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CASE REPORT

Kawasaki disease and human bocavirus—potential association?

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Abstract Kawasaki disease (KD) is an acute febrile multisystem vasculitic syndrome of unknown etiology, occurring mostly in infants and children younger than 5 years of age. We present a 13-month-old male with KD from whom was found human bocavirus DNA in nasopharyngeal secretions. Human bocavirus DNA in a patient with KD raised question about the coincidental or possible etiological association.

Introduction

The cause of Kawasaki disease (KD) is unclear and there is no specific method of diagnosis; clinical suspicion is based on the identification of defined clinical criteria.[1] KD is a multisystemic vasculitis of small to medium size vessels.[1,2] The natural history of KD reveals that coronary artery aneurysms occur as a sequel of the vasculitis in 20% to 25% of untreated children. Although the cause of KD remains unknown, clinical trials have established effective therapies, despite the absence of a proven cause. Intravenous immunoglobulin plus aspirin lowers the rate of coronary artery aneurysms from 20% to between 3% and 5%.[3]

Immunopathological mechanisms involved in the pathogenesis of KD are unclear. Although its etiology remains unknown, the clinical and epidemiological features of this disease suggest that it is infectious.[1,4] Epstein-Barr virus, adenovirus, and cytomegalovirus have all been considered as possible agents that are involved in KD.[5,6] The recently discovered human bocavirus (HBoV) is the first member of the family Parvoviridae, genus Bocavirus, to be potentially associated with human disease.[7] Several studies have identified HBoV in respiratory specimens from children with acute respiratory disease but the full spectrum of clinical disease and the epidemiology of HBoV infection remain unclear.[8,9,10] A study using nasopharyngeal aspirates from children hospitalized with fever also revealed HBoV nucleic acid in five patients hospitalized with KD.[2]

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Case report

A 13-month-old male child, previously healthy, with updated vaccination, including antimeningococcal and antipneumococcal vaccine, was admitted to our hospital on October 2006 after 5 days of fever because of a suspicion of KD. Fig. 1.

On Day 1, he had fever with rash (on trunk and limbs) and presented with leukocytosis, neutrophilia, and elevated C-reactive protein (4.0 mg/dL). A progressive worsening of the general state was verified; and on Day 4, he was treated with ampicilin (80 mg/kg/d, 6/6 hours). On Day 5, he maintained fever; irritability; and developed mouth enanthem, glossitis, rash with perioral desquamation, swelling of the hands and feet, conjunctivitis, and jaundice. On clinical examination, he had tachycardia, systolic murmur, and hepatomegaly. Laboratory evaluation at admission in our hospital, on Day 5, showed 15,860/mL leukocyte count with 15.3% neutrophils, hemoglobin 10.3 g/dL, platelet count 225,000/mL, C-reactive protein 13.7 mg/dL, and elevation of transaminase (63/86 UI/L). Renal function, cultures (blood, urine, and feces), and serology for adenovirus, cytomegalovirus, Epstein-Barr virus, and parvovirus B19 were within normal limits or negatives.

Chest X-ray revealed a bibasal nonspecific interstitial infiltrate. Echocardiography (Day 2) showed a slight mitral valve insufficiency and normal coronary arteries; and on Day 6, left coronary aneurysm was identified (Fig. 1), which confirmed the diagnosis of KD. Detection of adenovirus, influenza virus A and B, parainfluenza virus 1—3, and respiratory syncytial virus in nasopharyngeal secretions by an immunofluorescence were negative. HBoV was identified in nasopharyngeal secretions by real time polymerase chain reaction (PCR) followed by sequencing of PCR product.

Treatment with gammaglobulin (2 g/kg) in a single dose and high dose of diary antiplatelet aggregate led to rapid resolution without relapse, progressive normalization of the liver function, and transitional thrombocytosis. Cardiac outcome was excellent with resolution of coronary aneurysm.

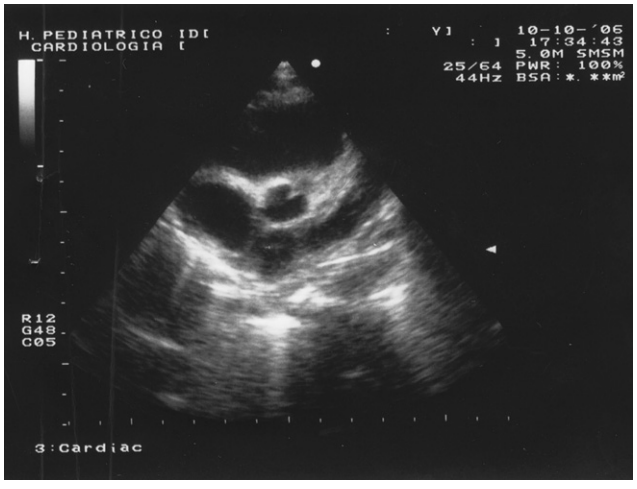

Figure 1. Coronary echocardiography showing a left aneurysm.

Discussion

During the past 30 years, identifying of a definitive infectious agent that causes KD has not been possible. Certain intracellular pathogens and superantigens from bacteria have been implicated in its immunopathogenesis. Several lines of evidence support the fact that KD is an infectious disease, such as acute onset of a self-limited illness, presence of fever, increased susceptibility in younger age groups, and geographic clustering of outbreaks with a seasonal predominance (later winter and early spring). Various bacteria, such as *Streptococcus pyogenes*, *Staphylococcus aureus*, *Mycoplasma pneumoniae*, and *Chlamydophila pneumoniae* have been sporadically isolated from patients with KD. Suspected viral agents, especially lymphotrophic viruses, such as adenovirus, Epstein-Barr virus, parvovirus B19, herpesvirus 6, parainfluenza type 3 virus, human immunodeficiency virus, measles virus, rotavirus, dengue virus, and varicella-zoster virus have been implicated as potential causes of KD, but no proof has emerged to incriminate one agent.[11]

This new parvovirus, genus Bocavirus (HBoV), has been identified in nasopharyngeal secretions from children with acute febrile respiratory infection. The potential of causing other nonrespiratory diseases has been under discussion.[12,13] Later publications reported the virus in the gastrointestinal tract and serum, referring to a systemic dissemination.[14,15]

The detection of HBoV DNA in a patient with KD raised question about the coincidental or possible etiological association. Based on the clinical, epidemiological, and immunological features of KD, the pathogenesis of KD could be a hyperimmune reaction in genetically susceptible children to a ubiquitous virus. Catalano-Pons et al.[2] have also identified HBoV by PCR in five (31.2%) patients with KD, suggesting that this emerging virus may also play a pathogenic role in some cases of KD. Additional studies are required to understand the physiopathology of this new virus.

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