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CLINICAL VIGNETTE

A Case Report of Kawasaki Disease Triggered By Vaccine-Attenuated Chicken Pox

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Introduction

Kawasaki disease is a common childhood vasculitis initiated by a still unidentified immunological trigger, which has frequently been hypothesized to be infectious in nature. Although the acute disease is self-limited, delay in proper diagnosis and treatment can result in serious cardiac complications. Here we present a case of Kawasaki disease, which occurred closely after a bout of vaccine-attenuated varicella zoster.

Case Report

A 3-year-old Asian-American boy was brought by his mother to the local urgent care, complaining of five days of persistent fevers and sore throat, followed by the onset of red eyes and swelling of the hands and feet. One-week prior, he had developed several 1-2 mm papules on his face and arms, with no other associated symptoms. His pediatrician diagnosed him with breakthrough varicella, a milder form of chicken pox increasingly recognized in children since 1995, when the vaccine was licensed for use in the United States.

Three days later, the boy's appetite markedly diminished, and the next day he became febrile to 100 degrees Fahrenheit. Subsequently he began complaining of mid-epigastric and right upper quadrant abdominal pain, causing him to sleep face down in his bed with his knees tucked up into his chest. He also complained of anterior neck pain that prevented him from flexing his neck. At one point, he developed a transient diffuse, macular erythematous rash involving his chest, back, and groin.

Over a five-day period, he continued to suffer from anorexia, persistent high-grade fevers (as high as 102.8 degrees Fahrenheit), and increasing irritability. On the day of presentation, he began to cry inconsolably. His parents noticed that the whites of both his eyes had now become pink, and his hands and feet were swollen.

In urgent care, he was febrile to 100.1 degrees Fahrenheit, tachycardic with a heart rate of 113 beats/min, and breathing rapidly at a rate of 36 breaths/min. He appeared tired and uncomfortable, but was interacting appropriately with his mother. Head and neck exam showed bilateral conjunctival injection without purulent discharge, erythema of the lips and oral mucosa, and a 2 cm right-sided tender anterior cervical lymph node. Tympanic membranes and oropharynx were both clear. His heartbeat was rapid but regular without any murmurs, and lung fields were clear bilaterally. The abdominal exam was positive for right upper quadrant tenderness to palpation but no rebound, guarding, or organomegaly. Extremities revealed non-pitting edema of the bilateral hands and feet, with palmar erythema and mild desquamation. No synovitis was noted. There was a subtle maculopapular rash characterized by blanching erythema diffusely covering the trunk.

After evaluation in urgent care, he was admitted to the hospital for further work-up and management, with a presumptive clinical diagnosis of Kawasaki disease. On admission, complete blood count was notable for leukocytosis of 11.6 x $10^3/\mu L$ with a left shift. Electrolytes and urinalysis were unremarkable. A liver panel revealed both marked transaminase elevation (AST 118 U/L, ALT 304 U/L) and cholestasis (alkaline phosphatase 352 U/L, total bilirubin 2.2 mg/dL). Non-specific inflammatory markers were markedly elevated, with an erythrocyte sedimentation rate of 53 mm/hr and a high-sensitivity C-reactive protein level was 182.7 mg/L. Serology for Epstein-Barr virus was negative. Blood and urine cultures did not grow out any organisms. A chest radiograph was normal. The electrocardiogram showed sinus tachycardia at a rate of 124 beats/min. An echocardiogram showed normal cardiac anatomy and function, with no evidence of coronary artery aneurysm or pericardial effusion.

The patient was promptly started on IVIG at 2 gm/kg and high-dose aspirin 270 mg every 6 hours. By the next morning, he was smiling and hungry, and remained afebrile from that point on. All of his remaining symptoms of illness resolved by hospital day #3.

One week later, he was back to his usual state of health. Repeat laboratory examinations revealed a dramatic drop in the inflammatory markers (ESR 5 mm/hr, hsCRP 0.26 mg/dL, WBC 8 x $10^3/\mu L$) and resolution of hepatic dysfunction (AST 50 U/L, ALT 50 U/L, alkaline phosphatase 231 U/L, total bilirubin 0.5 mg/dL).

Discussion

Kawasaki disease, also known as mucocutaneous lymph node syndrome, was first described in 1969 by Dr. Tomisaku Kawasaki, a Japanese pediatrician. It is a largely self-limiting necrotizing vasculitis of the small- and medium-sized arteries. It primarily affects children, with over 80% of cases in children under the age of five. Though the prevalence is highest in East Asia, it is a relatively common disease worldwide with the incidence in the United States of 4 to 5 cases in 100,000[1].

Diagnosis is made on clinical grounds, based on a persistent fever lasting at least 5 days, along with 4 out of 5 additional criteria: cervical lymphadenopathy (usually >1.5 cm), polymorphous rash, acral swelling, bilateral conjunctivitis without exudates, and mucous membrane changes of the upper respiratory tract (injected pharynx, injected/fissured lips, strawberry tongue).

These initial manifestations are not worrisome, however, there are potential cardiac sequelae. In the early stages of the disease, inflammation of the small vessels can cause pericarditis, myocarditis, and endocarditis with valvulitis. As the disease progresses, medium-sized vessels also become involved, leading to coronary artery aneurysm and thrombosis formation. Even though the disease course is self-limited, with full resolution of the inflammation, up to 20-25% of untreated patients can develop coronary artery stenosis and myocardial ischemia later in life[1].

Although the etiology of Kawasaki disease is still unknown, it has long been suspected that one or more infectious agents likely serve as an immunological trigger in a genetically predisposed host. Proposed but unproven agents include adenovirus, herpesvirus, Mycoplasma species, toxigenic streptococci, viridans streptococci, toxigenic staphylococci, Propioni-bacterium acnes, Erlichia chaffeensis, rickettsia species, Epstein-Barr virus, retroviruses, human coronavirus New Haven, measles virus, Chlamydia pneumoniae, Bartonella henselae, Coxiella burnetii, and house dust mite. Epidemiological studies seem to support this idea as well; Kawasaki disease displays a seasonal predominance in the late winter/early spring and a geographic clustering of outbreaks[2].

In this case, the child developed breakthrough varicella despite being vaccinated on schedule. The incidence of breakthrough varicella is about 2 percent[3] and has been attributed to either primary vaccine failure (i.e. the body not mounting an adequate response to produce the desired antibodies), or through waning immunity, which has led to the recommendation of a second dose of the vaccine at 4 to 6 years of age. These vaccine-attenuated varicella infections are generally milder cases, with a maculopapular rash rather than the distinctive vesicular one, and minimal or no systemic symptoms. We believe it was this infection which triggered the Kawasaki disease a week later.

There are a number of case reports in the literature regarding Kawasaki disease following infection with herpesvirus. Turkay et al. describe a similar case of a three-year-old boy with Kawasaki disease, who had developed chicken pox ten days prior to diagnosis and was also found to have concomitant Epstein-Barr virus with a positive anti-IgM antibody[4]. Ogboli et al., Kuipers et al., and Lee and Huang all diagnosed cases in patients with active chicken pox infection[5-7]. In our review of the existing literature, we did not find any other reports of Kawasaki disease after a mild breakthrough varicella.

Standard treatment is IVIG infusion (2 gm/kg) plus high-dose aspirin (80-100 mg/kg per day divided into 4 doses) as early as possible in the course of the disease. While Kawasaki is a self-limited disease, timely diagnosis and treatment serves to not only shorten the time course of the fever and laboratory abnormalities, but more importantly, to prevent long term complications. Early treatment has been shown to lower the rate of coronary aneurysm from 20% down to less than 3-5%[1].

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