Kawasaki disease recognition and treatment

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Abstract

Question If a child presents to my office with several days of fever and a few features of Kawasaki disease (KD) but does not meet the diagnostic criteria, could they still have KD and is treatment needed?

Answer Presentations of KD have a range of clinical signs and symptoms. With the lack of a criterion standard test, the diagnosis of KD relies on syndrome recognition and a high index of suspicion in cases where KD does not present classically. It is still possible to have KD even if not all of the criteria are met, and these children are referred to as having incomplete forms of KD. The diagnosis of incomplete KD is usually made in a child or infant who presents with a history of prolonged fever, a few clinical criteria for KD, and other supportive features such as positive laboratory or echocardiographic findings. It is important to recognize children with incomplete forms of KD to avoid poor outcomes such as coronary artery aneurysms.

Reconnaissance et traitement de la maladie de Kawasaki

Résumé

Question Si un enfant est fiévreux depuis plusieurs jours et présente quelques caractéristiques de la maladie de Kawasaki, mais que les symptômes ne répondent pas aux critères diagnostiques, pourrait-il quand même être atteint de la maladie de Kawasaki, et le traitement est-il nécessaire?

Réponse Le tableau clinique de la maladie de Kawasaki compte une vaste gamme de signes cliniques et de symptômes. En l'absence d'un test pour les critères standards, le diagnostic de maladie de Kawasaki repose sur la reconnaissance du syndrome et sur de forts soupçons dans les cas où la maladie se manifeste de manière atypique. Il est toujours possible d'être atteint de la maladie de Kawasaki même si les symptômes ne répondent pas à tous les critères; on parle alors de formes incomplètes de la maladie de Kawasaki. Le diagnostic de maladie de Kawasaki incomplète est habituellement posé lorsqu'un enfant ou un nourrisson se présente avec un historique de fièvre prolongée, quelques critères cliniques de maladie de Kawasaki, et d'autres caractéristiques à l'appui, telles que des résultats de laboratoire positifs et des observations à l'échographie. Il importe de reconnaître les enfants atteints des formes incomplètes de la maladie de Kawasaki afin d'éviter des conséquences néfastes, telles que l'anévrisme d'une artère coronaire.

Kawasaki disease (KD) is a childhood vasculitis affecting the medium-sized muscular arteries, mainly the coronary arteries. It was first described in 1967 by the Japanese physician Dr Kawasaki as a mucocutaneous lymph node syndrome.[1] The hallmark of KD is fever lasting 5 days or more, counting the day of fever onset as day 1, in addition to 4 or 5 of the principal clinical criteria (**Box 1**): cracking of lips or strawberry tongue, nonpurulent conjunctivitis, rash, erythema and edema of the hands and feet, and large unilateral cervical lymphadenopathy.

Beyond syndrome recognition based on a combination of the clinical features, the diagnosis might be supported by positive laboratory or echocardiographic findings. While there are no specific diagnostic tests for KD, elevated erythrocyte sedimentation rate or C-reactive protein level, leukocytosis, and anemia are common. Thrombocytosis is frequently present, albeit usually in the second week of illness. Elevated serum transaminase, γ-glutamyl transpeptidase, bilirubin, and hypoalbuminemia levels, as well as sterile pyuria, are frequently described in the literature.

The pathogenesis of KD is unknown and is likely to be multifactorial, with epidemiologic information suggesting 1 or more infectious agents triggering KD in a genetically predisposed host. It is recognized that children of parents who have had KD have twice the risk of developing the disorder, and that having affected siblings increases the risk to 10-fold.[2,3]

Kawasaki disease presentation is very similar to other infections, particularly viral infections, which complicates the differential diagnosis. Furthermore, there are seasonal peaks in the winter and spring, and frequent descriptions of concurrent infections[4-6]—all pointing to a likely infectious element of KD.

Other than infections, the differential diagnosis of KD is broad and includes toxin-mediated syndromes (staphylococcal scalded skin syndrome and toxic shock

Box 1. Criteria for the diagnosis of KD

Classic KD is diagnosed in the presence of fever for at least 5 days together with at least 4 of the 5 following principal clinical features.

- Erythema and cracking of lips, strawberry tongue, or erythema of oral and pharyngeal mucosa
- Bilateral bulbar conjunctival injection without exudate
- Rash: maculopapular, diffuse erythroderma, or erythema multiforme–like
- Erythema and edema of the hands and feet in the acute phase
- Cervical lymphadenopathy (≥ 1.5 cm in diameter), usually unilateral

KD—Kawasaki disease.

syndrome); hypersensitivity reactions such as Stevens-Johnson syndrome, drug reactions, or acrodynia (pain and pink discoloration in the hands and feet most often seen in children chronically exposed to heavy metals, specifically mercury); and systemic-onset juvenile idiopathic arthritis.

Incomplete KD

In many cases, children will present to the physician's office with fewer than 5 days of fever, or with fewer than 4 or 5 criteria but several findings compatible with KD. To avoid complications of KD (eg, coronary artery aneurysms)[7-11] and to ensure early referral for treatment, the possibility of incomplete KD should be considered in these patients. Further laboratory or echocardiographic evaluation is warranted to determine the likelihood of incomplete KD and whether treatment is necessary. While in the past children with criteria below the threshold number were considered to have "atypical" KD, the American Heart Association and the American Academy of Pediatrics have recommended that the term *incomplete KD* be used, as these patients lack sufficient clinical signs to fulfil the classic criteria but do not demonstrate atypical features.[12]

It is estimated that 10% to 20% of children diagnosed with KD do not fulfil criteria for KD.[13,14] Children with incomplete KD can present at any age[15,16] but are more likely to be infants, who are at high risk of developing coronary artery aneurysms.[17-20]

Family physicians should consider the diagnosis of incomplete KD in any infant or child with prolonged unexplained fever, even if only a few principal features of KD are present.

Timely treatment

One of the prominent complications of KD is coronary artery aneurysms, documented in up to 25% of untreated patients.[21] Timely treatment with intravenous immunoglobulin (IVIG) has been shown in clinical trials to reduce the risk of coronary artery aneurysms from 25% to 4%.[22,23]

Some children are at high risk of IVIG resistance,[24] mostly those with young age (< 12 months), low albumin levels, thrombocytopenia, fever of less than 4 days, low sodium levels, or elevated transaminase levels.[25-27]

Acetylsalicylic acid is used in conjunction with IVIG, despite lack of clear evidence of any effect in prevention of coronary artery abnormalities.[28] A moderate (30-50 mg/kg/d) to high dose (80-100 mg/kg/d) is provided until fever subsides, and a low dose (3-5 mg/kg/d) is prescribed for 6 to 8 weeks afterward (around the time the follow-up echocardiogram is performed).

The role of corticosteroids in the treatment of KD is a source of controversy and should be determined with a pediatrician experienced in the management of children with KD.[15]

Recovery

Most children with KD or incomplete KD will recover without any long-term sequelae, but up to 5% might have life-altering coronary artery aneurysms despite standard therapy. This has implications for long-term cardiac morbidity and requires anticoagulation therapy.[22,23,29] Early referral to an emergency department, a pediatrician, or a rheumatologist is imperative for accurate diagnosis and judicious therapy.

Conclusion

The diagnosis of KD should be considered in any child with prolonged unexplained fever and any of the 5 principal clinical findings associated with the condition. However, early recognition and consideration of incomplete KD is essential for timely laboratory and echocardiographic evaluation and treatment of these patients who are at risk of delayed diagnosis and have higher rates of coronary artery aneurysms.

Competing interests
None declared

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