

KAWASAKI DISEASE IN INFANCY AND CHILDHOOD

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Diagnosis

The diagnosis can be made where there is fever plus at least four of the five features listed under early manifestations. One of the most serious complications is the delayed development of coronary artery aneurysms, which will develop in at least 20% of untreated patients. Risk factors for the development of coronary aneurysms include male sex, age less than 12 months and older than 5 years, fever lasting more than 10 days, low serum albumin and/or Haemoglobin, and clinical signs of cardiac involvement (arrhythmias, pericardial effusion)

Febrile infants less than a year old may present with less <4 characteristic features. The diagnosis of atypical Kawasaki disease can be made in this situation if coronary artery disease is present.

Early Clinical Manifestations

A multisystem illness with fever and rash, which occurs mainly in children less than 5 years old. Within 3 days of the abrupt onset of fever, the other characteristic features usually appear:

- Bulbar conjunctivitis (no exudate)
- Mucositis: red cracked lips, red mouth and throat, strawberry tongue
- Polymorphous generalized rash that can be morbilliform, maculopapular, scarlatiniform or may resemble erythema multiforme
- Induration of the hands and feet with red palms and soles
- Cervical lymphadenopathy (usually a solitary, unilateral node > 1.5 cm in size)

Other Findings

Extreme irritability, severe abdominal pain, diarrhoea and vomiting are common. Other features may include:

- Urethritis with sterile pyuria (70% of cases)
- Hepatic dysfunction (40% of cases)
- Arthritis or arthralgias (35%)
- Aseptic meningitis (25%)
- Pericardial effusion or arrhythmias (20%)
- Gallbladder hydrops (<10%)
- Carditis with congestive heart failure (< 5%). This can occur at any time in the first 3 weeks, and usually resolves by 6 to 8 weeks.
- Other arterial aneurysms (e.g. iliac, femoral, renal, axillary) may occur

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Late Manifestations

- The lips usually begin to dry, crack and fissure by day 6 of the illness
- The skin of the fingertips, palms ± soles begins to peel in weeks two and three
- With no treatment, the average length of fever is 12 days, and when the fever resolves the child may remain irritable for a further 2 to 3 weeks.

Coronary Aneurysms

Coronary aneurysms usually appear 2 to 4 weeks into the illness, but can be found as early as 3 days. Appearance later than 6 weeks is uncommon. In some children with mild coronary dilatation, the coronary artery size may return to baseline within 8 weeks of the onset of disease. In others, the arteries frequently return to normal size over 1 to 2 years. However, the lumen of the vessel may remain abnormal, or there may be coronary stenosis.

75% of fatalities occur within six weeks of the onset of symptoms, but myocardial infarction and sudden death can occur months to years after the acute episode.

Differential Diagnosis

Viral infections e.g. measles, adenovirus, enterovirus
Scarlet fever
Staphylococcal scalded skin syndrome
Toxic shock syndrome
Polyarteritis nodosa
Bacterial cervical lymphadenitis
Drug hypersensitivity reactions
Stevens-Johnson syndrome
Leptospirosis
Mercury hypersensitivity

Recurrence

Second episodes are rare in previously affected children.

Epidemiology

The peak age of occurrence in the United States is 18 to 24 months, with 80% of affected children being less than 5 years old. Children older than 8 years rarely have Kawasaki's disease. The incidence is higher in the Asian community. There can be clinical overlap with polyarteritis nodosa and toxic shock syndrome.

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Investigations

The ESR and CRP are usually raised during the first two weeks of the illness. Thrombocytosis (platelet count > 450) after day 10 of the illness is also common. ECG and CXR are the initial cardiological investigations.

Inpatient pediatric cardiology review and echocardiogram are indicated if:

- there are ECG changes suggestive of myocardial ischaemia
- there is a murmur of mitral regurgitation
- there are signs of congestive heart failure
- the diagnosis is unclear
- there is persistent fever after IV immunoglobulin
- the child presents beyond 10 days of illness

Adequate visualization of the coronary arteries is difficult in young, irritable children. The timing and site of the echocardiogram, and the need for sedation, should be discussed with the Paediatric Cardiologist on a case-by-case basis.

There is no indication for early echocardiography in those who present early (< 10days) have no ischaemia on their ECG, and respond to IVIG. This is supported by NZPSU surveillance data and report (the AHA recommend echo for all at presentation but this remains unproven).

Treatment

Specific therapy must be given early to be most effective, so it should be given when the diagnosis is strongly suspected.

- Intravenous immunoglobulin. If given with aspirin **within 10 days** of the onset of fever, IVIG relieves symptoms and reduces the risk of coronary aneurysm. There is some evidence that IVIG is less effective by day 8-10 compared to the day 1-7. The dose is **2 grams per kg, over 10 to 12 hours** - Evidence level A. In about 10% of children, the fever may not respond to the first dose of IVIG within 48 to 72 hours, or may recur. In this situation, a second dose of IVIG may be given. Be aware of the possibility of isoimmune haemolysis with IntragamP, particularly in blood group A patients
- IVIG should be given later than 10 days, if there are signs of continuing inflammation (fever, high ESR) or evolving coronary artery disease
- Aspirin. Give at a dose of 30-50 mg/kg in the first week of the illness. There is no evidence that the dose of salicylate effects aneurysm formation. Level A evidence. Reduce the dose to 3 to 5 mg/kg/day once the fever is under control. If the coronary arteries are normal at 6 weeks, stop the aspirin. If there are coronary artery aneurysms, continue low-dose aspirin (see below) with or without warfarin or other antiplatelet medication. *Aspirin is available in 300mg soluble tablets and 650mg enteric-coated tablets. Use soluble tablets dissolved in water to administer part doses, and consider enteric coated tablets for older children.*

Note: several children with Kawasaki disease have developed Reye syndrome while on high dose Aspirin. It is important therefore to change to low dose Aspirin as soon as possible, and to warn the parents to discontinue Aspirin if the child develops influenza or chickenpox.

Children should remain in hospital until afebrile for 24 hours

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Subsequent Immunisation

Children who have had IVIG should not have measles vaccine for 12 months. Alternatively, a child at high risk of measles could be vaccinated, then re-vaccinated a year later. Varicella vaccine should be delayed at least 5 months.

Follow-up

48 hours after discharge

Paediatric review to exclude ongoing fever

4 - 6 weeks after presentation

Starship cardiology outpatient clinic/day stay for clinical review, ECG, echocardiogram

Further Follow-up

Dependent on risk stratification:

No coronary changes. No follow-up required. Low dose aspirin can be discontinued

Mild coronary artery ectasia. Low dose ASA. Repeat echocardiogram at one year. Stop ASA if no change or improving at this time. Consider exercise stress echocardiography after 10 years of age

Small-to-medium single coronary artery aneurysm. Continue low dose ASA. Annual review with ECG ± echocardiogram. Consider angiography. Consider stress echocardiography after 10 years of age. Advise against highly competitive sporting activities.

Multiple small aneurysms or one or more giant aneurysms. Low dose ASA ± warfarin. Annual review with ECG and echocardiogram. Consider dobutamine stress testing < 10 years of age. Exercise stress echocardiography after 10 years of age. Advise against competitive sporting activities.

Coronary artery obstruction. Low dose ASA ± warfarin. Holter monitor. Consider angiography. Consider repeating angiography ± thrombolysis if new ischaemic symptoms or ECG changes develop. Annual review with stress echocardiography. Advise against competitive sporting activities. Consider Beta blockers

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References

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