Austin Journal of Allergy

Austin Publishing Group

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Case Report

Methicillin-resistant Staphylococcus Aureus Bacteremia Complicated with Atypical Kawasaki Disease

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Received: July 25, 2014; **Accepted:** August 20, 2014; **Published:** August 22, 2014

Abstract

We report a 10-month-old boy initially presented with iatrogenic methicillin-resistant Staphylococcus aureus bacteremia. After a full dose and course of adequate antibiotic treatment, the diagnosis was complicated with atypical Kawasaki disease three weeks later. Two courses of intravenous immunoglobulin and steroid pulse therapy were prescribed.

Keywords: Kawasaki disease; MRSA; Bacteremia; Fever

Introduction

Kawasaki disease (KD) is the leading cause of acquired heart disease in children. Several case reports revealed KD patients with superantigen-secreting bacterial infections, which led to clinical trials to evaluate the association between superantigen-producing bacteria and KD. Most trials found superantigen-secreting bacteria from the rectum, pharynx, axilla, groin or skin [1,2], but never in the blood. We report a 10-month-old boy who is the first alive KD patient with S. aureus infection in the blood.

Case Report

A 10-month-old boy was admitted due to intermittent fever with chills for 4 days. On physical examination, the patient appeared fair. His vital signs were blood pressure of 79/48 mmHg, body temperature of 40.3°C, heart rate of 130/min, and respiratory rate of 34/min. Body weight was 11kg and body length was 74 cm. Examination of the oral cavity revealed a slightly injected throat.Auscultation showed clear breathing sound without cardiac murmur and normal bowel sound, too. There was no skin rash or joint swelling. The hemoglobin level was 13.4 g/dl, and hematocrit was 39.7%. The white blood cell counts were 2630/mm^3 with 43.7% neutrophils and 52.1% lymphocytes. The platelet counts were 96000/mm^3. C-reactive protein and urine routine were within normal limit.

On day 2, maculopapules on the trunk and face were noted, and fever subsided. After no more fever and skin rash gradually improved, discharge was arranged in the morning of day 4 under the impression of a diagnosis of roseola infantum. However, spiking fever up to 39°C was noted at the discharge night. He was then admitted again.

On physical examination, the patient appeared irritable. His vital signs were blood pressure of 118/85 mm Hg, body temperature of 37.5°C, heart rate of 142/min, and respiratory rate of 24/min. Physical examination included throat, eye, nose, heart and lung, abdomen and neurology with all negative findings. There was no palpable lymphadenopathy. The skin revealed improved maculopapuleson the trunk and faces sparing to upper and lowers extremities. Laboratory measureswere within normal limits. Blood culture was done and the result was pending.

On day 7, spiking fever persisted, but maculopapules continually improved. Vancomycin prescribed due to initial blood culture: methicillin-resistant Staphylococcus aureus. The physical examination showed a right hand abscess (2cm*3cm) at the previous intravenous site. Leukocytosis (white blood count: 17900 with segment 80%), C-reactive protein up to 19.5 mg/dl, and the pus culture from right hand abscess also found methicillin-resistant Staphylococcus aureus. Under the impression of bacteremia (Staphylococcus aureus) due to iatrogenic skin infection, Vancomycin was continually prescribed for one week. On day 14, the right hand abscess improved after irrigation, debridement, and dressing. However, spiking fever persisted, and body temperature was up to 39-40°C 2-3 times/day. We shifted antibiotics to Targocid and Fosfomycin due to Vancomycin cannot control fever. Further survey including blood culture, urine culture, and stool culture showed negative findings. Abdominal echo showed no hepatosplenomegaly and no abdominal abscess. Gallium scan revealed no definite evidence of active inflammation or gallium-avid tumor. On the re-evaluation physical examination, the patient appeared fair while no fever. There was no palpable lymphadenopathy, skin rash, edema or joint swelling. At the same time, leukocytosis and elevated C-reactive protein decreased. The hemoglobin level was 10.6 mg/dl. The erythrocyte sedimentation rate was 77 mm/hr. The procalcitonin level was 0.59 ng/mL.On day 20; we shifted antibiotics to Daptomycin, Fosphomycin, and Rocephin due to persistent spiking fever up to 39°C 2-3 times/day. Three cultures of stool, blood, urine were negative. Tests for Epstein-Barr VirusIgM, IgG were negative. Immunology measures of IgA, IgM, IgG were in the normal range according to his age to rule out any immunodeficiency. Rheumatoid factor was less than 10 IU/ml. Liver enzymes of aspartate amino transferase (90 IU/l) and alanine aminotransferase (93 IU/l), renal function and cardiac enzymes were normal. The hemoglobin level was 9.5 g/dl, and hematocrit was 39.7%. The white blood cell counts were 10630/mm^3 with 66% neutrophils and 29% lymphocytes. The platelet counts were 297000/mm^3. Urine routine was normal. On

Citation: Pan HS, Chen FL and Sun HL. Methicillin-resistant Staphylococcus Aureus Bacteremia Complicated with Atypical Kawasaki Disease. Austin J Allergy. 2014;1(2): 3.

day 22, we found mild non-purulent conjunctivitis, edema over the hand, red lip, strawberry tongueand a hemoglobin level was 8.6 g/dl, and hematocrit was 26.9%. The white blood cell counts were7620/mm^3 with 43% neutrophils and 35% lymphocytes. The platelet counts were 493000/mm^3. C-reactive protein was 4.45mg/dL. Atypical KD was suspected, we prescribed intravenous immunoglobulin (2 g/kg in a single infusion) and low dose aspirin (3 to 5 mg/kg per day), and the fever subsidedgradually. On day 24, desquamation on right fingers tip and relapsed fever were noted. Fever was up to 38.6ºC, once per evening. On day 26, the follow up lab data revealed the hemoglobin level was 7.4 g/dl, and blood smear found no hemolysis or premature cells. The white blood cell count was 9520/mm^3 with 47% neutrophils and 40% lymphocytes. The platelet counts were 577000/mm^3. C-reactive protein was 3.11 mg/dL. The erythrocyte sedimentation rate was >140 mm/hr.Arranged heart echo found LCA with mild dilation with irregular intima, and the EKG showed ST elevation at VL, V5, V6. Atypical KD was confirmed. On day 27, we prescribed the second course of intravenous immunoglobulin (2 g/kg in a single infusion) due to a fever of 38.8, once per evening persisted. On day 30, pulse therapy of Solumedrol 30 mg/kg/dose was given for one dose, and the fever finally subsided. Under the stable condition, discharge was arranged with a diagnosis of atypical KD plus bacterimea due to methicillin resistant Staphylococcus aureus. Low dose aspirin and a vasodilator (Dipyridamole) were prescribed for three months. After one year, all clinical data, manifestations and cardioecho were improved.

Discussion

KD was first addressed by Tomisaku Kawasaki as an acute febrile mucocutaneous lymph node syndrome in 1967. Understanding of the etiology and pathogenesis of KD is always an important and worthwhile public health concern. Several lines of epidemiological and clinical observations suggest that KD is caused by an infectious agent. Furthermore, the fever, clinical findings, and immunological reaction between KD, toxic shock syndrome, and streptococcal toxic shock syndrome are similar, which created a differential diagnosis of three diseases with a superantigen-mediated etiology. The evidence to support the theory that superantigen-producing microbes play a role in KD was as below.

First, an increase in the number of T cells expressing a specific T cell receptor (TCR Vβ2) region resulted from a toxin with superantigenic activity, and TCR Vβ2 skewing in patient with KD was also found [3]. Second, the clinical features between KD and staphylococcal and streptococcal toxin-mediated disease are similar. Previous case reports revealed children who were initially diagnosed with toxic shock syndrome and the illness progressed to KD, including the development of coronary artery disease [4]. Due to the manifestation in those cases, several studies were done to find the association between superantigen-producing bacteria and KD [1,2]. However, there were also conflicting results [5,6]. Third, serological responses to superantigens produced by S. aureus and group A Streptococcus also supported the role of superantigen-producing microbes. Some studies reported that KD patients had those serological findings [3,7].

The first and third evidence supporting the theory that superantigen-producing microbes play a role in KD were indirect. Thus, culture of superantigen-producing microbes may be relatively important. However, it is recognized that as many as 50% of healthy adults are colonized with staphylococcus aureus. Isolation of bacteria from the blood is a precise method to prove the infection. In those studies [1,2,5,6], cultures were obtained from the pharynx, rectum, axilla, and groin. Our case is the first live KD patient with the isolation of S. aureus from the blood.

In patients with KD who are initially treated with IVIG and aspirin, 10 to 15 percent of them continue to havefever or fever persists or returns within 48 hours. Some patients respond to additional doses of IVIG therapy while other patients with KD are resistant to IVIG therapy even after multiple doses. Retrospective studies [8,9] have reported some clinical factors that increased the likelihood of patient no responsiveness to initial IVIG therapy. Those factors, for example, less than one year of age, elevated C-reactive protein (≥8 mg/dL), and elevated liver enzymes were consistent with our patients. The mechanism of action of IVIG in KD is not understood, thus, the reason that some patients with KD fail initial IVIG therapy is not clear. Alternatives to IVIG retreatment [10] are needed because multiple doses of IVIG may incompletely control recalcitrant cases of KD. Clinical trials [11] discuss the treatments for patients with KD resistant to IVIG therapy who were given aregimen of methylprednisolone ,despite IVIG, who demonstrate ongoing signs suggestive of active vasculitis (eg, persistent fever) . Our patient had resolution of fever after one dose of methylprednisolone. There was no significant abnormal cardia-sonogram finding after treatment with low dose aspirin

Although there is still debate about the etiology, cumulative evidence suggests that KD is a response to superantigens. More attention must be focused on KD in patients with a superantigen-producing microbial infection.

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Austin J Allergy - Volume 1 Issue 2 - 2014
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Citation: Pan HS, Chen FL and Sun HL. Methicillin-resistant Staphylococcus Aureus Bacteremia Complicated with a Typical Kawasaki Disease. Austin J Allergy. 2014;1(2): 3.