Pediatr Nephrol (2005) 20:99–101
DOI 10.1007/s00467-004-1669-8

BRIEF REPORT

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Necrotizing fasciitis in a child: a rare complication of idiopathic nephrotic syndrome

Received: 16 April 2004 / Revised: 2 August 2004 / Accepted: 3 August 2004 / Published online: 10 November 2004

Abstract In nephrotic syndrome there is an increased tendency for bacterial infections due to immunological changes secondary to proteinuria, treatment (including steroids), and other as yet unknown causes**.** However, necrotizing fasciitis (NF) is an uncommon complication of the disease and has rarely been reported in nephrotic children. We report a 14-month-old boy with nephrotic syndrome who developed sepsis and NF as a complication. He was treated successfully with intensive medical and surgical treatment.

Keywords Nephrotic syndrome · Necrotizing fasciitis · Infection · Treatment

Introduction

There is an increased tendency for bacterial infections in nephrotic syndrome due to immunological changes secondary to proteinuria, treatment (including steroids), and other as yet unknown causes. Peritonitis, cellulitis, or sepsis due to *Streptococcus pneumonia* and *Hemophilus influenzae* are common infections associated with this disease [1]. A disturbance in the humoral immune defense mechanisms, edematous subcutaneous tissue, and increased fragility of the skin due to stretching predispose nephrotic patients to cellulitis, but necrotizing fasciitis (NF) is a rare complication [1, 2]. We present a child with nephrotic syndrome complicated with sepsis and NF, which is extremely rare in childhood.

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Case report

A 14-month-old boy was admitted to our hospital with diffuse body swelling and diarrhea. He was being treated at a local hospital for nephrotic syndrome with prednisolone at a dose of 60 mg/kg per day when he developed diarrhea. He was referred to our hospital because of persistence of symptoms despite steroid and ceftriaxone therapy. Physical examination revealed a well-developed boy (weight 11 kg, height 76 cm) in a good general condition, with normal blood pressure and body temperature, but with generalized edema and ascites with mild abdominal tenderness. Laboratory tests revealed hemoglobin 9.4 g/dl, leukocyte count 10,800/mm^3 with neutrophil predominance on the peripheral blood smear, platelets 640,000/mm^3, erythrocyte sedimentation rate 150 mm/h, C-reactive protein >172 mg/l (normal 0–5 mg/l), antistreptolysin O titer <49 IU/ml (normal <200 IU/ml), blood urea nitrogen (BUN) 31 mg/dl (normal 0–23 mg/dl), creatinine 0.5 mg/dl (normal <0.9 mg/dl), glucose 88 mg/dl (normal 80–110 mg/dl), sodium 133 mEq/l (normal 130–145 mEq/l), potassium 3.7 mEq/l (normal 3.5–5 mEq/l), calcium 7.4 mg/dl (normal 8.4–10.9 mg/dl), phosphorus 5.5 mg/dl (normal 4.5–5.5 mg/dl), alkaline phosphatase 61 IU/l (normal <448 IU/l), uric acid 7 mg/dl (normal 2–6.1 mg/dl), total protein 3.3 g/dl (normal 5.6–8 g/dl), albumin 1 g/dl (normal 3–5.4 g/dl), aspartate aminotransferase 34 IU/l (normal <44 IU/l), alanine aminotransferase 28 IU/l (normal <45 IU/l), total bilirubin 0.15 mg/dl (normal 0.3–1.2 mg/dl), cholesterol 228 mg/dl (normal 124–200 mg/dl), and triglycerides 220 mg/dl (normal 37–124 mg/dl). Urine density was 1020, with 3+ proteinuria, 7–8 leukocytes, many granular casts, and bacteria on microscopic examination. C3, C4, and immunoglobulin levels were normal except for low IgG levels. Viral markers for hepatitis A, B, and C, Epstein-Barr virus, cytomegalovirus, and human immunodeficiency virus were negative. Since he had ascites with mild abdominal tenderness, paracentesis was performed and revealed leukocytosis with 90% neutrophils in the peritoneal fluid. Ultrasonography showed enlarged and hyperechogenic kidneys.

With the diagnosis of nephrotic syndrome, peritonitis, and urinary tract infection, the steroid dose was reduced and intravenous amikacin and cephazolin were started empirically. In two urine cultures obtained by bag collection, first *Proteus* [100,000 colony forming units (cfu)/ml] and then *Proteus* plus *Klebsiella pneumonia* (both 100,000 cfu/ml) were detected. Paracentesis culture grew *Streptococcus pneumonia* that was sensitive to cephazolin. However, blood culture was sterile. On the 3rd day of admission the general condition of the patient deteriorated, with the body temperature increasing to 38.8°C, and he became unconscious with convulsions. On the lower extremities pink-purple ecchymotic skin lesions with demarcating borders developed (Fig. 1a). He showed findings consistent with sepsis and disseminated intravascular coagulation (hemoglobin 7.1 g/dl, white cell count 7,600/mm^3,

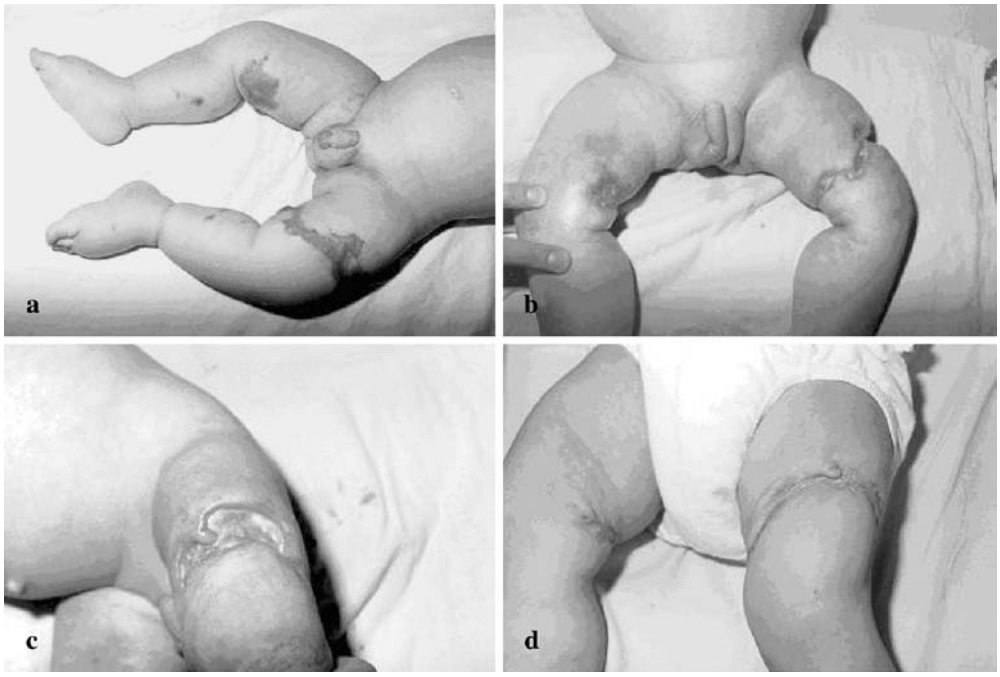

Fig. 1a–d Evolution of the skin lesions: **a** pink-purple-colored ecchymotic lesions with demarcating borders, **b–c** necrotic dark blue/purple-colored lesions extending to muscles, **d** healed lesions with little scar formation

platelets 36,000/mm^3, prothrombin time 51.7 s, activated partial thromboplastin time 61.6 s), and his renal function began to deteriorate (BUN 44 mg/dl, creatinine 1 mg/dl). Echocardiography was normal. Hypodense lesions in the left frontal subcortical white matter were detected by cranial tomography. These were consistent with chronic ischemia without any acute bleeding. The antibiotic treatment was changed to a combination of imipenem, amikacin, clindamycin, and vancomycin, and he was given blood transfusions and intravenous immunoglobulin (IVIG) therapy for 3 days because of severe infection. On the 4th day of admission his general condition deteriorated and he developed melena. The skin lesions on the lower extremities transformed into the bullous form. At the end of 1st week these lesions became necrotic with clear-cut borders and dark-blue/purple discoloration, involving subcutaneous tissue and muscles. This led to the clinical diagnosis of NF (Fig. 1b, c). Although initial cultures from the lesions did not grow any microorganisms, *Pseudomonas* was isolated from later cultures; this responded clinically to the antibiotic treatment. Therefore histological examination was not performed. In addition to intensive antibiotic treatment, wound care was carried out with twice daily surgical debridement lasting for months. The necrotic lesions healed and the boy was discharged on the 113th day of hospitalization. Since 3+ proteinuria and hypoalbuminemia (1.5 g/dl) persisted, he was restarted on prednisolone (60 mg/m^2 per day) on discharge. He responded to therapy and had a steroid-sensitive relapse 4 months later. Since then, he has been followed in remission for the last 8 months, with normal urinalysis, normal albumin and immunoglobulin levels, and with little scarring on the left leg (Fig. 1d).

Discussion

An increased tendency for bacterial infections is still a problem in nephrotic syndrome, although the use of antibiotics such as penicillin has reduced the rate of mortality due to infectious complications from 40% to about 4% [1, 3]. In patients with nephrotic syndrome, the humoral defense system and activation of the alternative complement pathway are impaired due to hypogammaglobulinemia secondary to immunological dysregulation, and urinary loss of factor B, factor I, and, factor D [4, 5]. There is also splenic hypofunction in these children causing plasma lymphocyte dysfunction [6]. All these factors, together with the use of corticosteroids and immunosuppressive treatments, increase the risk for infection in nephrotic patients [1]. The classic infection in children with nephrotic syndrome is *Streptococcus pneumonia* peritonitis. Edematous subcutaneous tissue and stretched skin also increase the probability of cellulitis secondary to *Hemophilus influenzae* [7]. However, invasive infections of the soft tissue such as NF are extremely rare, but have been reported in adult nephrotic patients [2].

NF is an uncommon, life-threatening soft tissue infection characterized by rapidly spreading inflammation and necrosis of the skin, subcutaneous tissue, and fascia. Old age, diabetes, cancer, immunosuppression, sepsis, trauma, and extensive surgery all predispose to polymicrobial NF. In contrast, about 50% of cases of streptococcal NF occur in young and previously healthy individuals [8]. Causative microorganisms proliferate in an environment of local tissue hypoxia in those patients with trauma, recent surgery, or immunosuppression. In NF, group A hemolytic streptococci and *Staphylococcus aureus*, alone or in synergism, are frequently the initiating infecting bacteria. However, other aerobic and anaerobic pathogens, including *Bacteriodes, Clostridium, Proteus, Pseudomonas,* and *Klebsiella*, may be present. The clinical disease is expressed by the spreading of the organism through the tissue above the deep fascia, causing thrombosis of vessels resulting in gangrene of subcutaneous fat and dermis. This prevents penetration of antibiotics into the tissue and causes spread of the suppurative process.

Because of gas-producing bacteria, subcutaneous emphysema might be detected [9].

In our patient, nephrotic syndrome, subcutaneous edema, stretching of the dermis, and thrombocytosis might be the underlying risk factors for the development of NF, probably caused by the blood-borne bacteria. Previous usage of corticosteroids is another contributory factor for the increased risk of infection. The NF in our patient was thought to be polymicrobial in origin, since *Streptococcus pneumonia* was isolated from the peritoneal fluid and *Proteus* and *Klebsiella* from the urine. Although the patient had the clinical picture of sepsis, blood culture was sterile, which might be due to previous antibiotic therapy before his admission.

The NF in this patient should be differentiated from ecthyma gangrenosum (EG), which is difficult as we did not have histological confirmation. Since EG is usually the cutaneous finding of *Pseudomonas* sepsis, and we were unable to isolate the bacteria from the blood, the diagnosis of NF is more likely [10]. Moreover, isolation of *Pseudomonas* from the lesions during follow-up but not from the initial cultures might indicate a secondary infection rather than an initial triggering factor. The extent and the clinical course of NF are somewhat more severe than EG. This patient had a severe clinical course with rapidly progressing lesions, although he showed a favorable outcome, probably due to prompt diagnosis and intensive medical and surgical treatment. In addition, the absence of the nodular stage of the skin lesions and the blue-black eschar in our patient, which are more characteristic for EG, also favor the diagnosis of NF.

Intensive medical and surgical treatment is of vital importance to reduce the mortality and morbidity, since NF has a rapid and severe clinical course with a mortality rate of about 70%–80%. In addition to antibiotic therapy, IVIG and hyperbaric oxygen are other supportive treatment modalities. However, clinical success cannot always be achieved because of disseminated intravascular coagulation and widespread thrombosis that prevents antibiotic penetration into infected tissue [8]. Our patient was treated with several antibiotics, IVIG, and blood transfusion, together with intensive surgical debridement lasting for more than 3.5 months. This careful treatment contributed to the satisfactory end result.

IVIG is not a routine treatment in patients with nephrotic syndrome, especially minimal change disease. It is mostly considered as an adjunct therapy for infection prophylaxis. In some studies there has been evidence for induction or maintenance of remission with IVIG in nephrotic patients resistant to conventional treatment protocols. However, other studies have reported no effect of IVIG on the duration of remission [11, 12]. In our patient, however, the main indication for IVIG was sepsis and the immunocompromised status.

In conclusion, although NF is a rare, life-threatening soft tissue infection, prompt diagnosis and appropriate medical and surgical treatment can be life saving despite very high mortality. Although there are some reports of NF in adult nephrotic patients in the literature, this case represents an extremely rare example of NF in pediatric idiopathic nephrotic syndrome.

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