

Kawasaki Disease: An Incomplete Presentation

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Citation

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Abstract

A 15 week old female infant presented with unresolving pyrexia. No focus of infection was found. She had conjunctivitis, oral mucosal changes and a skin rash. Investigations showed the presence of hydropic gall bladder and coronary artery aneurysms. She responded to treatment with gammaglobulins and aspirin.

Kawasaki disease is a multi-system disorder with predominant effects on the heart. It carries high mortality with late diagnosis. When all the classic diagnostic criteria are not met, a high index of suspicion should lead to further investigations towards making a diagnosis of Kawasaki disease. It also has significant pathological effects on other organ systems.

CASE REPORT

A 15-wk old Caucasian female infant was admitted with a 2-day history of febrile illness with dry cough and rash. She had a self-limiting episode of diarrhoea and vomiting 4 days prior to this. She was born at term. She had no major preceding illnesses. On examination she was pyrexial (38 deg C), tachypnoeic with intercostal recession, tachycardic, irritable with a florid macular blanching rash. Oral thrush, a swollen tongue and non-exudative conjunctivitis were evident. There were no palpable lymph nodes. Investigations showed a negative urine dipstick for infection. CSF analysis showed a white cell count of 21×10^6 (predominantly lymphocytes), $RBC < 1$, normal protein and glucose. Gram stain was negative. She was commenced on empirical intravenous cephalosporins. Urine culture was negative and chest radiograph was normal. Blood culture grew *Staphylococcus aureus* sensitive to flucloxacillin, which was commenced intravenously. Throat swab was negative.

However, she continued to be pyrexial. CRP, which was initially elevated improved with antibiotics but the child, remained unwell clinically. Further investigations were initiated for a focus of sepsis. A subsequent CXR remained unremarkable. An Ultrasound of the abdomen done in pursuit of an infective collection showed a grossly distended gallbladder with echogenicity. The cystic duct was distended, but the common biliary duct and hepatic duct were normal. Other viscera were normal. CT head ruled out an infective/ inflammatory process of the brain.

A cardiology referral was sought due to continuing pyrexia,

rash, conjunctivitis, hydrops of gallbladder and thrombocytosis (tab.1). Echocardiogram showed the presence of aneurysmal dilatation of right coronary artery with good ventricular function. Hence a diagnosis of Kawasaki's disease was made.

She was then started on 2 g/kg of intravenous gammaglobulin and aspirin 5mg/kg. A dramatic improvement in the clinical condition was noted and the pyrexia settled. A subsequent echocardiogram showed aneurysmal dilations of right coronary artery measuring 6.5 mm. Hence aspirin was increased to 30mg/kg and heparin was commenced. She was subsequently warfarinised. In view of her age, low molecular weight heparin was substituted for warfarin later. She was discharged home with a plan to continue regular aspirin and low molecular weight heparin for a year with regular Factor Xa assays and regular cardiology follow up.

Figure 1

Table 1

Day of illness	D7	D11	D13	D14	D16	D24	D30
WCC	35.4	14.8	15.2	14.1	12.8	11.4	15.4
Platelets	841	1299	1196	1092	966	646	458
Neutrophils	22.1	5.4	4.9			3.8	4.7
CRP	200	35.8	36.4	29.2	20.3	15.9	

Figure 2

Figure 1 shows transthoracic echocardiogram during the first week of illness. This demonstrates the parasternal short axis view of the aorta with aneurysmal dilation of right coronary artery (RCA) measuring 4.9 – 6.2 mm.

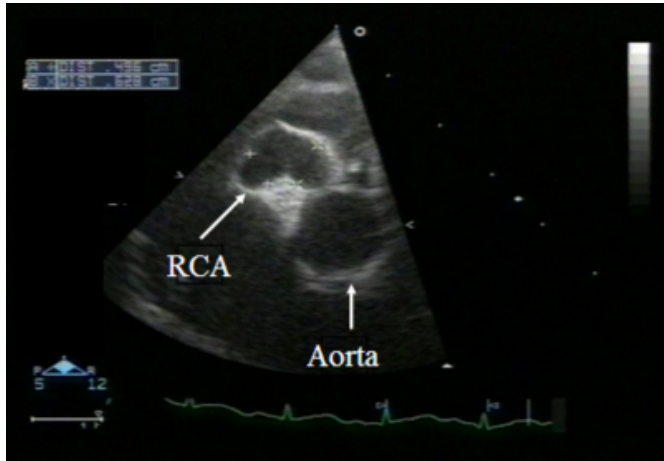


Figure 3

Figure 2 demonstrates the dilated right and left coronary arteries along the atrioventricular groove on the apical five chamber view on transthoracic echocardiogram. (RCA Right Coronary artery; LCA Left Coronary Artery)

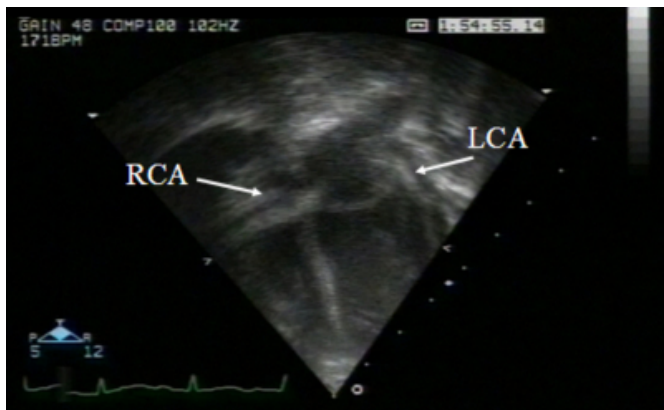


Figure 4

Figure 3 demonstrates dilation of RCA and an aneurysm at the mid portion of RCA on non-selective aortic angiography.

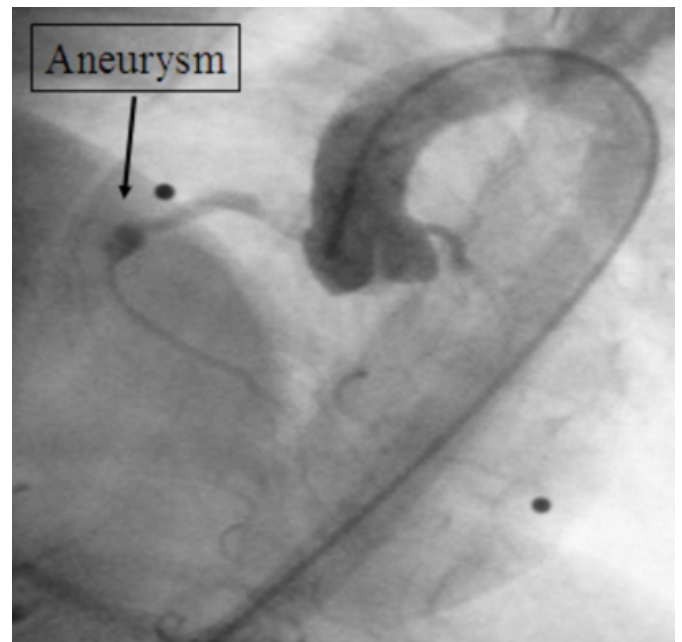
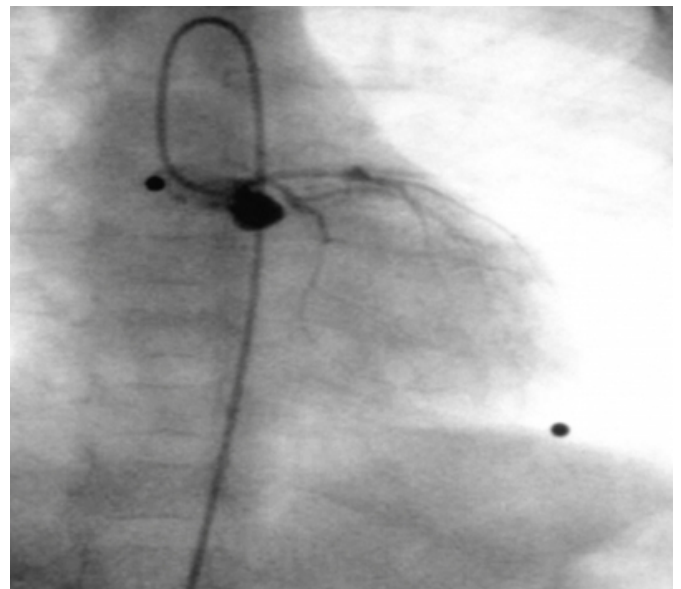


Figure 5

Figure 4 demonstrates multiple aneurysms on the Left Anterior Descending and Left Circumflex artery of the left coronary system on non-selective aortic angiography.



DISCUSSION

Kawasaki Disease is the most common cause of acquired heart disease in children in the developed world. It is most common in Japan followed by USA, UK and Australia. Japanese immigrants to various countries retain their high incidence rates suggesting a genetic predisposition. It seems

to be a rare diagnosis in developing countries or at least under reported.

KD is an acute febrile vasculitis that usually affects children under 5 yrs with the incidence peaking between 9 and 11 months of age. Our patient had a rather early presentation at 15 weeks of age. A superantigen toxin with an activity similar to streptococcal and staphylococcal superantigen toxins has been implicated^{1,2,3}. Kawasaki disease still remains a diagnosis of exclusion as it mimics sepsis.

- Fever of $> 38.5^{\circ}\text{C}$ for at least 5 days plus 4 of the following features
- Bilateral conjunctival injection
- Diffuse and polymorphous rash – usually lasts upto a week.
- Oral changes – erythema/fissuring of lips, strawberry tongue, congested oropharynx.
- Painful cervical lymphadenopathy > 1.5 cm in diameter
- Changes in peripheral extremities – erythema/swelling of hands and feet in the first week, desquamation usually occurs in the 2nd – 3rd weeks into the illness.

Our patient had pyrexia with conjunctivitis, rash and oral changes and only incompletely met the diagnostic criteria. Irritability is almost always a feature which our patient had. The diagnosis of Kawasaki disease in incomplete cases is made by the presence of coronary artery aneurysms on echocardiography⁴. The initial echo on this child demonstrated coronary aneurysmal dilatation, which clinched the diagnosis.

The other clinical sign, which may be important to recognise in populations/individuals who have had BCG vaccination, is the erythema and induration at the BCG immunisation site. This is believed to be due to cross reactivity between the heat shock proteins and the T cells of patients with Kawasaki disease^{5,6}.

Common differential diagnoses are Scarlet fever, Toxic shock syndrome, Exanthem fevers, Mycoplasma infection, Stevens-Johnson syndrome and Infectious mononucleosis.

Laboratory investigations may show neutrophilia initially and by the end of the first week changing to lymphocytosis.

Thrombocytosis is usually a feature in the 2nd or 3rd week of presentation. This child had a thrombocytosis noticed a week after her initial presentation.

The initial treatment of Kawasaki disease is with Intravenous Gammaglobulin 2 g/kg as a single infusion over 12 hrs followed by Aspirin 30-50 mg/kg/day in 4 divided doses until afebrile for 2-3 days. Aspirin is continued for 6-8 weeks as anti-platelet therapy at a dose of 3-5 mg/kg/day once daily. If the 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 inflammation⁸. Persistence or re-occurrence of fever is managed with further doses of gammaglobulin, methylprednisolone or cytotoxic drugs. Plasmapheresis and use of monoclonal antibodies to TNF α have also been reported⁷.

The most common and life threatening complication of Kawasaki disease is the development of coronary arterial aneurysms. Coronary arterial aneurysms usually develop within 6-8 weeks from the onset of illness. The other cardiac complications include myocarditis, pericarditis, congestive heart failure, pericardial effusion, valvular insufficiency and arrhythmias.

Mortality rates have been reported to be 0.08% in Japan and 3.7% in the UK⁴. About 50% of aneurysms regress within 5 yrs. Mild dilatation (3-4mm) regresses within 2 years and 80% of aneurysms with moderate dilatation (4-8mm) regress within 5 years. Giant aneurysms ($>8\text{mm}$) are unlikely to resolve and may progress to stenosis or complete obstruction within a few years of the initial diagnosis⁷. The largest aneurysm in this child had a diameter of 6mm on echocardiography. Myocardial infarction is a well known complication occurring in 73% of children within the first year after diagnosis. The mortality rate is 22% from the first episode. Of the 16% who had a second myocardial infarction, mortality rate increases to 62%⁷. Diarrhoea, vomiting, abdominal pain and hydrops of the gall bladder may occur. Liver enlargement with dysfunction is known to occur in about 15% of patients⁷. Gastrointestinal symptoms were the initial presenting features in this child.

Hydrops of the gall bladder was demonstrable on abdominal ultrasound in this child.

Neurological complications can be seen in upto 30% of cases in the form of irritability, aseptic meningitis, cerebral infarction, seizures and encephalopathy. Facial palsy has

been reported, though transient. There have been reports that Kawasaki disease can also affect the renal, pulmonary, musculo-skeletal and haematological systems.

Follow up depends upon stratification of patients according to their relative risk of myocardial ischemia. This stratification allows individualisation of patient management to reduce the risk of thrombosis, frequency of clinical follow-up and diagnostic testing, and indications for cardiac catheterization and coronary angiography.⁸

In summary, a high index of suspicion is needed in cases of unresolving pyrexia in babies and children. Diagnosis of Kawasaki disease should be suspected and actively sought for in this group who do not show all the classic signs by performing a baseline echocardiogram to look for coronary artery aneurysms.

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