Necrotizing Fasciitis

Report of 39 Pediatric Cases

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Background: Necrotizing fasciitis (NF) is a severe, life-threatening soft tissue infection. General features and risk factors for fatal outcome in children are not well known.

Objective: To characterize the features of NF in children and the risk factors for fatal outcome.

Design: Retrospective, comparative, observational, and longitudinal trial.

Setting: Dermatology department of a tertiary care pediatric hospital.

Patients: All patients with clinical and/or histopathological diagnosis of NF seen from January 1, 1971, through December 31, 2000.

Main Outcome Variables: Incidence, age, sex, number and location of lesions, preexisting conditions, initiating factors, clinical and laboratory features, diagnosis at admission, treatment, evolution, sequelae, and risk factors for fatal outcome.

Results: We examined 39 patients with NF (0.018% of all hospitalized patients). Twenty-one patients (54%) were boys. Mean age was 4.4 years. Single lesions were seen in 30 (77%) of patients, with 21 (54%) in extremities. The most frequent preexisting condition was malnutrition in 14 patients (36%). The most frequent initiating factor was varicella in 13 patients (33%). Diagnosis of NF at admission was made in 11 patients (28%). Bacterial isolations in 24 patients (62%) were polymicrobial in 17 (71%). Pseudomonas aeruginosa was the most frequently isolated bacteria; gram-negative isolates, the most frequently associated bacteria. Complications were present in 33 patients (85%), mortality in 7 (18%), and sequelae in 29 (91%) of 32 surviving patients. The significant risk factor related to a fatal outcome was immunosuppression.

Conclusions: Necrotizing fasciitis in children is frequently misdiagnosed, and several features differ from those of NF in adults. Immunosuppression was the main factor related to death. Early surgical debridement and antibiotics were the most important therapeutic measures.

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Necrotizing fasciitis (NF) is a rare, rapidly progressive, and potentially fatal infection of the superficial fascia and subcutaneous cellular tissue.1,2 Necrotizing fasciitis is frequently polymicrobial, and the combination of aerobic and anaerobic bacteria contributes to the quick progression and severity of the disorder.3 Necrotizing fasciitis has been known since antiquity.4 In 1871, Jones5 gave the first clinical description of “hospital gangrene.” In 1924, Meleney7 wrote a classic report on NF, emphasizing the importance of early diagnosis and surgical treatment to reduce mortality. In 1952, Wilson8 proposed the term necrotizing fasciitis to replace terms like gangrenous erysipelas, hospital gangrene, acute cutaneous gangrene, nonclostridial crepitant cellulitis, streptococcal gangrene, synergistic necrotizing cellulitis, Meleney cellulitis, and others. In addition, Wilson8 differentiated NF from disorders like erysipelas, cellulitis, and clostridial myonecrosis with muscle involvement. At present, a popular synonym is flesh-eating bacteria disease.9

Series of NF in children are scarce and include few cases.1,10-14 With less than 100 in the literature.1,2,10-24 The present series of 39 cases is, to our knowledge, the largest reported.

We found 39 patients with a diagnosis of NF during the 30-year study period, representing 0.018% of all hospitalized patients. Of these, 21 (54%) were boys, and 18 (46%) were girls. Ages ranged from 10 days to 15.5 years (mean ± SD age, 4.4
PATIENTS AND METHODS

STUDY DESIGN

We performed a retrospective, observational, comparative, and longitudinal study.

SAMPLE POPULATION

We included all clinical records of patients hospitalized in the National Institute of Pediatrics, Mexico City, Mexico, with a diagnosis of NF from January 1, 1971, through December 31, 2000. We included all patients aged 1 day to 18 years of either sex with a diagnosis of NF.

STATISTICAL CONSIDERATIONS

The sample size needed to be considered significant was calculated as 35 to 40 patients. We used a commercial statistical software package (SPSS Base System; SPSS Inc, Chicago, Ill) for data analysis. All studied variables were analyzed in univariate form using t or χ² test (P<.05 was considered significant). Significant factors in the univariate analysis to predict risk for death were included in a logistic regression multivariate analysis.

years ± 4.7 months). The number and location of lesions, preexisting conditions, initiating factors, bacterial isolations, complications, evolution, and sequelae are shown in the Table.

The signs and symptoms at the time of diagnosis were fever in 36 patients (92%), vomiting in 21 (54%), hypotension and irritability in 13 (33%) each, prostration in 11 (28%), hyporexia in 8 (21%), altered consciousness in 6 (15%), impaired peripheral perfusion in 5 (13%), hypothermia in 2 (5%), and hypertension in 1 (3%). Local signs and symptoms of pain, hard edema, and erythema in all patients; local warmth in 33 (85%); and functional limitation in 29 (74%). Ecchymoses and necrosis were each recorded in 28 patients (72%), hemorrhagic blisters in 25 (64%), purulent secretion in 16 (41%), serous blisters in 14 (36%), local delayed capillary refill in 7 (18%), and crepitus in 4 (10%).

Serum laboratory findings showed hemoglobin levels ranging from 4.0 to 14.8 g/dL (mean level, 9.5 g/dL); hematocrit levels, 12% to 48% (mean level, 29%); white blood cell count, 300 to 72000 cells/µL (mean, 16 532 cells/µL); neutrophil levels, 18% to 87% (mean level, 59%); lymphocyte levels, 8% to 70% (mean level, 32%); monocyte and eosinophil levels, within the reference ranges; bands, 0% to 33% (mean, 4%); and platelet count, 10 to 400 × 10³/µL (mean, 188.4 × 10³/µL).

Results of radiographic studies performed in 13 patients (33%) showed soft tissue swelling in all and gas in 3 (8%).

Diagnoses at admission were cellulitis in 23 patients (59%), NF in 11 (28%), and gangrene in 5 (13%). Concomitant diagnoses were recorded in 17 patients (44%), ie, septicemia in 10 (59%) of these and humeral osteomyelitis, febrile neutropenia, hemorrhagic varicella, septic arthritis, malnutrition, acute diarrhea, and disseminated intravascular coagulation in 1 patient each of the remaining 7.

Initial antibiotic treatment included amikacin sulfate, clindamycin phosphate, and gentamicin sulfate. A single antibiotic was used in 5 patients (13%); 2 antibiotics in 30 (77%); and 3 antibiotics in 4 (10%). The most frequent antibiotic combinations (22 patients [56%]) were an aminoglycoside or third-generation cephalosporin plus clindamycin, antistaphylococcal penicillin, and a first-generation cephalosporin or fosfomycin. Treatment with clindamycin plus cefoperazone sodium is recommended as soon as NF is diagnosed.

Necrotizing fasciitis is rare in children.10 It has been reported in 0.03% of hospitalization causes25 and in 0.08 per 100 000 children per year.13 Our 39 patients (1.34 cases per year) represented 0.018% of all our hospitalized patients. Necrotizing fasciitis is more common in middle-aged adults, without sex, race, or geographic predilection.26 In adults, the lower extremities are more frequently affected, followed by the trunk and head.7,27 In children, most lesions are reported in the trunk.10-13 In newborns, NF originates from omphalitis.28 In our series, the lower extremities constituted the most commonly affected area (17 patients [44%]).

Necrotizing fasciitis in the genital area is known as Fourmier gangrene. It is more common in diabetic patients and in immunosuppressed males39 or after genital surgical procedures30 or rectal perforation.31 Fourmier gangrene is seldom reported in children.32-34 In our series, 5 patients had genital involvement. Of these, involvement was primarily genital in 2, owing to an inadequate setting of a Foley catheter tube in one and after an orchectomy in the other. The remaining 3 cases resulted from the extension of neighboring lesions (abdomen and thigh). In this group, 1 patient with immunosuppression died.

Location in the neck is a rare but severe presentation associated with high mortality.35,36 Owing to carotid...
## Features in 39 Patients With Necrotizing Fasciitis*

<table>
<thead>
<tr>
<th>Patient No./Sex</th>
<th>Age</th>
<th>Location/No. of Lesions</th>
<th>Underlying Factors</th>
<th>Initiating Factors</th>
<th>Tissue Bacteriology</th>
<th>Blood Bacteriology</th>
<th>Complications</th>
<th>Outcome</th>
<th>Sequelae</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/F</td>
<td>11 y</td>
<td>UE and LE/2</td>
<td>None</td>
<td>None</td>
<td>Morganella morganii</td>
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<td>Sepsis, Ost</td>
<td>Survived</td>
<td>US, FJL, D</td>
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<td>2/F</td>
<td>1 y</td>
<td>Trunk/1</td>
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<td>Varicella</td>
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<td>None</td>
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<td>D</td>
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<td>Sepsis, DIC, Ost, pneumonia</td>
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<td>US, FJL, D</td>
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<td>Malnutrition</td>
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<tr>
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<tr>
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<td>None</td>
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</tr>
<tr>
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<td>None</td>
<td>Survived</td>
<td>D, US</td>
</tr>
<tr>
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<td>Varicella</td>
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<td>Survived</td>
<td>D, US</td>
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<tr>
<td>23/F</td>
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<td>None</td>
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<td>Survived</td>
<td>US</td>
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<tr>
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<td>Sepsis, DIC, SH</td>
<td>Survived</td>
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</tr>
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<td>25/M</td>
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<td>Traumatic wound</td>
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<td>Sepsis, DIC, SH</td>
<td>Survived</td>
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<td>S. aureus</td>
<td>None</td>
<td>Toe necrosis</td>
<td>Survived</td>
<td>Toe amp</td>
</tr>
<tr>
<td>27/F</td>
<td>3 mo</td>
<td>LE/1</td>
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<td>Burn</td>
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<tr>
<td>28/M</td>
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<td>Survived</td>
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<td>None</td>
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<tr>
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<td>ALL</td>
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<td>Survived</td>
<td>LFU</td>
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<td>31/M</td>
<td>11 mo</td>
<td>Head/1</td>
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<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>Survived</td>
<td>D, US</td>
</tr>
<tr>
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<td>LE/1</td>
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<td>Diarrhea</td>
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<td>Survived</td>
<td>LFU</td>
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<td>33/M</td>
<td>3 y</td>
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<td>Malnutrition</td>
<td>Varicella</td>
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<td>Survived</td>
<td>US</td>
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<td>34/F</td>
<td>9 mo</td>
<td>Trunk, LE/2</td>
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<td>None</td>
<td>K pneumonia, E cloacae</td>
<td>None</td>
<td>Ost</td>
<td>Survived</td>
<td>D, US, FJL</td>
</tr>
<tr>
<td>35/M</td>
<td>10 mo</td>
<td>Trunk/1</td>
<td>Malnutrition</td>
<td>Diarrhea</td>
<td>Proteus aegerinosus, E cloacae</td>
<td>None</td>
<td>Sepsis</td>
<td>Survived</td>
<td>LFU</td>
</tr>
<tr>
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<td>Trunk/1</td>
<td>Malnutrition</td>
<td>Varicella</td>
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<td>None</td>
<td>Survived</td>
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<td>37/M</td>
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<td>Close injury</td>
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<td>None</td>
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<td>Survived</td>
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<td>Malnutrition</td>
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<td>Survived</td>
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<td>Sepsis, pneumonia</td>
<td>Survived</td>
<td>D</td>
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</tbody>
</table>

*UE indicates upper extremities; LE, lower extremities; Ost, osteomyelitis; US, unsightly scar; FJL, functional joint limitation; D, deformity; RF, respiratory failure; ALL, acute lymphoblastic leukemia; BMB, bone marrow biopsy; DIC, disseminated intravascular coagulation; GABHS, group A β-hemolytic streptococcus; HS, hypovolemic shock; SH, septic hepatitis; CR, carotid rupture; MR, myelomeningocele rupture; JRA, juvenile rheumatoid arthritis; MOF, multiple organ failure; LS, laryngeal stenosis; IMI, intramuscular injection; amp, amputation; and LFU, lost to follow-up.

†Indicates herniorrhaphy.

‡Indicates orchiopexy.
artery and mediastinal dissemination. Three of our patients presented with NF in the neck. Of these, one died of tracheal compression and another of carotid rupture (both causes were diagnosed at autopsy). The patient with tracheal compression presented with severe respiratory failure. At admission, intubation was unsuccessful, and tracheostomy could not be performed due to severe edema.

Predisposing factors vary with age. Diabetes is the main factor in adults, but other chronic diseases, such as hypertension, peripheral vascular disease, renal failure, obesity, alcoholism, and malnutrition, are important underlying factors. Nonsteroidal anti-inflammatory drugs have been implicated as a predisposing factor, although the relationship remains controversial. Some cases in children have been associated with immunosuppressive diseases such as acute lymphoblastic leukemia. In our series, half of the patients presented predisposing factors, the most frequent being malnutrition in 14. Immunosuppression was a factor in 6 patients, due to acute lymphoblastic leukemia in 3 and drug-induced in 3.

Initiating factors reported in the literature include minor injuries, surgical and traumatic wounds, contusion, and varicella. In a number of cases, initiating factors cannot be identified. In newborns, omphalitis, circumcision, and placement of electrodes for the monitoring of vital signs have been reported as initiating factors. In our series, initiating factors were determined in 85% of patients, the most frequent being varicella.

Clinical manifestations in NF start around a week after the initiating event, with induration and edema, and another of carotid rupture (both causes were diagnosed at autopsy). The patient with tracheal compression presented with severe respiratory failure. At admission, intubation was unsuccessful, and tracheostomy could not be performed due to severe edema.

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Clinical manifestations in NF start around a week after the initiating event, with induration and edema, followed by erythema or purple discoloration (Figure 1) and increasing local fever. Pain is important in the early stages, and sometimes crepitation can be found. Tissue necrosis with nerve involvement results in hypsensitivity or anesthesia. Forty-eight to 72 hours later, the skin turns smooth, bright, and serous, or hemorrhagic blisters develop (Figure 2). Without treatment, necrosis develops, and by the fifth or sixth day, the lesion turns black with a necrotic crust (Figure 3). Removal of the crust shows fascial tissue and a brown grayish secretion. Subcutaneous cellular tissue is friable and easily removable. Sometimes the presence of gas (produced by aerobic and anaerobic bacteria) is recognized through tissue crepitation. This sign, although infrequent, is highly suggestive of NF. Necrosis of the superficial fascia is always more extensive than that indicated by the extension of skin necrosis.

Systemic signs and symptoms are a consequence of the toxic process and septicemia. A high fever is disproportionate in relation to the size of cutaneous lesion. Consciousness disturbance correlates with the severity of the process. Multiple organs and systems can be involved, and abscesses of the liver, lungs, spleen, brain, and pericardium may develop. Tissue edema may deplete the vascular volume and provoke hemocoagulation, hypotension, obtundation, and shock. Tachypnea, hyperglycemia (with osmotic diuresis), and fever aggravate the hypovolemic state.

Tissue bacteria are isolated in about 76% of cases. In our series, positive tissue cultures were found in 24 cases (62%). A polybacterial cause of NF is well documented. In our series, the isolates in 17 (71%) of 24 cases were polymicrobial.

Group A β-hemolytic streptococcus has been the most frequently incriminated agent since Meloney’s findings, and a recent increase in its frequency has been reported. Many other bacteria may be involved. Fungi such as Aspergillus, Mucoraceae, and Candida albicans rarely are etiologic agents.

Pseudomonas has been implicated as an important causal
agent in patients with neutropenia. In our series, *Pseudomonas* was the main causal agent, always in association with other bacteria. The results of gram stain should not be used as a guide to therapy because of the polymicrobial nature of NF.

The diagnosis of NF was suspected initially in only 11 (28%) of our patients. Cellulitis was the most frequent initial diagnosis, made in 23 (59%) of our patients. These findings suggest that the diagnosis of NF is often overlooked and, consequently, that specific therapeutic measures are delayed. Over time, the trend in our series was toward an improvement of the survival rate.

In the presence of a soft tissue infection unresponsive to treatment and with rapid health deterioration, NF should be suspected. The diagnosis is confirmed during surgical debridement by the presence of liquid necrosis of the superficial fascia. In doubtful cases, the results of a frozen-section biopsy during surgery may confirm the diagnosis. Elements for histological diagnosis include necrosis of the superficial fascia; leukocytic infiltrates with polymorphonuclear cells predominant in fascia, subcutaneous fat tissue, and dermis; arterial and venous fascial thrombosis; angitis with fibrinoid necrosis; visible bacteria in the fascia and dermis on results of gram stain; and absence of muscular damage. A skin biopsy was performed in 16 (41%) of our patients, and the findings were in all cases compatible with the clinical diagnosis of NF.

Anemia, found in 29 (74%) of our cases and reported in 70% to 90% of cases in the literature, is probable due to hemolysis. Leukocytosis was present in 25 (64%) and leukopenia in 5 (13%) of our cases. Thrombocytopenia, longer coagulation time, hypofibrinogenemia, and circulating fibrin degradation products can be a marker of disseminated intravascular coagulation. Disseminated intravascular coagulation was a complication in 11 (28%) of our cases and was fatal in 5 of them. Abnormal results of liver function tests, prerenal azotemia, hypocalcemia, hypoalbuminemia, and an increased creatine phosphokinase level may be present.

A differential diagnosis should be made with other infectious or necrotic processes with similar appearance. Among the more benign infectious processes, early cellulitis may present in a form similar to NF, but the edema in NF is harder. Cellulitis and NF present with signs of toxicity, but cellulitis responds to conventional treatment in 24 to 48 hours, whereas in NF, necrosis will progress if surgical treatment is not initiated. Erysipelas presents with well-defined erythematous edges, soft edema, and the absence of necrosis and systemic toxicity. Gaseous gangrene produces a quickly progressive myonecrosis that involves deep fascia with early crepitation, severe local pain, and few cutaneous changes. Pyoderma gangrenosum has a slow evolution and is frequently associated with ulcerative colitis, rheumatoid arthritis, and myeloma. In cutaneous necrosis caused by the extravasation of intravenous drugs, the positive history findings are helpful. Ecthyma gangrenosum is due to *Pseudomonas aeruginosa* and consists of pustules with an erythematous base that burst in hours and turn into punched, quick progressive lesions with purpuric raised edges, more frequently located in the anogenital region, axillae, abdomen, and legs of children. Purpura fulminans often appears after varicella and starts with ecchymotic areas in the extremities with inflammation, hemorrhage, and necrosis. In our series, cellulitis and purpura fulminans were the most frequent initial diagnoses.

Once vital signs are stable and the hydroelectrolytic balance is stabilized, extensive debridement of necrotic tissue must be performed (Figure 4), and the procedure must be repeated as many times as needed. Sudarsky et al reported a decrease in mortality from 50% to 0% in selected patients with appropriate early treatment. Freischlag et al concluded that mortality doubles when surgery is delayed for more than 24 hours. Initially, the combination of clindamycin and a third-generation cephalosporin that covers *P aeruginosa* seems adequate. Once culture findings and bacterial sensitivity are obtained, antibiotics should be administered accordingly. Antibiotics alone, because of their inability to reach the poorly vascularized and necrotic fascia, have little effect if surgery is not performed. In our series, the median time from admission to surgery was 2 days. Owing to severe multiple organ failure treated in the intensive care unit in a 4-year-old boy (patient 28 in the Table), the time from admission to surgery was 29 days. Skin grafts should be applied as soon as there is no evidence of infection and granulation tissue appears. When indicated, total parenteral nutrition must be given.

The benefit of hyperbaric oxygen in NF remains controversial. Other poorly tested therapies include high doses of intravenous immune globulin, granulocyte transfusion, granulocyte colony-stimulating factor (in granulocytopenic patients), and bovine thymic extract (Thymostimulin).

Mortality rates in adults range from 8% to 100%. In newborns, the mortality rate can be as high as 87.5%. The average mortality in children ranges from 10% to 60%, with a mean of 20%. Most deaths are due to sepsis or multiorgan failure. In our series, mortality was average (18%), mostly owing to infectious complications (eg, sepsis, septic hepatitis, and pneumonia) or volemic alterations (disseminated intravascular coagulation and hypovolemic shock). One patient died owing to tracheal compression, and another, owing to carotid rupture.

In the multivariate analysis, immunosuppression, hypothermia, and hypotension were the significant risk fac-

![Figure 4. Necrotizing fasciitis after extensive surgical debridement of necrotic tissue.](https://example.com/image)
Necrotizing fasciitis is a severe multisystemic disorder with prominent cutaneous features that can compromise life if diagnosis and treatment are delayed. After the first month of life, the location of lesions is the same in adults and children. The most frequent predisposing factor in our patients was malnutrition. In 19 children (49%), predisposing factors were not identified. The most frequent initiating factor was varicella. The most important risk factor for death in our series was immunosuppression. On the basis of our findings, antibiotic treatment with clindamycin plus cefopaxime sodium is recommended as soon as NF is diagnosed. According to the findings of bacterial cultures and antibiograms, this regimen may be modified. Surgical debridement should be performed as soon as the patient’s condition is stabilized.

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CONCLUSIONS

REFERENCES


