}. However, we were unable to obtain regular fungal, viral or anaerobic bacterial cultures during the period of this study, mainly due to non-availability of the necessary culture media. Cases of *Vibrio vulnificus*, *Vibrio parahaemolyticus*^{13,14} and other halophilic marine vibrios have earlier been reported as causes of NF. These organisms belong to the family *Vibrionaceae* and are inhabitants of seawater. They are facultative organisms, which can cause a variety of infections, including gastro-enteritis, otitis externa and conjunctivitis¹⁵. Although *V. vulnificus* is the most common cause of soft tissue infections, *V. alginolyticus* is the most halophilic of the pathogenic *Vibrio species*¹⁵. These organisms are commonly found

in patients with immunosuppression¹²⁻¹⁴, and their virulence is related to their ability to produce haemolysis, haemagglutination and proteases¹⁵. More recently, Yamane et al¹⁶ reported two cases of fatal NF caused by *Photobacterium damsela* in Japan. Other new varieties of NF recently described are caused by phycomycoses, particularly *Rhizopus arrhizus*¹⁷ and *Cryptococcus neoformans*¹⁸. Unlike the NF caused by the commonly recognized bacteria, marine vibrios and *Photobacterium damsela*, the clinical presentation of phycomycotic NF is insidious¹. In agreement with some studies^{4,19,20}, gram-positive bacteria were the most frequently isolated organisms. The predominant bacterial cause of NF has been the subject of debate. While some report gram-positives as the commonest^{4,19,20}, other reports^{5,9} favour gram-negatives; although recent studies⁹ report an increasing aetiological contribution by the latter. However, it is well established that in NF, there is a synergistic relationship between gram-positive and gram-negative bacteria^{1,8,9,14}. Consequently, the resultant effect is usually far more fulminant than the regular effect attributable to the individual pathogen¹⁴.

The initial choice of antibiotics (cephalosporins and metronidazole) was based on previous knowledge of the microbiology of NF and local sensitivity patterns^{8,9,11}. These antibiotics, as well as quinolones and aminoglycosides, were found to have the highest sensitivity in the study (Table I). While some researchers¹⁷⁻²¹ have found quinolones to be very effective in the management of NF, others^{8,9,20} reported the initial use of a combination of penicillin, aminoglycoside and metronidazole to be essential. The resistance noted in this study to antibiotics like ampicillin, cloxacillin and tetracycline may be a result of their abuse (in the local environment). Most of these drugs are commonly found with vendors and in chemist shops and can be obtained without prescription. They are also frequently prone to adulteration. We avoided quinolones as our first line of antibiotics in children in our study because of their suspected effect on the growth plate of bones, although this risk is now considered minimal²².

Conclusion

We conclude that NF is largely polymicrobial, deriving significant contributions from both gram-positive and gram-negative organisms. Elucidating the prevailing pattern in any locality requires periodic analysis. The results of this study would enable a more objective initial

empirical antibiotic treatment of NF while the results of antibiotic sensitivity are being awaited.

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