

KAWASAKI DISEASE: WHAT TO DO WITH INCOMPLETE CASES?

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The original criteria for the diagnosis of Kawasaki disease were drawn up by a committee appointed by the Japanese Ministry of Health. These were created primarily for the purposes of epidemiological surveillance, and to help exclude patients with rheumatic fever and Stevens-Johnson syndrome.¹ Cardiac ultrasound has subsequently provided a readily available, non-invasive method for detecting coronary artery abnormalities. Together with the lack of any “gold standard” specific diagnostic test for Kawasaki disease, this has led to the recognition that children presenting with incomplete clinical manifestations are also at risk of developing coronary artery abnormalities. This has been demonstrated in a number of publications, including a retrospective review in both children meeting the diagnostic criteria of Kawasaki disease, and those with incomplete criteria but treated with intravenous immunoglobulin (IVIG).² In this study cervical lymph node changes were the least commonly seen diagnostic feature, followed by the extremity changes.

Those seeking guidance on the diagnosis and management of Kawasaki disease can do no better than to refer to two recent reviews.^{3–4} Both cover diagnosis and management. Maconochie⁴ particularly focuses on the differential diagnosis, diagnostic criteria, recommended investigations, and clinical assessment that are needed when Kawasaki disease is suspected. The Kawasaki Disease Research Group guidance in 2002 also covered treatment including those failing to respond to initial IVIG and aspirin treatment.

The management of those children who do not satisfy the diagnostic criteria is not supported by strong evidence. None of the randomised controlled trials of IVIG provide information on the efficacy of treatment in these children.⁵ Both recent UK guidelines recommend that children under the age of 1 year with incomplete features should be treated with IVIG, though the criteria required for such treatment were not specified. Neither gives criteria for treating older children with incomplete features. Both stress seeking expert advice, and the 2002 guideline includes a contact telephone number for general paediatricians within the London area (this number is no longer functioning).

In the absence of strong evidence, any guidance on the management of incomplete cases is arbitrary and potentially contentious. In 2004 the American Academy of Pediatrics (AAP) and the American Heart Association published an “endorsed clinical report” providing guidance for paediatricians on the diagnosis and management of Kawasaki disease.⁶ This included an algorithm suggesting an approach to suspected incomplete Kawasaki disease. This forms the basis of the algorithm presented in fig 1.

KEY PRACTICE RECOMMENDATIONS

- ▶ Kawasaki disease should be considered in the differential diagnosis of every child with fever of at least several days' duration accompanied by rash and non-purulent conjunctivitis, especially in children < 1 year old and in adolescents, in whom the diagnosis is frequently missed.
- ▶ Diagnostic pitfalls include mistaking:
 - rash and mucosal changes for an antibiotic reaction
 - sterile pyuria for partially treated urinary tract infection
 - cerebrospinal fluid (CSF) pleocytosis for viral meningitis.
- ▶ The diagnosis is guided by:
 - the number of positive clinical criteria
 - the age of the child (those under 6 months with persistent fever for seven days and evidence of inflammation needing an echocardiogram even in the absence of positive clinical criteria)
 - the absence of clinical features suggesting another diagnosis, and
 - the laboratory C reactive protein (CRP) and erythrocyte sedimentation rate (ESR) results.
- ▶ In those with raised CRP (30 mg/l or above) and/or ESR (40 mm/h or above) the results of a number of other supplementary investigations (full blood count, plasma albumin, alanine aminotransferase, urinary white cell count, and echocardiogram) contribute to the decision as to whether to treat with IVIG.
- ▶ There is an option to wait and watch the febrile child with less elevated CRP or ESR, as well as some children with negative echocardiogram. Those with persisting fever are clinically re-evaluated (with repeat CRP and ESR) after a further two days.

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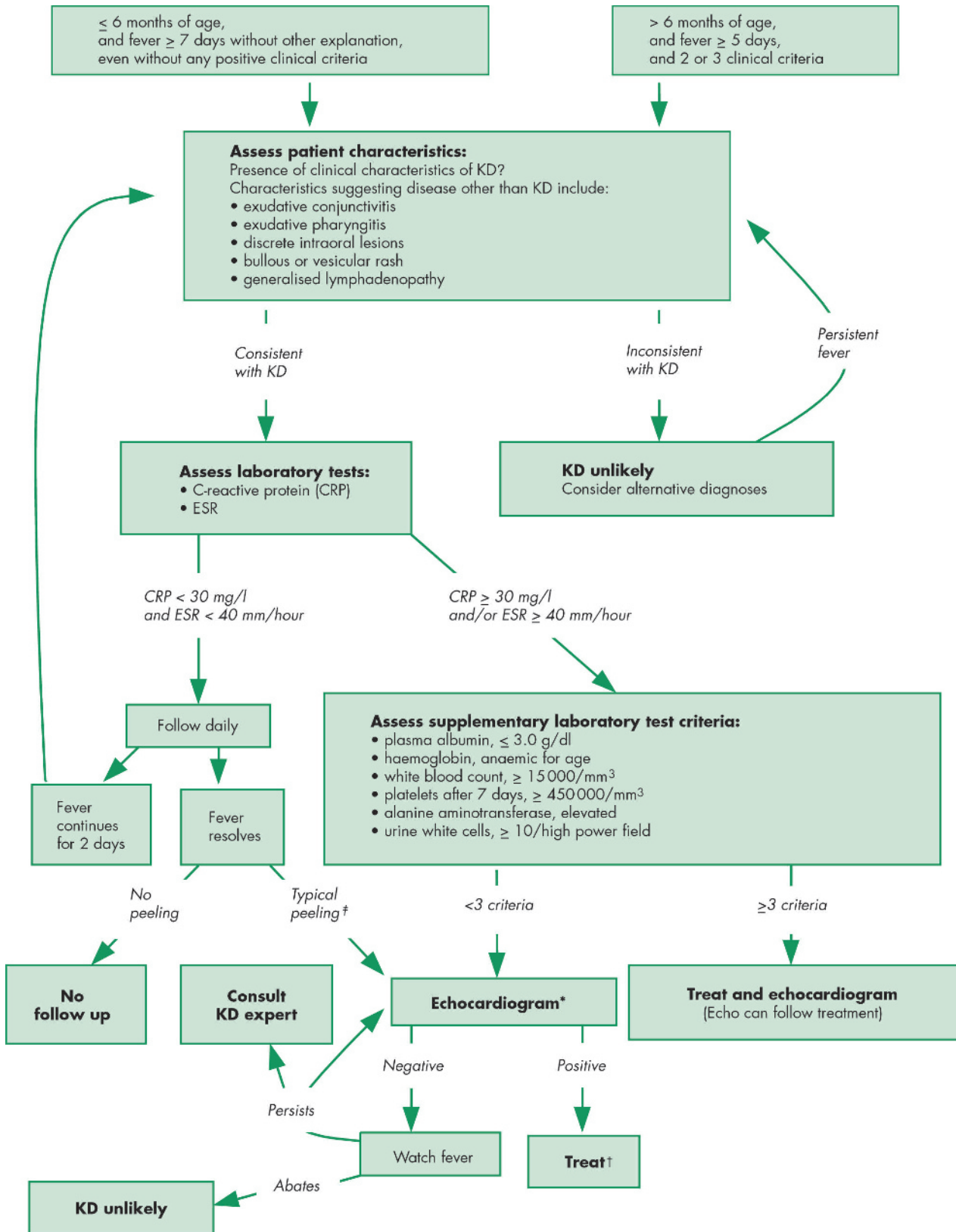


Figure 1 Investigation and management of children presenting with incomplete criteria. *Positive if any of three conditions are met: (1) z score of left anterior descending coronary artery (LAD) or right coronary artery (RCA) 2.5 or more; (2) coronary arteries meet Japanese Ministry of Health criteria for aneurysms; (3) three or more other suggestive features exist, including perivascular brightness, lack of tapering, decreased left ventricular function, mitral regurgitation, pericardial effusion, or z scores in LAD or RCA of 2–2.5. †If echocardiogram is positive, treatment should be given to children within 10 days of fever onset and those beyond day 10 with clinical and laboratory signs (CRP, ESR) of ongoing inflammation. ‡Typical peeling begins under the nail bed of fingers then toes. Adapted from Newburger *et al.*⁶

Table 1 Recommended investigations and clinical assessment to exclude Kawasaki disease

- ▶ Full blood count and film
- ▶ Erythrocyte sedimentation rate and C reactive protein
- ▶ Blood culture
- ▶ Antistreptolysin O titre and antiDNAse B
- ▶ Nasal and throat swab bacterial and viral culture
- ▶ Stool culture
- ▶ Urea and electrolytes
- ▶ Liver function tests
- ▶ Clotting screen
- ▶ Autoantibody screen
- ▶ Viral titres for enterovirus, adenovirus, parvovirus, Epstein Barr virus, cytomegalovirus
- ▶ *Mycoplasma pneumoniae* titres
- ▶ Urine microscopy—dipsticking for proteinuria and haematuria
- ▶ ECG/echocardiography/chest x ray

ECG, electrocardiogram.

- ▶ Echocardiogram criteria for treatment are included.
- ▶ Children with illness of more than 10 days' duration and changes on echocardiogram are treated with IVIG if they have persisting clinical and laboratory signs of inflammation.
- ▶ Advice from an expert should be considered at any point in the process.

COMMENTARY

The AAP guideline does not document full details of the methodology used to reach its recommendations. In particular, the underpinning literature search and the methods used to reach a consensus are not documented. In view of this, other approaches to decision making may be equally or even more appropriate, and the guidance reproduced here should not be seen as necessarily defining current best practice. Nonetheless, the authors' attempt to assist clinicians

in this specific aspect of diagnosis is hopefully of value to paediatricians.

Other causes should be actively sought in all children presenting with incomplete clinical manifestations. The recommended investigations³ are reproduced for ease of reference (table 1). Some of these tests also contribute to the AAP algorithm for suspected Kawasaki disease.

It is emphasised that the full AAP article⁶ should be read. The guidance also covers other aspects of Kawasaki disease, giving particularly detailed guidance to cardiologists on the investigation for and treatment of coronary artery abnormalities (including reference ranges for coronary artery sizes by body surface area), as well as long term follow up and prognosis. This article should not be seen as a substitute for obtaining specialist advice when there remains diagnostic uncertainty, but may help to ensure that all relevant clinical details and test results are available when seeking help.

In summary, the AAP guidance provides one approach to the investigation and management of children presenting with incomplete Kawasaki disease.

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CORRECTION

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In the footnote to table 3, the formula for urinary fractional excretion of magnesium is incorrect. It should read: Urinary fractional excretion of magnesium = $([Ur\ Mg]/[Pl\ Mg]) \times [Pl\ Cr]/[Ur\ Cr] \times 100\%$ and all units should be in mmol/l.