Oral Diseases (2009) 15, 133–141. doi:10.1111/j.1601-0825.2008.01496.x
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INVITED REVIEW
HOT TOPIC

Cervico-facial necrotizing fasciitis

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Necrotizing fasciitis of the cervical facial region is a rare entity that has seen an increasing prevalence in the last 20 years. It is most common in patients with an underlying systemic disease leading to immunosuppression, but can be seen in healthy adults and children. It is characterized by soft tissue destruction which is disproportionate to its clinical symptoms and signs, with rapid progression and fatal outcome, if not treated rapidly and radically. We present a review of the etio-pathogenesis and management of this challenging disease.
Oral Diseases (2009) **15**, 133–141

Keywords: necrotizing fasciitis; cervico-facial; invasive group A streptococcus

Introduction

Severe life threatening necrotizing infections have been recognized as entities throughout history. The synonym for cancrum oris, derives from the ancient Greek word noma, meaning 'to devour' and a classic specific description of necrotizing fasciitis (NF) was also given by the Greek 'father of medicine' Hippocrates (Adams, 1771). The term NF was first used by Wilson (1952). Prior to his times, the infection had been described using a number of different names including, malignant ulcer, gangrenous ulcer, gangrenous erysepalis, necrotizing cellulitis, phagedenis ulcer, phagedena gangaenosa, Fournier's gangrene (Fournier, 1883) hospital gangrene, and Melaney's gangrene (Melaney, 1924). It was Melaney's work in China that first isolated a hemolytic streptococcus from patients with this disease in 1924. However, Joseph Jones, a Confederate Army surgeon in 1871, is generally regarded as having given the first modern account of NF, (which he called hospital gangrene) (Jones, 1871). He delineated cases of gangrene amongst the Confederate soldiers of the American Civil War, which were characterized by skin discoloration followed by the loss of superficial and deep tissue. In civilian life, NF has been regarded as relatively rare especially in the cervico-facial region.

In this modern era of sensationalism in the media, stories of flesh eating bacteria and antibiotic resistant super bugs have raised public consciousness regarding this disease, which is actually becoming more prevalent. The rate of NF has increased since the late 1980s, which may be attributed to a recent mutation in a sub-group of group A Streptococci (Martin, 1993). An epidemiologic study on invasive group A Streptococcal infections (defined as NF, streptococcal toxic shock syndrome or isolation of the organism from a normally sterile site), found 5400 cases in a population of 29.7 million (3.5 cases per 100 000) (O'Loughlin *et al*, 2007). The authors estimated that 8950–11 500 cases of invasive group A Streptococcal infections occur a year in the USA. The case fatality rates for NF were 24%. The authors recommended the introduction of a multivalent vaccine. This increasing incidence may be related to an increase in virulence of the organism and a comparative increase in susceptible (immune suppressed) hosts. Currently, there are 93 validated M serotypes of group A streptococci and >130 emm genotypes reported from the United Kingdom (Tanna *et al*, 2006).

Etiology

Necrotizing fasciitis is most common in the abdominal wall, perineum, and limbs and <10% of cases involve the cervico-facial region. As is the case in any infection, the disease involves a precipitating event, an infectious agent and a host. The commonest precipitating event is an odontogenic infection, and Whitesides *et al* reported 12 cases and Wong *et al* reported 11 cases of odontogenic infections complicated by NF (Whitesides *et al*, 2000; Wong *et al*, 2000). In Wong *et al*'s series, the incidence of NF was 2.6% in patients hospitalized with infections on the OMS service. Other causes are tonsillar abscesses, parotitis, otitis media, trauma, or surgery of the head and neck mostly as isolated case reports. Peritonsillar abscess as a cause for NF is rare and a review in 2003 found only 12 published cases in the world literature (Skitarelić *et al*, 2003). Interestingly, the overall mortality in this group of 33% was higher than

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Received 14 July 2008; revised 20 August 2008; accepted 15 September 2008

the 25% reported for NF from odontogenic infections. In children, odontogenic infections are rarely a cause of NF and varicella infections appear the main precipitating cause (Eneli and Davies, 2007). In this epidemiologic survey from Canada, NF occurred in 2.93 children per million, with higher rates in children <5 years, 58% of cases of NF related to group A streptococcal were associated with varicella (Eneli and Davies, 2007).

Although classically regarded as a beta hemolytic group A streptococcal infection, NF is usually a polymicrobial infection with synergistic activity between aerobic and anaerobic organisms. McGurk in a comprehensive review categorized three types of NF depending on the organisms involved (McGurk, 2003). First, in temperate climates group A streptococcus $\pm$ *Staphylococcus aureus*; secondly, in up to 60% of cases, polymicrobial infections occur with anaerobes predominating including peptostreptococcus, prevotella, porphyromonas, bacteroides, and clostridia: and finally, in tropical climes vibrionacae may cause NF. However, many different organisms have now been described as contributing to the pathogenesis of NF. Lin *et al* reported a series of 47 patients with NF of the head and neck from Taiwan. Klebsiella pneumonia was found in 26% of cases with streptococci and staphylococci also being common (Lin *et al*, 2001). Case reports of rare bacterial species as causative organisms in cervico-facial NF such as multidrug resistant Burkholderia cepacia with peptostreptococcus (Marioni *et al*, 2006) and stomatococcus mucilaginosis (Lowry and Brennan, 2005). Lowry and Brennan illustrated that NF can be caused by a wide variety of bacteria (Lowry and Brennan, 2005). In health care today, the problem of antibiotic resistant 'super bugs' can be a major cause of morbidity and mortality. Methicillin resistant *S. aureus* (MRSA) has been identified as the causative organism in 39% of NF, and it is recommended that MRSA-directed antibiotics be considered promptly in NF (Lee *et al*, 2007). In another publication with a total of 843 patients who had MRSA cultured from their wounds, 14 patients were diagnosed with NF and the authors state that community associated MRSA causing NF should be recognized as an emerging entity (Miller *et al*, 2005).

Regarding the host, NF is most commonly seen in immuno-compromised patients and although healthy adults and children can be affected, this is relatively rare. In systemic diseases such as diabetes, renal failure, AIDS, liver cirrhosis, and lymphomas/leukemias, there is an increased risk, also in elderly and obese patients. In Lin *et al*'s series, 89.4% of cases had systemic diseases with 34 of 47 cases (72.3%) having diabetes, while Wong *et al* found that 63.4% of patients were immunocompromised with 4 of 11 (36.3%) affected by diabetes. Whitesides reported a series of patients from our institution, 45% had diabetes 36% obesity and alcoholism and 18% HIV infection (Whitesides *et al*, 2000). Medical therapy such as steroids or chemotherapy for cancer can also cause immune compromise and be associated with NF. In one case report, NF leading to septic shock occurred 9 months following completion of chemoradiation therapy for head and neck cancer (Maluf *et al*, 2007).

Diagnosis

Necrotizing fasciitis is a rapidly progressive disease that can progress from a small innocuous wound to a fulminant necrosis of the skin with septic shock and death very rapidly in hours to days. In view of the rapid evolution of NF and its fatal outcome without early treatment, immediate diagnosis is essential to reduce both morbidity and mortality. Early diagnosis is confounded in the initial onset of disease by the fact that the rate of necrosis is disproportionate to the systemic signs and symptoms. Severe pain may be present in a small wound or infection accompanied by redness, swelling, and a warm skin. However, at this point, there may be no temperature, tachycardia or raised white cell count, and it is hard to differentiate this clinical picture from a routine cellulitis. As the disease evolves, the skin initially becomes pale, then mottled and purple looking and finally obviously gangrenous. Blistering of the skin occurs with overlying anesthesia and in cases where gas forming organisms are prominent, surgical emphysema will be elicited on palpation (Figure 1a–c). There is increasing edema with fluid weeping from the wound and frequently a marked fetor. At this stage, the patient will become systemically ill showing the signs of septic shock with hypotension, tachycardia, and malaise. If untreated, there is progression of the skin necrosis and exposure of the underlying soft tissues and bone (Figure 2). The patient becomes increasingly ill with progression to organ failures most commonly renal, hematologic or acute respiratory distress syndrome. A clinical staging of disease progression has been proposed based on the cutaneous signs (Wang *et al*, 2007). Stage I (early) includes clinical signs of tenderness, erythema, swelling, and calor. Stage II (intermediate) involves blistering or bullae. Stage III involves crepitus, skin anesthesia, and skin necrosis. In this study, it was found that 41% of patients presented with blistering but had late signs e.g. skin crepitus, necrosis, and anesthesia were rare (0–5%). However, by day 4, 77% of patients had blisters and in addition late signs of skin crepitus, necrosis, and anesthesia were present in 9–36%. Overall, 59% of patients were Stage I at day one, but 68% progressed to Stage 3 at day 4.

Complete blood count may be helpful if the white count is significantly raised; however, this is not always true in the early phases of the disease. Cultures and gram stains can help direct antibiotic therapy. CT scanning may aid in early recognition of NF (Figure 3). In one study of 14 patients with NF of the head and neck, constant features in all cases were diffuse thickening and infiltration of the cutis and subcutis, diffuse enhancement and/or thickening of the superficial and deep cervical fascia, enhancement and thickening of platysma, sternomastoid, and strap muscles and fluid collections in multiple neck compartments (Becker *et al*, 1997). Other features that were not seen in all patients included gas collections (64%), and 50% with mediastinitis and pleural and pericardial effusions.

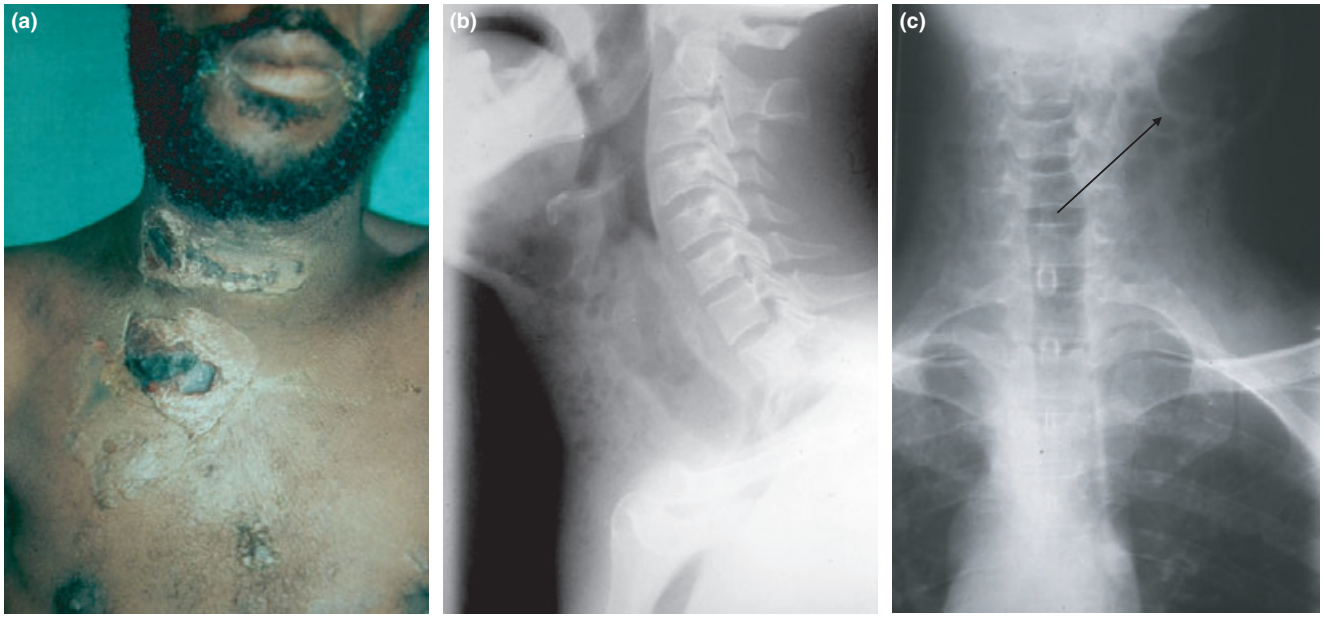

Figure 1 (**a**) Diabetic patient with submandibular swelling secondary to an abscessed mandibular molar tooth, showing necrosis and gangrene of the skin of his neck and supraclavicular region. Crepitus is palpable in the neck. (**b**) Lateral cervical radiograph shows gas in the neck. (**c**) PA cervical film shows large areas of gas (see arrow)

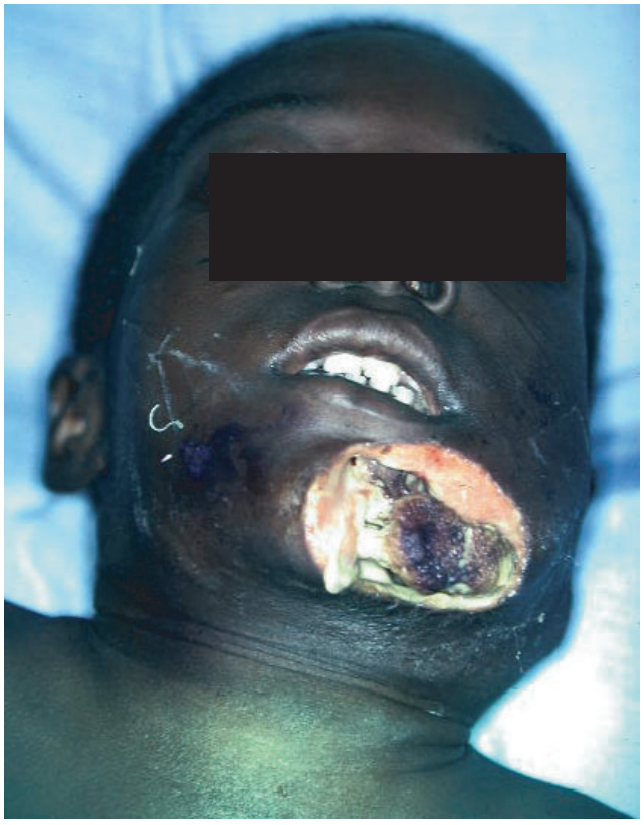

Figure 2 A 12-year old girl with leukemia has rapidly progressive facial NF with sloughing of the necrotic skin and subcutaneous tissues over the chin

If NF is clinically suspected, the surgeon should not, however, delay surgical treatment to obtain scans or culture results.

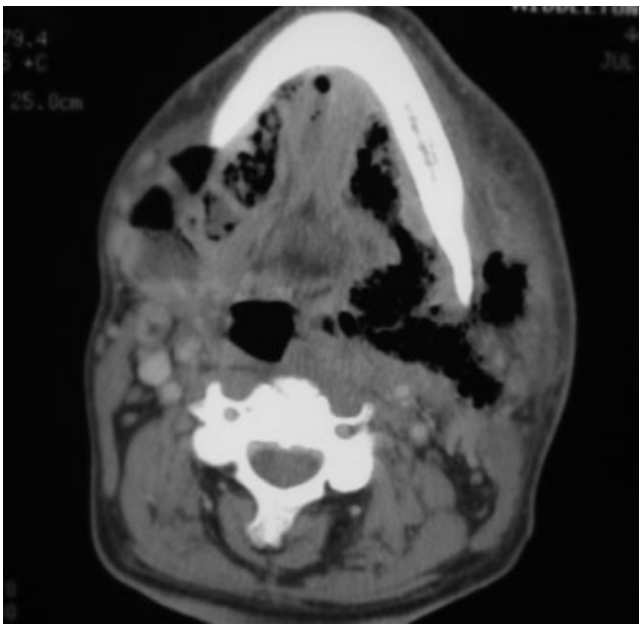

Figure 3 Axial CT shows large areas of gas in the fascial spaces tracking between muscles

Pathogenesis

In true NF, the infection is related to the fascia and subcutaneous fat while the overlying skin is spared, unlike erysipelas, which affects the superficial layers of the skin and lymphatics, and cellulitis, which involves deeper subcutaneous tissues, but not the fascia. In its classical form, the underlying muscles are not affected, but a necrotizing myositis may occur as part of the

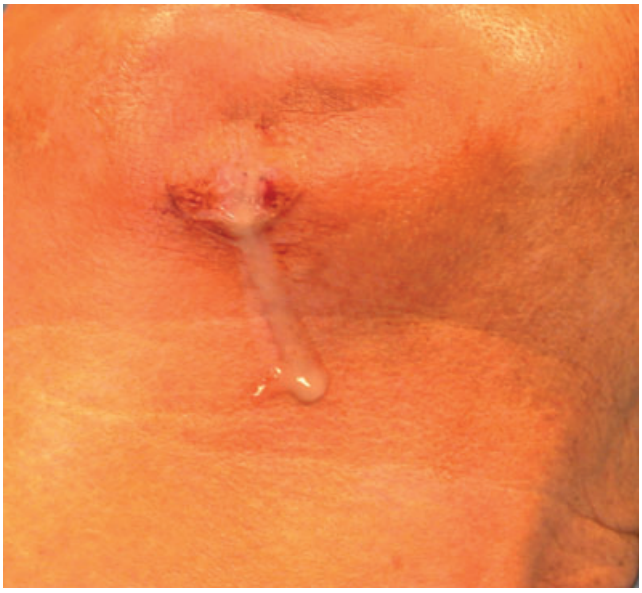

Figure 4 Example of 'dishwater puss' drainage

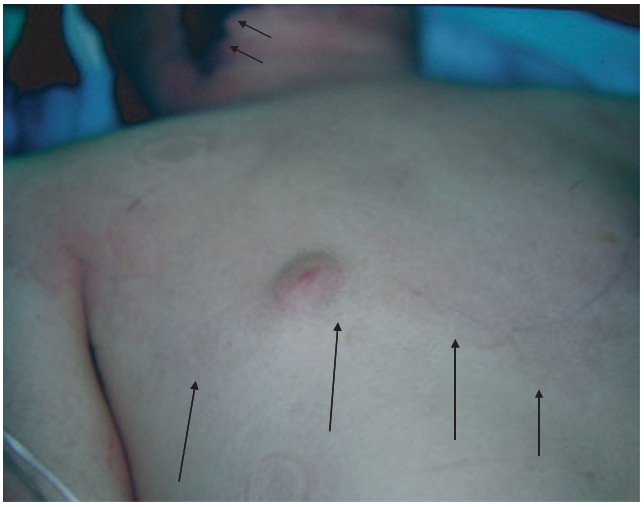

Figure 5 A young man with cervicofacial NF postwisdom teeth extraction. The two short arrows in the upper part of the figure show an area of purple black necrosis in the skin of the submandibular region. Although the skin of the chest wall and neck appears intact, the long arrows mark the advancing lines of skin erythema

spectrum of NF particularly when gas forming organisms such as Clostridia are prominent. Early in the disease process, necrosis and liquefaction of the fascia and fat occur possibly mediated by the collagenase and hyaluronidase produced by group A streptococci. This liquefaction breakdown of the fat causes edema and separates the skin from the underlying tissues producing edema fluid and the pathognomic 'dishwater pus' (Figure 4), which has an offensive odor in the presence of anaerobes. As the process progresses, the perforating veins supplying the skin become thrombosed reducing venous return from the skin and increasing edema and purplish mottling (Figure 5). Because of the inflammatory response, a dense infiltrate of polymorphonuclear cells migrates to the subcutaneous tissue and the skin surrounding the infected area is erythematous. At this stage, the redness and swelling of the skin can still be taken for a cellulitis and spread of the infectious process along the fascial planes of the neck can widely undermine the skin into the face and thorax. The clinician may not be able to appreciate the extent of skin that is already devitalized by the cutaneous erythema alone. Further necrosis and liquefaction of the fat and fascia lead to arterial thrombosis with ischemic death of the skin, which is first pale then purple and finally black. At this point, blistering of the skin and leaking of foul smelling fluid from the skin surface will be seen. The dead skin will be anesthetic to sensory testing. NF can progress very rapidly and if unrecognized or not treated appropriately, the skin will slough to expose the underlying muscle, which may be relatively unaffected. If a myositis is present then dead muscle frequently with a marked fetor and gas formation will expose the underlying bone. The molecular inflammatory factors produced will lead to a systemic response with fever, tachycardia and eventually septic shock.

Summary of diagnosis and pathogenesis

Diagnosis	*Pathogenesis*
Early pallor of skin	Early liquefaction of fascia and fat
Late mottling and cyanosis of skin	Venous thrombosis
Pitting edema	Infiltration of polymorphonuclear cells
Blistering	Spread along fascia planes
Crepitus of skin	Arterial thrombosis
'Dish water' pus	Death of skin and underlying fascia
Fetor odor	
Clinical signs of septic shock	

Management

It should be emphasized that the single most important treatment modality for NF in determining the outcome and mortality is surgery. The earlier the recognition of the disease and the sooner surgical debridement is undertaken, the better the prognosis. However, depending on the stage of the disease and when the patient is first seen, the management of these patients is divided into four areas. The first stage is prompt resuscitation of the patient, which is followed by early aggressive surgery as the second stage. The third stage of treatment will be supportive critical care (including adjuvant antibiotics). Lastly, a reconstruction/rehabilitation phase will commence after the infection is resolved, wounds are stable, and the patient has recovered from the septic shock.

Resuscitation

If the patient is systemically ill when first admitted, attention will be directed to immediate medical resuscitation to allow the patient to be taken to the OR as soon as possible. At this stage, fluid resuscitation for septic

shock, insulin and fluids for diabetic keto-acidosis, steroids and tranfusions for immuno-suppressed patients and correction of electrolytes in renal failure may all be essential. In patients with profound hypotension and/or multiorgan failure, ionotropes may be required. Patients who have septic shock have a significantly worse prognosis (Lin *et al*, 2001), although we and others have reported treating such patients successfully (Ricalde *et al*, 2004). Decisions regarding the patient's airway may also need urgent decisions at this stage with intubation and early tracheotomy recommended (Durrani and Mansfield, 2003). Medical management with antibiotics will be initiated at this stage (see below), but surgery should not be delayed to await the results of cultures or scans.

Surgery

The definitive treatment for this disease is radical debridement of all the necrotic fascia and subcutaneous tissue along with the overlying dead skin and the involved muscles, if necessary (Figure 6). Following incision of the skin, extensive underlying necrosis will be recognized. Usually, there is copious grey-white dish water pus with an offensive odor. The skin can be easily stripped from the underlying fat and fascia by blunt finger dissection and the skin edges do not bleed. The area of the dead skin is greater than perceived clinically and can best be delineated by cutting back the skin that dissects easily by finger pressure until the edges bleed. The necrotic fascia and fat are stripped from the muscle as a jelly like necrotic mass and sent for histology and deep anaerobic and aerobic cultures. Wound cultures and blood cultures are extremely important to direct antibiotic therapy (Chattar-Cora *et al*, 2002) in the face of what is usually a polymicrobial infection. The muscle is usually healthy and bleeds readily but if involved, (usually by gas forming organisms) should also be debrided (Figure 7a–c). Surprisingly, nerve trunks are often intact and branches of the facial nerve may be spared if possible. At this stage, no attempt should be made to close the wound or reconstruct the area primarily, but the wound should be packed open. The

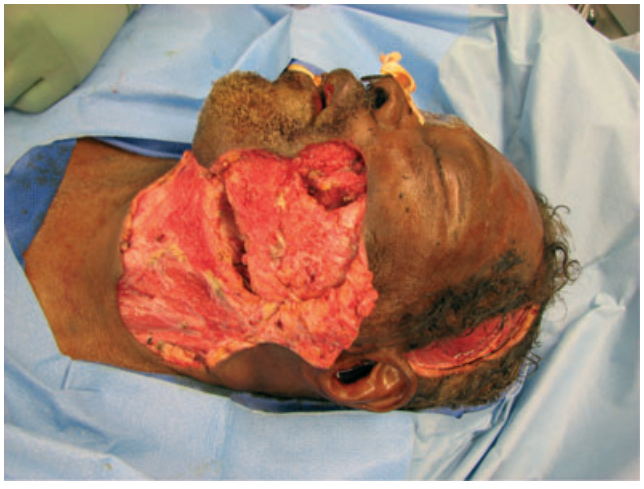

Figure 6 Debilitated diabetic patient, status postchemotherapy for renal carcinoma. Debridement of the face and neck for necrotizing infection from an odontogenic source

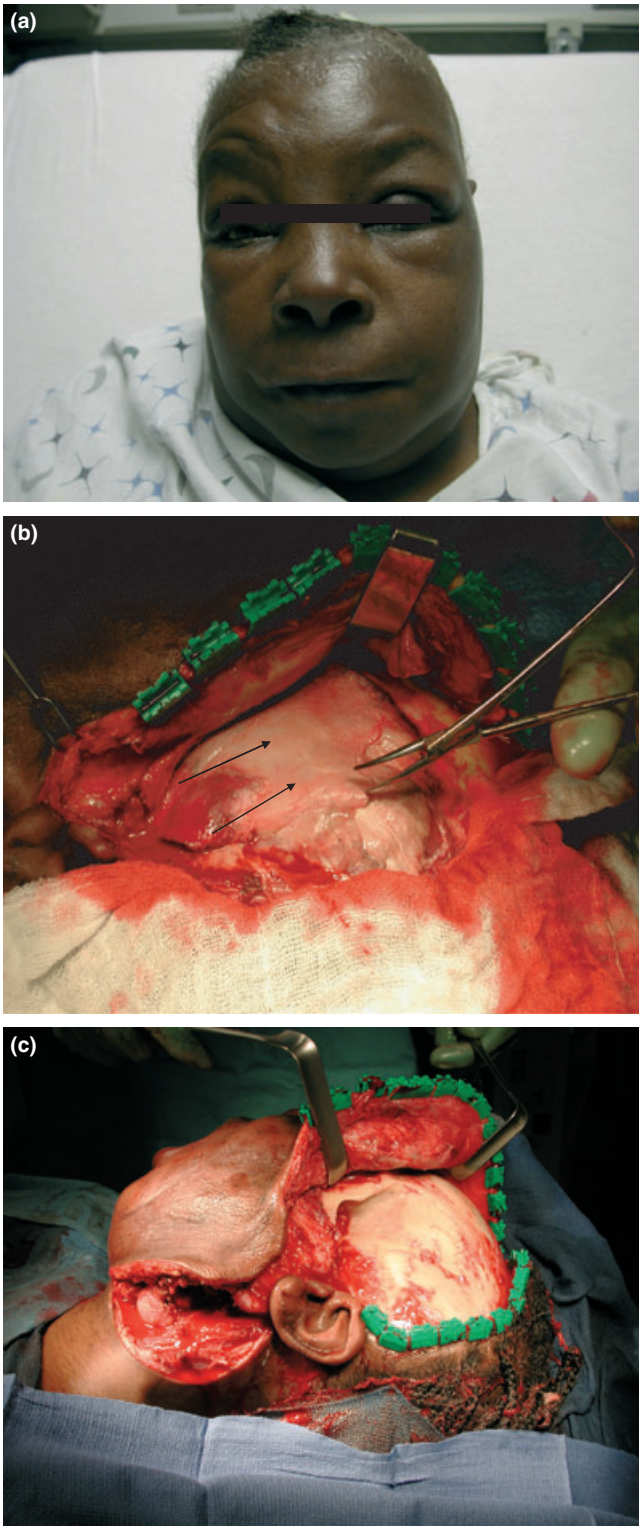

Figure 7 (**a**) Patient with AIDS presents with swelling of the left face and peri-orbital edema. (**b**) Initial submandibular exploration reveals myonecrosis of the masticatory muscles. Subsequent hemicoronal flap shows the temporalis muscle to be necrotic and avascular (arrows). (**c**) Following excision of all dead muscle

only closure may be the use of local muscle flaps to cover important structures such as the carotid artery although blow out in NF is very rarely reported (Tovi *et al*, 1991). The wound can be packed with wet-to dry gauze soaked in saline, with dilute hydrogen peroxide if anaerobes are suspected or the use of Clorpactin^{TM} (Guardian Labs, div United – Guardian Inc. Drug Development Company, Hauppage, NY, USA) (hypochlorous acid) gauze soaked packing. Other authorities have recommended packing with moist Providone iodine guaze (Ahrenholz, 1998). If pseudomonas is cultured, dilute acetic acid is also useful to clean the wound. At this stage, the surgeon must decide whether to convert the endotracheal tube to a tracheotomy and also to prepare the patient to be brought back to the OR within 24 h. It is usually the case that the initial debridement does not prevent some progression of the disease and further cutting back of non-bleeding skin edges is required. On average, the patient will go back to the OR at least three times for wash outs, debridement, and packing until the wound is stabilized. Alloderm (allogenic cadaver dermis) may be used as a temporary dressing in wounds with extensive open areas. An alternative, which we have found useful, is the vacuum-assisted wound closure (Huang *et al*, 2006).

Medical Therapy

Obviously, the main medical priority in these patients other than initial stabilization and resuscitation with attention to any underlying compromising systemic condition is the immediate initiation of antibiotic therapy. Today, we realize that in addition to covering for group A streptococci, anaerobic and broad spectrum coverage is essential, with the understanding that antibiotic resistant bacteria such as MRSA are frequently present. Usually, a triple antibiotic regime is required which will include a penicillinase/methicillinase resistant penicillin for streptococci and staphylococci, an aminoglycoside such as vancomycin (or a third generation cephalosporin) for gram negative bacteria, and anaerobic cover using clindamycin or metranidazole. Antibiotic therapy will be changed in response to cultures, but initial triple therapy is currently the standard of care.

Postoperatively, the patient will be managed in an ICU setting with attention given to ventilation and nutrition and correction of any organ failure (pulmonary, renal, hematologic). Most of these patients are extremely ill with hospital stays of 26.4 days mean (Lin *et al*, 2001), 24.9 days mean (8–52 days) (Gozal *et al*, 1986), and 31 days with 14 in the ICU (Whitesides *et al*, 2000). In one study, the average length of ICU stay was 21 days (Mohammedi *et al*, 1999). Polyspecific immunoglobulin given intravenously has been used for invasive group A streptococcal infections and specifically for NF (Haywood *et al*, 1999). In this study of 16 patients who received immunoglobulin and four who did not, there was no difference in outcomes or mortality. The authors, however, commented on a low mortality rate of 20%. There are few other reports that emphasize the use of immunoglobulin (Hanna *et al*, 2006). Another adjunctive therapy that has been suggested in the treatment of NF to reduce morbidity and mortality is hyperbaric oxygen (Gozal *et al*, 1986; Riseman *et al*, 1999; Banerjee *et al*, 1996). However, it should be noted that there are no controlled trials to delineate its effectiveness and at least one paper has shown that mortality rate and the number of debridements required was higher in patients treated with hyperbaric oxygen (Shupak *et al*, 1995). One very recent paper advocating the use of hyperbaric oxygen reports 13 cases of cervical NF with a zero mortality rate (Stenberg *et al*, 2004). Lastly, appropriate nutritional support should commence as soon as possible because these patients are usually in a profound catabolic state. There is a greater chance of achieving stabilized wounds, which is obviously required for reconstruction, by optimizing their caloric intake.

Reconstruction/Rehabilitation

Because of the patient's immune suppression during the acute phase, immediate reconstruction is contraindicated. Once multiple debridements have ensured a stable wound with good vascular granulation, and the ability of the skin edges to stick to the wound, reconstruction can be considered. Usually, the major problem is to provide skin coverage, which may involve an extensive area and require skin grafting treating this like a burn wound. However, this will inevitably cause contracture and in areas such as the neck, (Figure 8) flap coverage to

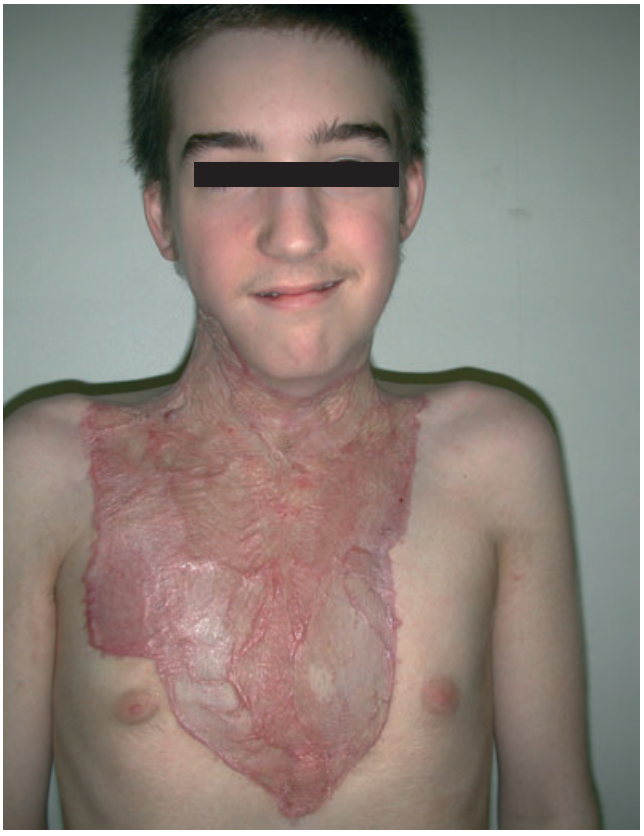

Figure 8 The patient survived and is seen 1 year later. Note contractures from skin grafting

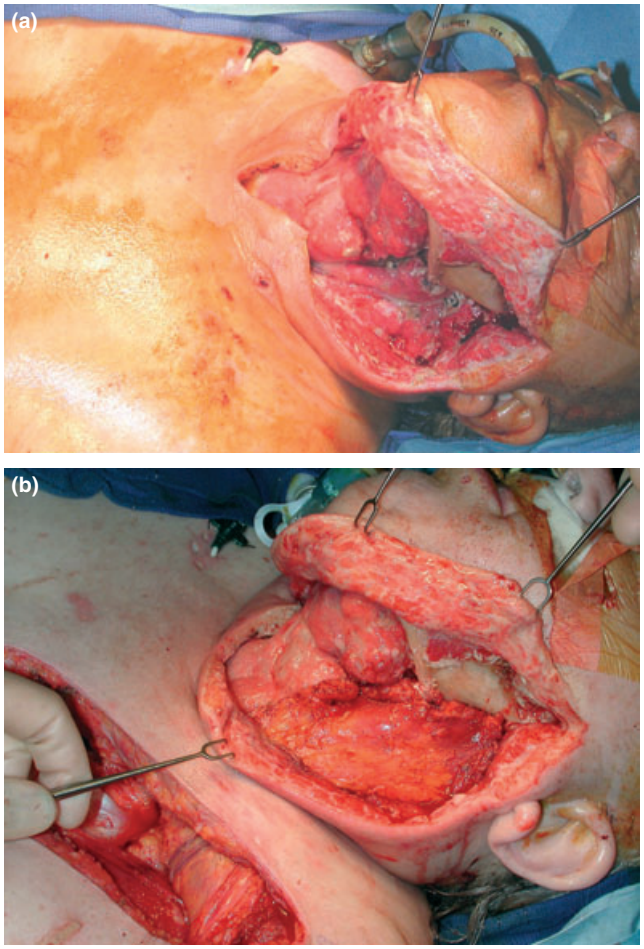

Figure 9 (**a**) Necrotizing infection of the neck from unknown source with great vessels exposure. (**b**) Pectoralis major flap performed for great vessel coverage

allow good mobility is the preferred method of choice. The reconstructive decisions and options are dependent upon the local, regional, and systemic disease processes. The authors have encountered NF/myonecrosis wounds in the cervicofacial region which created exposure of great vessels in the neck, or result in direct communication between the neck and oral cavity because of loss of intraoral tissue (Figure 9a,b). In these types of cases, skin grafting is not amendable, and recruitment of vascularized tissue should strongly be considered with the employment of either regional or free flaps. The pectoralis major, latissimus dorsi, and trapezius regional flaps have been utilized at our institution as a muscle only, or myocutaneous flap to reconstruct these types of wounds (Figure 10a,b). The pectoralis major flap may not be the best 'first choice' especially when treating large defects, which also involve the chest wall. Free tissue transfer has been utilized in our unit and described in the literature (Whetzel *et al*, 1999). Free flaps such as the anterior lateral thigh flap or the scapular/parascapular flap can provide a large surface area of tissue coverage; these flaps can provide upwards of 10 × 25 cm of skin coverage, and multiple flaps can be harvested if needed. Obviously, the utility of free tissue transfer will

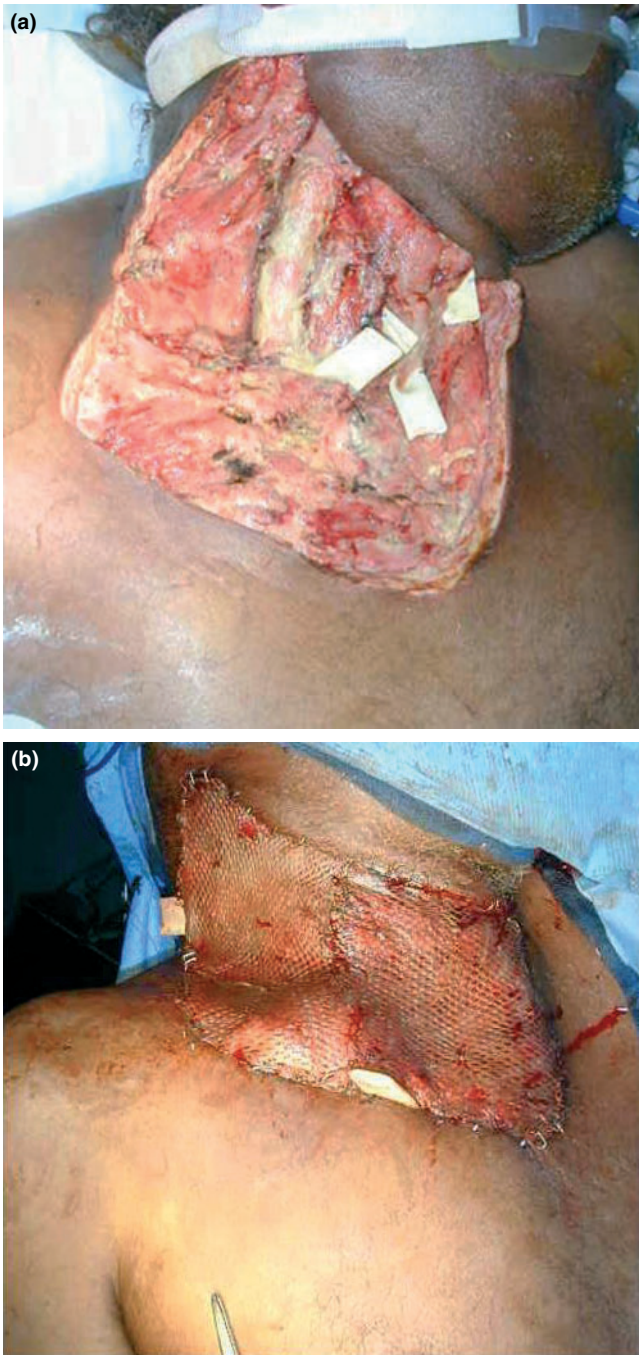

Figure 10 (**a**) Necrotizing infection of the neck from skin source, with great vessel exposure. (**b**) Latissimus Dorsi regional flap with skin graft for wound coverage

be dependant upon the patient's systemic condition, wound stability, and recipient vessel availability. It is preferable to utilize recipient vessels outside the confines of the wound; however, this maybe difficult at times because of pedicle length and flap geometry limitations.

Prognosis

Prognosis for survival will depend both on the severity of the NF and the patient's systemic condition. In those

patients who have an associated myonecrosis, mortality is higher and early reports gave an 80% mortality rate in patients with invasive group A streptococcal infections and myonecrosis (Stevens, 1992). In another series with an overall mortality of 20% from NF, those patients who also exhibited myonecrosis had a 37.5% mortality (Haywood *et al*, 1999). Also, NF can easily spread along the fascial spaces of the prevertebral fascia and the carotid sheath into the mediastinum, which is associated with a worse prognosis. In a review of 59 cases by Banerjee *et al*, the mortality rate for cervical NF was only 19%; however, 44% of his cases had mediastinitis and amongst this group the mortality was 38% (Banerjee *et al*, 1996). In a review of the literature and experience with 21 cases of cervical NF that involved the mediastinum, Mora *et al* recommended that cervical drainage alone was sufficient if only one superior mediastinal space was involved, but thoracotomy and drainage of mediastinal collections would be necessary when mediastinal involvement was more extensive (Mora *et al*, 2004). The incidence of postoperative complications in the thoracotomy group was 40%; despite this, their overall mortality was only 9.5%. In a recent small series of cervico-facial NF, mortality rates have ranged between 0% (Stenberg *et al*, 2004; Whitesides *et al*, 2000), 15% (Mohammedi *et al*, 1999), 18% (Wong *et al*, 2000) and 27.6% (Lin *et al*, 2001). These figures are better than those reported for NF at other sites and may be because of earlier presentation and diagnosis for head and neck sites or the better overall vascularity of the region.

Patients with initial hypotension, underlying cancer, and organ failure will have a worse outlook as will those with inadequate surgery (Mohammedi *et al*, 1999). Morbidity is high in survivors because of scarring, deformity, and loss of function caused by the life saving radical debridement. Numerous complications have been reported and include empyema, lung abscess, jugular vein thrombosis, perforation of the pharyngeal wall, airway obstruction, rupture of major vessels, pericardial effusions, and brain abscess.

Conclusion

Necrotizing fasciitis of the cervico-facial is a rapidly evolving life threatening infection, which requires prompt diagnosis and management. Radical surgical debridement combined with triple broad spectrum antibiotics give the best chance for survival. Even with radical and intensive therapy, the fatality rate remains approximately 20%.

Author contributions

Both authors were involved with the written text and providing photos.

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