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Toxic Shock Syndrome and Purpura Fulminans Due to *Streptococcus Pyogenes* in a Child

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Abstract

We report the case of 4 years old boy with toxic shock syndrome and purpura fulminans due to *Streptococcus pyogenes*. Treatment consisted of antibiotics, intravenous Gamma globulin and cardiorespiratory support. The child had ischemia and necrosis of several phalanges of his fingers and toes, and he required amputation of the distal phalanges. Therapy was successful and he survived.

Introduction

Group A Streptococcus (GAS) or *Streptococcus pyogenes* follows *Staphyloccocus aureus* as the second most common cause of Toxic Shock Syndrome (TSS) caused by Gram positive cocci. It's reported mortality is 5-10% in children and 30-80% in adults. GAS can also present as purpura fulminans and Necrotizing Fasciitis (NF), with a related mortality as high as 50%. The treatment consists of bactericidal antibiotics to diminish the bacterial burden, associated with antimicrobials that inhibit bacterial protein synthesis and help to immunomodulation of the inflammatory response secondary to superantigen production and supportive treatment directed at correcting the multiorganic compromise.

Case Report

A 4 year old boy presented to a local hospital because of 12 hours of up to 104°F fever, diminished appetite, 4 episodes of vomit and diffuse abdominal pain. His mother reported loss of conscience of one minute duration, profuse sweating and central cyanosis. There was no diarrhea, skin lesions, cough or pharyngeal sore.

His physical exam confirmed a temperature of 104°F, a 160/min Heart rate, respiratory rate 44/min, an arterial pressure of 65/40, dry oral mucosae, periorbital petequiae, a slow capillary refill of 3 seconds, with tachypnea but normal pulmonary auscultation.

Fluid resuscitation was begun, along with early respiratory support to avoid deterioration and protect airway. He was started on broad spectrum antibiotics with vancomycin and cefotaxime. His labs reported leukocytosis (46.900), neutrophils 79%, lymphocytes 10%, anemia (Hb 8.7 g/dL), trombocytopenia (29.000 platelets), an elevated C reactive protein (24.4 mg/dL), normal bleeding times, elevated liver enzymes (AST 450 U/L, ALT 147 U/L) and serum creatinine (1.8 mg/dL), hypoalbuminemia (2.5 g/dL), and CPK 9425 U/L. Twenty four hours after admission, he presented with multiple purpuric lesions on his fingers and toes, progressing to ischemia and finally necrosis (Figure 1). Three days after, his blood cultures taken at admission reported *S. pyogenes*. With a diagnosis of toxic shock syndrome due to GAS, penicillin, clindamycin and Intravenous Immunoglobulin (IVIG) at 2g/kg were begun.

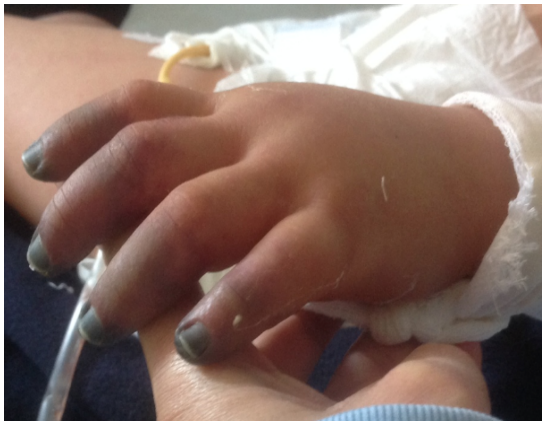

Figure 1: Distal necrosis from the 2nd to the 5th finger of his left hand and isquemia of the medial phalanges

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He received continuous heparin infusion to delimit the ischemic lesions. After one week, plastic surgery amputated the distal phalanges of the 2nd to 5th left fingers and debrided his right hand finger tips. After the 11th day of hospitalization he could be taken of the mechanical ventilation, stayed on noninvasive respiratory support, and a diffuse rash consisting of pustules, scabs and vesicles appeared and he was diagnosed with chickenpox in addition to the toxic shock syndrome. His chest X-rays showed basal right consolidation compatible with pneumonia, for which he received 7 days of intravenous acyclovir and completed a total of 14 days of penicillin and 10 days of clindamycin. The patient fully recovered and was discharged.

Discussion

Group A Streptococcus (GAS) is a common cause of infections in children that can range from mild to severe disease. The mild infectious episodes include acute tonsillitis, pharyngitis, impetigo, cellulitis and erysipelas. The severe invasive infections due to GAS are reported with an incidence of 2-4/100.000 persons. They include bacteremia with sepsis (14%), pneumonia (11%), necrotizing fasciitis (6%), and toxic shock syndrome (13%). The related mortality of the TSS is less in pediatrics (5-10%) than adults (30-80%), also lower than TSS secondary to *S. aureus* [1,2].

The TSS secondary to GAS is defined as an invasive infection with bacterial isolation from a sterile site, associated with hypotension and two or more organic dysfunction including: renal or hepatic dysfunction, coagulopathy, acute respiratory distress syndrome, skin rash or skin and soft tissue necrosis [3].

Its presentation as Purpura Fulminans (PF), as our patient presented with, is a potentially mortal infection, and results in a prothrombotic state of disseminated intravascular coagulation in severe septic patients. It is characterized by rapidly progressive skin hemorragiae, tissue necrosis and multiorganic failure. Most commonly responsible pathogens include *N. meningitidis, S.pneumoniae, S. aureus, Klebsiella pneumoniae, Enterococcus* and less frequently *S. pyogenes* [4].

The TSS is caused by the pyrogenic streptococcal exotoxin with acts as a superantigen with activation of a big population of T-Lymphocytes that induce an excessive inflammatory cytokine response (TNF, IL1-IL6). These cytokines are responsible for the clinical manifestations of toxic shock syndrome with fever, rash, hypotension, coagulopathy, hepatic and renal dysfunction. Also characteristic is Creatine Phosphokinase (CPK) elevation as result of rhabdomyolysis. In children, the primary source of infection can be frequently the skin and soft tissues, a penetrating trauma, surgical wounds, septic arthritis, varicella skin lesions and less common, cervical adenitis. However, in up to 50% of cases, the initial infection source remains unknown [2,5].

The diagnosis of TSS is confirmed with: isolation of GAS in normally sterile corporal fluids (blood, synovial fluid, cerebrospinal fluid) associated with shock and two of the following: renal injury, thrombocytopenia or coagulopathy, elevated liver enzymes or bilirrubins higher than 2 times normal, acute respiratory distress syndrome, generalized erythematous, macular or desquamatous rash in the following 5-7 days, soft tissue necrosis including myositis, necrotizing fasciitis or gangrene. Blood cultures are positive in more than 60% of the patients, unlike TSS secondary to *S. aureus*, for which only in 5% of cases, the microorganism can be identified [6,7]. The primary treatment is based on three important components: directed antimicrobials to diminish the bacterial burden and inhibit protein synthesis which is related to the toxin production, immunomodulation of the inflammatory response caused by the superantigens and support therapy to correct multiple organ failure.

Although GAS is multisensitive to microbials including B-lactams, Glicopeptides and Quinolones, the drug of choice consists of penicillin, without any reports of resistant strains worldwide. Adding clindamycin is based on its inhibition of protein synthesis, diminishing toxin production, M protein synthesis, and tumoral necrosis factor released by macrophages. It also potentiates phagocytosis and is recommended as adjuvant therapy or Penicillin [3,5,7]. Daptomycin has also been evaluated *in-vitro* to inhibit protein synthesis [8].

Intravenous Immunoglobulin [9] modulates the inflammatory response, reinforces humoral reponse to GAS, neutralizes superantigens, blocks inflammatory cytokines (IL-1,6, IL-1 γTNF) and increases streptococcal opzonization. The recommended dose is 2 g/kg in one dose. It diminishes mortality in TSS but not in necrotizing fasciitis [10].

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