The Complexities of the Diagnosis and Management of Kawasaki Disease

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KEYWORDS

• Coronary artery aneurysm • Prolonged fever • Systemic inflammation
• Myocardial infarction • Acquired pediatric heart disease

KEY POINTS

- The diagnosis of Kawasaki disease (KD) requires a high index of suspicion. Infants and children may present with "soft" or incomplete clinical features, yet still develop significant coronary artery abnormalities.
- Asian children have the highest incidence of KD of all ethnic/racial groups. Siblings and children of KD patients are at increased risk.
- Laboratory and echocardiographic findings can help establish the diagnosis in nonclassic cases. In particular, a child with prolonged fever, laboratory evidence of systemic inflammation, and a coronary artery *z* score of 2.5 or higher has a very high probability of having KD.
- Prompt treatment with intravenous gammaglobulin and aspirin can be life-saving. Children who do not have resolution of fever with this primary therapy are at increased risk of developing coronary artery abnormalities, and additional anti-inflammatory therapies should be administered.

INTRODUCTION

Although Kawasaki disease (KD) has been recognized in Japan and the United States for decades, the etiology and pathogenesis of the illness remain major pediatric mysteries. The abrupt onset of clinical signs such as fever, exanthem, and enanthem in previously healthy children, the rarity of recurrence, the very young age group affected, and the well-documented epidemics and outbreaks of illness are strongly suggestive of infectious etiology, as well described in a classic epidemiologic study from the 1980s.[1] The very high incidence of the illness in Japan, where approximately

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1 in 90 children develop KD by age 5 years,[2] is highly suggestive of a ubiquitous infectious agent affecting young susceptible children who are genetically predisposed. Key features of KD are presented in **Box 1**. It is important to understand the major pathologic features of KD arteriopathy, briefly summarized in **Box 1**, because these features predict the adverse clinical outcomes observed in KD patients who develop coronary artery abnormalities.[3] Moreover, knowledge of the many organs and tissues involved in the systemic inflammation of KD assists in understanding the many possible clinical manifestations of the illness (**Box 2**).[4] Risk factors for KD and the development of coronary artery abnormalities are summarized in **Box 3**.

INCIDENCE AND MORTALITY RATES

The incidence of KD varies in different countries throughout the world (**Table 1**) and remains unknown in many regions, especially in those that continue to have a high prevalence of measles, which shares many clinical features with KD. In Japan, there is high recognition and early treatment of the condition, and mortality rates have fallen from 1.4% in 1970 to 0.01% in recent years; fatality rates began to decrease markedly after the introduction of intravenous gammaglobulin therapy in the late 1980s.[8] In the United States, fatality rates are also very low; fatal cases are often associated with delayed or missed diagnoses.[3] Peak months of KD incidence vary somewhat by country, but a consistent theme seems to be a peak during the winter in nontemperate climates.[9]

PATIENT HISTORY

The history is particularly important in KD, as some clinical features of the illness may begin and abate before the patient's presentation. It is recommended that the parent or guardian is asked nonleading questions about symptoms to avoid introducing recall bias. **Box 4** lists common features in the history of children with KD. Excessive irritability, refusal to bear weight, redness and swelling of the hands and feet, and an

Box 1
Key features of Kawasaki disease (KD)

An acute onset of prolonged febrile illness in previously healthy children.

The leading cause of acquired heart disease in children in developed nations.

A systemic inflammatory illness affecting many organs and tissues, but leading to long-term consequences almost exclusively confined to medium-sized muscular arteries, particularly the coronary arteries.

KD arteriopathy is characterized by 3 linked pathologic processes: necrotizing arteritis, subacute/chronic arteritis, and luminal myofibroblastic proliferation. Necrotizing arteritis occurs in the first 2 weeks after onset and can result in necrosis of the coronary arteries; if the necrosis is extensive, giant coronary artery aneurysms can form, which are associated with severe outcomes. Subacute/chronic arteritis begins in the first 2 weeks and can continue for months to years after onset. It is closely associated with luminal myofibroblastic proliferation, an active proliferative process of smooth muscle cell–derived myofibroblasts and their matrix products, which can lead to progressive arterial stenosis.

The etiology remains unknown, but clinical and epidemiologic features support an infectious cause.

Genetic factors play a role in susceptibility, with Asian children at highest risk. However, children of all racial and ethnic groups can develop KD.