

Asymptomatic Kawasaki Disease in a 3-Month-Old Infant

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Kawasaki disease (KD) is the leading cause of acquired heart disease in children in the United States. It is a systemic vasculitis characterized by diffuse inflammation of medium and small blood vessels. If untreated it can lead to myocardial infarction, ischemic heart disease, or sudden death. Early recognition and treatment decrease the incidence of coronary consequences, resulting in improved clinical outcomes. Incomplete KD is much less likely to fulfill major clinical diagnostic criteria. Infants <12 months of age are more likely to have an incomplete presentation, and children <6 months of age are more likely to develop cardiac complications. We present a case of a 3-month-old, previously healthy white boy who was noted to have a new transient cardiac murmur during a routine health assessment. He was completely asymptomatic, and physical examination was otherwise within normal limits. An echocardiogram was performed and showed abnormal dilation of several coronary arteries, consistent with the coronary ectasia associated with KD. Laboratory evaluation was significant for values suggestive of systemic inflammation. Based on these results, a presumed diagnosis of incomplete KD was made and treatment administered. Close surveillance was undertaken, and serial laboratory studies and imaging showed gradual resolution of inflammatory markers and cardiac ectasia. This unique case of incomplete KD without any of the physical signs normally associated with the disease emphasizes the spectrum of presentation and the possibility of missing a diagnosis of incomplete disease, reinforcing the need to remain vigilant.

Kawasaki disease (KD) is a self-limited systemic vasculitis of small and medium vessels that typically occurs in infants and young children. Untreated, it can lead to myocardial infarction, ischemic heart disease, or sudden death.¹⁻³ The annual incidence of KD is ~112 cases per 100 000 children <5 years old, and although it is historically more likely to occur in those of Japanese descent, it has been found in all ethnic groups.⁴ The incidence of incomplete KD is unknown, probably because of diagnostic uncertainty, as the clinician must rely on clinical judgment and adjunctive findings such as cardiac ectasia on echocardiogram.⁵

Clinical diagnosis of KD includes the presence of fever for ≥ 5 days, without a known cause, with ≥ 4 of the following: bilateral bulbar conjunctivitis; injected or fissured lips, injected pharynx, or strawberry tongue; erythema of the palms or soles and edema of the hands or feet early in the illness, or periungual desquamation during convalescence; polymorphous rash; or cervical lymphadenitis with at least ≥ 1 node >1.5 cm in diameter. Incomplete KD is less likely to fulfill major clinical diagnostic criteria, with conjunctivitis, peripheral extremity changes, and cervical lymphadenopathy most likely to be absent,⁶ and infants appear to

abstract

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Dr Pinches participated in care of the patient and drafted, revised, and reviewed the manuscript; Dr Dobbins participated in care of the patient and assisted in drafting, revising, and reviewing the manuscript; Ms Cantrell assisted in the initial data search and acquisition of resources and reviewed the manuscript; Dr May directed the care of the patient, interpreted the echocardiograms and provided documentation of the same, and critically reviewed the manuscript; Dr Lopreiato directed care of the patient and critically reviewed the manuscript; and all authors approved the final manuscript as submitted.

DOI: 10.1542/peds.2015-3936

Accepted for publication May 4, 2016

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

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FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

To cite: Pinches H, Dobbins K, Cantrell S, et al. Asymptomatic Kawasaki Disease in a 3-Month-Old Infant. *Pediatrics*. 2016;138(2):e20153936

be more likely to have incomplete presentation.^{4,7}

Laboratory values showing elevated acute phase reactants, though not included in diagnostic criteria, can support a diagnosis in uncertain cases. A diagnosis of incomplete KD can be made with increased clinical suspicion, elevated erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP), and ≥ 3 abnormal laboratories or echocardiogram findings. Abnormal laboratory values include CRP ≥ 3 mg/dL, ESR ≥ 40 mm/hour, white blood cell count (WBC) $\geq 15\,000$ cells per mm^3 , normocytic, normochromic anemia, pyuria, elevation of alanine aminotransferase, hypoalbuminemia, and platelets $>450\,000$ per mm^3 after 7 days of illness.⁴

Echocardiogram changes are not part of the diagnostic criteria but can support a diagnosis, particularly in incomplete cases. Lesions suggestive of KD include aneurysms with an internal cardiac artery diameter >2 SD over the body surface area-adjusted norm or >2 SD over the age-adjusted norm with 2 other findings, pericardial effusion, valvular regurgitation (particularly of the mitral valve), decreased left ventricular contractility, and coronary arteritis.^{4,5}

The decision to treat KD is based on the presence of clinical features, elevated ESR or CRP, and ≥ 3 abnormal laboratory findings or an abnormal echocardiogram.^{4,8} The standard regimen for initial treatment during acute illness, aspirin and intravenous immunoglobulin,⁴ has been shown to greatly reduce cardiac complications.² Additional interventions are available but beyond the scope of this discussion.^{4,9}

CASE PRESENTATION

Our patient is a 3-month, 12-day-old white boy noted to have a

new, nonradiating, otherwise unspecified murmur at the left upper sternal border by his primary care provider during a routine health assessment before a family overseas move with the military. At that time there were no signs or symptoms of illness (including rash, conjunctivitis, or fever), and the physical examination was within normal limits. There was no history of fever, dyspnea, excessive sweating, loss of consciousness, or cyanosis. Past medical history was unremarkable. He was a term infant born via cesarean delivery for failure to progress after failed induction. Birth weight was appropriate for gestational age. Newborn screening was normal, and vaccines were up to date. Medications included simethicone as needed for gas. Family history was notable for paternal grandfather with myocardial infarction in his 40s and maternal uncle with familial thrombocytosis. The patient was referred to cardiology for additional evaluation.

On examination by cardiology 5 days later, past medical history was reviewed in great detail with no new findings. He was well appearing, and on cardiac examination he had a regular rate and rhythm, normal S1 and S2, and no S3 or S4; no murmur was heard. Arterial pulses were equal and normal bilaterally, there was no edema, and capillary refill was <2 seconds. The patient had normal conjunctiva, without mucous membrane abnormalities, cervical lymph node enlargements, strawberry tongue, rash, or swollen extremities. Electrocardiogram showed normal sinus rhythm with normal intervals and voltage for age.

An echocardiogram was performed for clinical completeness and showed abnormal dilation of the left coronary artery, left anterior descending artery (LAD), and right coronary artery. The LAD had a z

score of $+6.2$ per the Boston data set, commonly used for patients with KD.¹⁰ There was no pericardial effusion, and size and function of the left ventricle were normal, with no mitral valve disease. The results of the echocardiogram were consistent with coronary ectasia associated with KD, although even on extensive questioning, the patient's parents did not recall any systemic findings that would correlate with this diagnosis. Laboratory evaluation was significant for a WBC of 21.3 cells per mm^3 , hemoglobin (Hb) of 9 g/dL, platelet count (PLT) of 1002 per mm^3 , and CRP of 1.679 mg/dL. A complete metabolic panel was normal.

A presumed diagnosis of incomplete KD was made. The patient was admitted to the hospital for treatment, with close echocardiogram surveillance to better demonstrate the trajectory of coronary enlargement. Upon admission the infant was stable and afebrile with vital signs as follows: heart rate 148 beats per minute, respiratory rate 36 breaths per minute, blood pressure 98/56 mm Hg, and oxygen saturation by pulse oxygen saturation probe 100% on room air. He again had a normal physical examination. Treatment with low-dose aspirin was begun, and a single infusion of intravenous immunoglobulin was administered. The patient tolerated the treatment well, and after a period of monitoring he was discharged from the hospital on continued aspirin therapy. During outpatient follow-up, the infant continued to have a normal physical examination, and electrocardiogram remained within normal limits for age. Laboratory studies and serial echocardiograms at 1 and 6 weeks after diagnosis showed gradual resolution of leukocytosis, thrombocytosis, and cardiac ectasia; CRP also normalized (Fig 1). The infant was treated with aspirin therapy for 6 weeks after diagnosis.

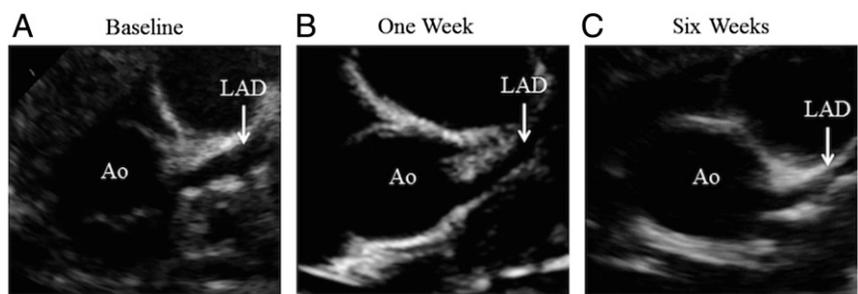


FIGURE 1

A, The LAD appears echobright, irregular, and dilated. It measures 2.7 mm (z score +6.2 for BSA). Laboratory values at this time were WBC 21 cells per mm^3 , Hb 9 g/dL, PLT 1002/ mm^3 , and CRP 1.68 mg/dL. B, The LAD appears less bright and more regular. It measures 2.1 mm (z score +3.2 for BSA). Laboratory values at this time were WBC 16 cells per mm^3 , Hb 10 g/dL, PLT 703 per mm^3 , and CRP 0.03 mg/dL. C, The LAD appears more normal for age and measures 1.7 mm (z score +1.0 for BSA). Laboratory values at this time were WBC 12 cells per mm^3 , Hb 11 g/dL, PLT 472 per mm^3 , and CRP not obtained. Ao, aorta; BSA, body surface area.

DISCUSSION

This young infant was diagnosed with KD after an incidental finding of cardiac ectasia on echocardiography. His only clinical sign may have been a transient heart murmur; he never displayed any other signs or symptoms typical of KD. He did not display clinical findings to support an alternative diagnosis of viral illness, systemic lupus erythematosus, or Behçet disease, which can mimic KD but do not involve the heart. Although mild transient coronary dilation may occur with some febrile illnesses, these typically do not reach z scores >2.5 .^{11,12} Thus, this case probably represents asymptomatic incomplete KD.

Resolution with appropriate treatment also supports the diagnosis of incomplete KD, with classification as a risk level II.⁴ Patients in this stratification present with transient coronary artery ectasia or dilatation (which resolves within the initial 6–8 weeks after the onset of illness) and are recommended to have antiplatelet therapy only in the initial 6 to 8 weeks after the onset of illness. There is no restriction of physical activity after 6 to 8 weeks of therapy. Risk assessment and counseling are recommended at 3- to 5-year intervals, and coronary angiography is not recommended. Our patient's

follow-up care was arranged accordingly.

KD is the leading cause of acquired heart disease in children in the United States.^{5,13} As our case demonstrates, it is important to maintain vigilance for incomplete KD, especially in infants <6 months old.¹³ Infants <12 months of age with an incomplete presentation are more likely to develop cardiac complications, probably because of an uncertain clinical picture delaying diagnosis.^{5,6,8,13–15} Early recognition and treatment decrease the incidence of coronary consequences,^{5,16} but children with complete presentation are significantly more likely to be treated earlier in the disease course than those with incomplete presentation.⁵ Nonetheless, as our case demonstrates, even at an unknown stage in the disease process treatment may improve coronary artery anomalies and reduce morbidity and mortality. After treatment, patients with typical and incomplete presentations with coronary vasculitis show similar rates of regression on follow-up visits.⁷

There is a need for more research into the pathophysiology and possible inciting causes of KD to more clearly delineate the spectrum of cases. For example, it is interesting to note that the

incomplete presentation of disease is prevalent in young infants such as our patient, particularly those <6 months of age, who have persistent maternal antibodies. It has been postulated that KD is caused by an unknown infectious agent, that an infected child might experience an asymptomatic disease course secondary to the presence of passively acquired maternal antibodies, and that, if this were the case, it would be fitting that only a small fraction of such patients would develop the overt clinical features of KD.⁴ Our case potentially substantiates this hypothesis, and we believe that the role of persistent maternal antibodies in these younger infants, which may modify the typical disease presentation, bears continued study.

This is a unique case of incomplete KD without fever or any of the other physical signs normally associated with the disease. Only through a fortuitous echocardiographic examination was the underlying cardiac and inflammatory process uncovered and treatment begun. Dr Kawasaki's guidelines were created before cardiac involvement was understood to be involved in this disease process, and were never intended to identify children at risk for developing coronary artery abnormalities. It is thus unsurprising that $\geq 10\%$ of children who develop coronary artery aneurysms never meet criteria for KD.¹⁷ Young infants with the coronary abnormalities described here should alert the clinician to possible incomplete KD, even in the absence of other symptoms of the disease.^{4,6,13}

ACKNOWLEDGMENTS

We acknowledge Ms Farahnaz Ghias, RDCS (AE/PE), for the outstanding echocardiographic images obtained on this infant. We also acknowledge the pediatric inpatient staff of the

ABBREVIATIONS

CRP: C-reactive protein
ESR: erythrocyte sedimentation
rate
Hb: hemoglobin
KD: Kawasaki disease
LAD: left anterior descending
artery
PLT: platelet count
WBC: white blood cell count

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Pediatrics 2016;138;

DOI: 10.1542/peds.2015-3936 originally published online July 1, 2016;

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