

Final Report of Completed Studies

Kawasaki disease

Background

There is no diagnostic test for Kawasaki disease. There is considerable variation in the sequence and type of presenting clinical features making rapid diagnosis difficult. Early treatment with intravenous gammaglobulin (IVGG) is known to significantly reduce the risk of cardiac sequelae. The aim is therefore to make an earlier diagnosis of Kawasaki disease and give prompt IVGG.

Kawasaki disease was monitored between May 1993 and June 1995. Information collected during this period of surveillance has enabled us to describe the clinical profile of Kawasaki disease in Australia, detailing the epidemiology, management and rate of cardiac sequelae.

Objectives

- To determine the incidence of Kawasaki disease
- To examine its management and short and long term morbidity and mortality

Case definition

Any child or adolescent up to 16 years of age with fever for five or more days and any four of the following, or any of the following plus coronary artery aneurysm:

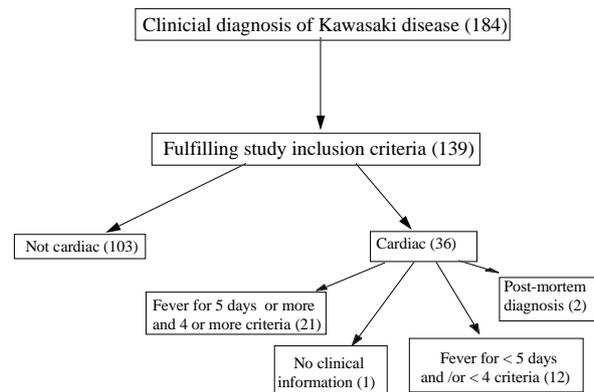
- bilateral conjunctival injection
- oral mucosal changes, such as injected pharynx, dry cracked lips, strawberry tongue
- changes of the peripheries, such as hand or foot oedema or erythema or desquamation (which may be in the napkin area and occur some time after presentation)
- rash
- cervical lymphadenopathy greater than 1.5 cm diameter

Note: measles and streptococcal infection should have been excluded

Results and discussion

Three hundred and sixty-nine cases of Kawasaki disease were notified during the 26 month surveillance period. Of these, 272 questionnaires were completed and returned (74% response rate). 65 notifications were duplicates and a further 23 were reporting errors, resulting in 184 cases thought by clinicians to have Kawasaki disease. Forty-five of these did not satisfy study inclusion criteria because they had fever for less than five days and/or less than four of the five clinical criteria (39) or they had documented streptococcal infection (6), resulting in 139 confirmed cases (Figure 10). Twelve cases with cardiac sequelae did not fulfil the other clinical diagnostic criteria.

Figure 10 Outcome of Kawasaki cases notified



The incidence of Kawasaki disease in Australia in 1994 was 3.7/100,000 children under the age of five years, which is similar to the incidence reported in the British Isles. Of the 139 confirmed cases, 16 were not admitted to hospital. The male to female ratio was 1.8:1. The median age at diagnosis was 2.8, with ages ranging from five weeks to 14.6 years. 75% of patients were aged less than five years and 20% were under one year. 72% of cases were European with a substantial minority reported to be Asian 14%. The geographic distribution of cases was widespread with no State over-represented in the number of Kawasaki disease notifications.

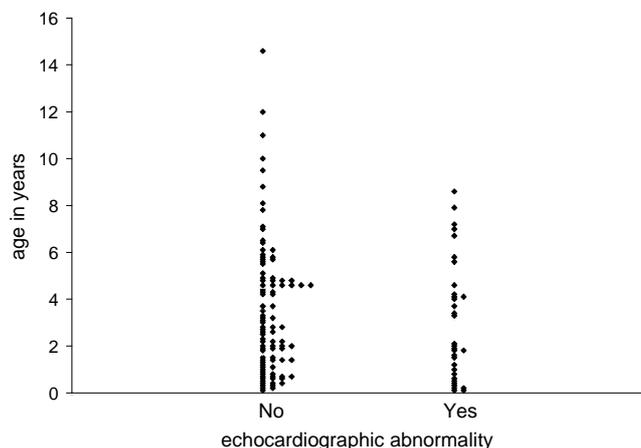
The median time to diagnosis from the onset of the first symptom was eight days. 66% of cases were diagnosed within the first ten days. Cervical lymphadenopathy was reported in only 43% of cases, while the other four clinical criteria were all reported in over 89%. Of note no particular type of rash was specific for the diagnosis. Rashes reported were mainly maculopapular/morbilliform (28%) or macular (25%) but a proportion were described as urticarial, pruritic and scarlatiniform. Many rashes were florid and confluent, others were pale, discrete and transient. Other associated symptoms were reported; respiratory symptoms, mainly cough, (40%), diarrhoea (24%), vomiting (4%) and arthralgia or arthritis (12%).

The median maximum ESR was 85, platelet count 577×10^9 /liter and WCC 16.5×10^9 /litre. Abnormal liver function tests were reported in nine cases, with clinical jaundice in two of these cases. Although abdominal ultrasound was not performed in all cases, hydrops of the gall bladder was reported in 23 children.

Cases received IVGG, high dose aspirin and low dose aspirin, in varying combinations. In total, 79% of cases received IVGG, 53% received high dose aspirin and 75% received low dose aspirin. Of the children receiving

IVGG, most cases were given a 2 gram/kg dose, the remainder received smaller doses with single or multiple treatments. Five patients were given high dose aspirin and no IVGG.

Figure 11 Age of children with and without cardiac abnormalities



Coronary sequelae were reported in 36 of the confirmed cases. Two died and the diagnosis was made at autopsy. Of the 34 patients with echocardiography abnormalities, 14 had aneurysms, 16 coronary dilatation, one had coronary ectasia and three had both dilatation and ectasia reported. Although cases with coronary artery sequelae tended to be younger, a proportion of cases over five years suffered cardiac complications (Figure 11). Time to diagnosis differed for cardiac (median 9.5) and non-cardiac groups (median 7.0), though not significantly. Other echocardiographic abnormalities were reported in an additional ten cases who satisfied other diagnostic criteria; pericardial effusion (4) and borderline coronary artery abnormalities such as “prominent”, “echogenic” or “possible abnormalities” of the coronary arteries (6). The proportion of all cases that fulfilled study inclusion criteria with documented coronary artery abnormalities was 25%.

Six cases satisfying the clinical diagnostic criteria were excluded because streptococcal infection was documented. One of these had coronary artery dilatation. Four received IVGG and three were treated within ten days of symptom onset. A further 39 cases were excluded because they had insufficient clinical criteria. Four of these were also documented to have streptococcal infection and eight cases which did not satisfy clinical criteria were reported to have cardiac abnormalities other than those sufficient for study inclusion: pericardial effusion (3), an aortic aneurysm (1), myocarditis with

effusion (1), “query coronary artery dilatation” (1), and “prominent coronary artery” (2). Five of the 39 cases not satisfying clinical criteria received IVGG within five days of symptom onset.

This study includes a large proportion of patients with cardiac complications who do not fit the clinical diagnostic criteria. The notification and treatment of cases not satisfying the study criteria indicates clinicians are concerned about potential cardiac sequelae in atypical cases. Unfortunately, at the time of this study, not all cases satisfying the diagnostic criteria were receiving 2g/kg of IVGG within ten days of symptom onset.

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