Group A Streptococcal Toxic Shock

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Introduction

Clinically, group A streptococcal (GAS) toxic shock resembles Toxic Shock Syndrome (TSS) caused by toxins produced in vivo by Staph aureus. The characteristic features of GAS shock, also known as Toxic Strep Syndrome, include rapid development of multiorgan failure, early and progressive renal dysfunction and in many patients, also the adult respiratory distress syndmme. Cardiac dysfunction is also significant, but may be either due to septicemia per se or represent acute toxic cardiornyopathy. Other major findings include generalized desquamation with epidermal bullous eruption, hemorrhages and most often lack of positive blood cultures. We report such a classic case proven by positive blood culture. The patient's history of gastroententis suggests the bowel mucosa to be the most likely portal of entry, which is unusual for GAS infection.

Case Report

A 68 year old female with history of type-TI diabetes mellitus, hypothyroidism and hypercholesterolemia presented with complaints of vomiting and diarrhea of four days duration, preceded by fever and left flank pain. She denied chills, rigors or urinary symptoms. Her medications included glyburide and levothyroxine. On admission, her blood pressure was 100/70 mm Hg, pulse 108/mm and temperature 38.9°C (102°F). Physical examination revealed warm skin without any rash and left costovertebral angle tenderness. Oral mucosa was dry but Skill turg or was fair. Chest and abdominal radiographs were normal. Electrocardiogram showed sinus rhythm with a first degree heart block. Urinalysis was positive for nitrate, leukocytes and bacteria. Complete blood count (CBC) on admission revealed leukocytosis of 2 $1.6x10^9$/L, hemoglobin 8.68 mmoLfL (14.0 gm/dl), hematocrit 0.42 (42 percent). platelet $212x10^9$fL and granulocyte 95 percent. Serum chemistry showed potassium 4.6 mmol/L, bicarbonate 18.2 mmolfL, glucose 11.93 mmol/L (217 ing/dl), blood urea nitrogen (BUN) 17.14 mmol/L (48 rng/dl), creatinine 185.64 umol/L (2.1 mg/dl) and amylase 2.2 ukat/L. Urine cultures were negative. She became hypotensive within a few hours of admission and was transferred to intensive care unit. Initial pulmonary capillary wedge pressure was 17 mm Hg. She was initially treated with cefazolin and gentanucin. Blood culture on admission grew B- hemolytic GAS within 24 hours. Cefazolin was changed to ampicillin. Initial partial thmmboplastin time was 44 seconds with a control of 30.1 seconds. On day 1 serum chemistry revealed BUN 58 mg/dl, creatinine 2.9 mg/dl, calcium 6.2 mg/dl, phosphate 6.4 mg/dl, total bilirubin 2.5 mg/dl, direct bilirubin 1.91 mg/dl, alanine aminotransferase 100 IU/L, aspartateaminotransferase 1951/L, LDH 585 IU/L, alkaline phosphatase 133 lU/L, total protein 4.9 mg/dl, albumin 2.4 mg/dl, amylase 468 IU/L, lactic acid 5.4 mmol/L and creatinine phosphokinase (CPK) 7529 lU/L. Repeat chest radiograph next day showed bilateral infiltrates and congestion. Serial cardiac enzymes and hepatitis profile were negative. An ultrasonogram revealed enlarged kidneys. She continued to be hypotensive, acidotic and oliguric despite fluid therapy, inotmpic support and bicarbonate infusion. She developed adult respiratory distress syndrome and was intubated on her first hospital day. The next day, she developed petechiae followed by a generalized fragile bullous eruption. This progressed to disseminated intravascular coagulopathy confirmed by high levels of fibrinogen degradation products anddecreasing levels of fibnnogen. The antibiotics were changed to intravenous vancomycin, metronidazole and penicillin-

sodium. Fever gradually subsided. All parameters of CBC and serum chemistry, however, deteriorated further with rising leukocytosis, creatinine, bilirubin, arnino transferases and decreasing hematocrit and platelets. Thrombocytopenia was treated with platelet transfusions. Albumin, calcium and potassium were supplemented. The coagulopathy was treated with fresh frozen plasma transfusions. She died on the fourth day of hospitalization after unsuccessful resuscitation. Autopsy results were significant for non-infective mitral valve vegetation, recent infarct of papillary muscle, pseudomembranous colitis, 1 cm hyperplastic polyp in transverse colon, severe atherosclerotic heart disease and hemorrhagic changes in all the viscera.

Discussion

Group A streptococcus (GAS) has been known for centuries to cause serious infections. Non-suppurative sequelae like rheumatic fever and glomerulonephritis have been the major cause of morbidity and mortality. Until 1970s, the incidence and severity of GAS infections and their sequelae had been declining but prevalence was still high[1]. In late 1980s severe GAS infections have been identified with increasing incidence especially in younger, healthier individuals[2]. Clinically GAS shock resembles Toxic Shock Syndrome (TSS) caused by toxins produced in vivo by Staph. Aureus characterized by a generalized etythematous eruption and often multi-organ failure. Correlation between TSS and streptococcal exotoxin had been suggested in early 1980s[3,4]. In 1988 Bartter et al[5] suggested the term Toxic Strep Syndrome after observing an association between group A-B hemolytic streptococci and features of toxic shock syndrome. TSS generally includes early features of fever, hypotension, diffuse erythroderma, oropharyngeal and/or vaginal hyperemia, vomiting, diarrhea and myalgia[6]. Multiorgan failure usually occurs early. Several aspects of GAS infection are consistent with the pathophysiology of toxin mediated injury, despite evidence of tissue invasion and. bacteremia[5]. The pyrogemc exotoxin A has been implicated as the mediator, but exotoxin B and C may also be involved[5,7]. In our patient, although physical examination and BUN was suggestive of mild dehydration, renal compromise was evident prior to development of hypotension and progressed to acute renal failure[5,8] . Rhabdomyolysis was evident from high and rising CPK level, negative MB fractions, urinalysis and mild metabolic acidosis[9,10] . No surgical intervention was done due to lack of localized infection. Diabetes mellitus could be the predisposing factor for myositis and bacterernia. Blood cultures are negative in about 40 percent of cases with established GAS infection based on other criteria[8]. Our patient only had the first blood culture positive for GAS with subsequent negative cultures. This paucity might have been due to the early antibiotic use or may suggest an inherent property of the organism for transient bacteremia. Progression of the condition was most likely toxin mediated. Skin and mucous membranes are the main sites of infection though the injury may be trivial even without a break in the skin[8]. GAS may be present as part of the bowel flora and be responsible for sporadic streptococcemia. Food borne spread of GAS has not been associated with gastrointestinal symptoms[11]. Could it be that viral gastroententis in this patient had lowered gastrointestinal mucosal resistance to GAS and be responsible for the infection? Both questions of transient bacterenna and gastrointestinal source will be answered as more cases and additional pathological factors are recognized.

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