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CASE REPORT

Giant coronary artery aneurysms in a 12-week-old infant with incomplete Kawasaki disease

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SUMMARY

Kawasaki disease (KD) is an acute inflammatory vasculitis that occurs worldwide and disproportionately affects male children, most commonly between the ages of 6 months and 5 years. KD can present with only a few features and thus be difficult to diagnose, particularly in the youngest and oldest patients. We describe a 12-week-old Caucasian female infant who presented with rash and fever but no other features of KD, who developed giant coronary artery aneurysms. Considering how common is the presentation of a febrile infant with a rash, this case highlights the importance of considering KD early in the differential diagnosis for any infant with unexplained fever. Furthermore, it emphasises how echocardiography can help in the investigation of a febrile child with no clear source of infection.

BACKGROUND

Kawasaki disease (KD) is an acute inflammatory vasculitis that preferentially affects medium-sized arteries, particularly the coronary arteries.¹ It is the leading cause of acquired cardiac disease in children in developed countries.² It is more common in boys than girls, and in those of Asian ethnicity.³ The aetiology is unclear, but epidemiological features such as the development of clusters of disease has led to the suggestion that an infectious or agent or toxin may be implicated.⁴ Most cases occur in children between 6 months and 5 years of age, but younger infants can also be affected.⁵ Although most patients recover fully, a proportion develops coronary artery aneurysms, which can result in severe acute and long-term sequelae. Aneurysms are more common in those patients in whom treatment is delayed or missed. Extremes of age have been identified as risk factors for coronary artery aneurysm development.⁶

Coronary artery aneurysms develop in up to 25% of untreated cases of KD with 2% to 3% of untreated cases dying due to coronary vasculitis.¹ Coronary artery dimensions are assessed in the UK by calculation of Z-score.^{7,8} A minority of patients develop giant coronary artery aneurysms; a recent study found an incidence of 2.6% in a cohort of American children with KD where giant aneurysm was defined as a maximum Z-score ≥ 10 . Giant coronary artery aneurysms are associated with 29% to 48% risk of adverse coronary artery events, including thrombosis, stenosis, myocardial infarction and death.⁹

The key features of Kawasaki disease are¹:

- ▶ fever: duration of 5 days or more, plus
- ▶ conjunctivitis: bilateral, non-suppurative
- ▶ cervical lymphadenopathy (often single and large)
- ▶ rash: polymorphous
- ▶ changes to lips or oral mucosa
- ▶ changes to extremities

The diagnosis of complete KD requires fever plus four of the other above features to be present—although not necessarily at the same time. However, it is recognised that KD may present with fewer features and that these cases remain at risk of developing coronary artery aneurysms. Thus, patients with some of the above features—along with evidence of systemic inflammation (such as elevated C-reactive protein (CRP) or erythrocyte sedimentation rate, or leucocytosis)—may be diagnosed with incomplete KD. Echocardiography may show evidence of coronary vasculitis. If present, this confirms the diagnosis, but a normal echocardiogram does not rule out KD.¹

As illustrated by this case, young infants are more likely than older children to present without the expected features of KD, putting them at greater risk of delayed diagnosis and associated sequelae.¹⁰

CASE PRESENTATION

A 12-week-old Caucasian infant was admitted to hospital with a history of fever and vomiting. The illness had started 5 days earlier with diarrhoea and a non-specific rash on her abdomen and back.

No fevers were noted by the parents until the day of admission, on which she vomited and had a low-grade fever of 37.8°C, prompting her parents to bring her to the emergency department. There was no history of infectious contact. She had been born at 41+2 weeks gestation via ventouse delivery, had no previous medical problems and was up to date with immunisations.

Clinical examination on admission identified a high fever of 38°C, and a blanching erythematous rash over her whole body which resolved shortly after admission.

INVESTIGATIONS

Admission blood results in her local hospital showed a normal white cell count of $11.7 \times 10^9/L$ but an elevated CRP of 64 mg/L. Blood platelets were high at $657 \times 10^9/L$ and haemoglobin



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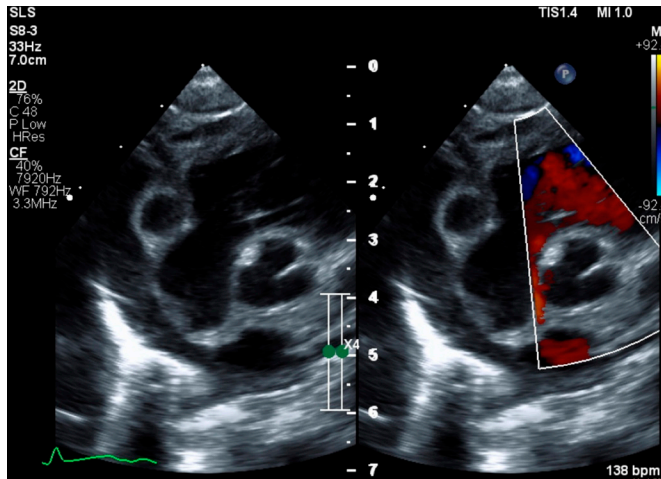


Figure 1 Pericardial effusion in short axis.

was slightly low at 10.1 g/dL. Alanine transferase, bilirubin and albumin were normal.

Urine dip, viral screen and initial chest radiograph were all normal. Initial and repeat lumbar punctures were unremarkable.

The patient developed recurrent fevers over 38°C, which did not settle in spite of treatment for presumed bacterial sepsis with intravenous ceftriaxone. One set of blood cultures grew *Moraxella osloensis*, so a 3-day course of azithromycin was added, but this organism was subsequently felt likely to be a contaminant. There were no other positive microbiology or virology investigations.

There was no lymphadenopathy, joint problems or desquamation of the extremities. Ultrasound examination of the abdomen and renal tract on day 11 of fever showed a grossly distended gallbladder. The same day an echocardiogram was performed, revealing a global pericardial effusion and aneurysmal right and left coronary arteries.

The patient was transferred to a tertiary cardiology centre for management of presumed incomplete KD. The echocardiogram was repeated, confirming these findings, with a pericardial effusion of 8 mm (figure 1), impaired myocardial function (fractional shortening 26%) and coronary artery Z-scores of +26 and +20.5 for the right (figure 2) and left (figure 3) coronary arteries, respectively, indicative of giant coronary artery

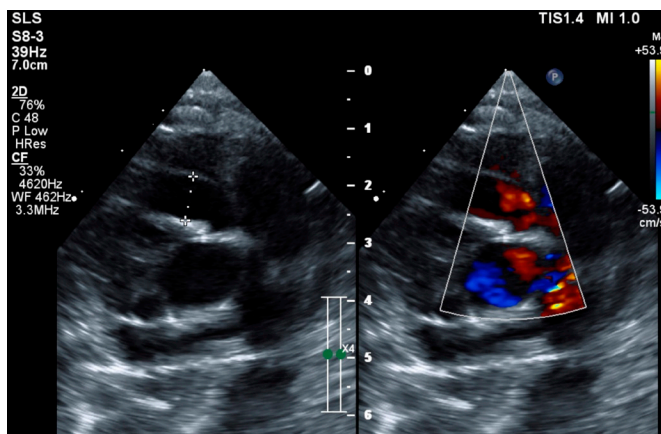


Figure 2 Right coronary artery.

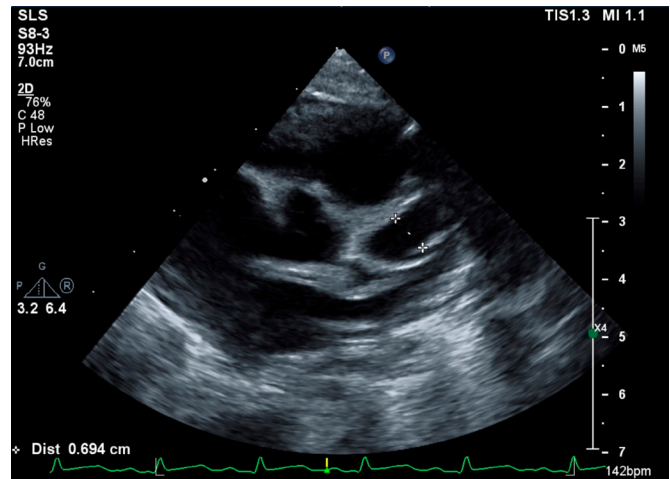


Figure 3 Left coronary artery.

aneurysms. It was possible to visualise the dilated right coronary artery, left anterior descending artery and circumflex artery down to the ventricular apex.

DIFFERENTIAL DIAGNOSIS

Prior to echocardiography:

- ▶ Bacterial sepsis
- ▶ Viral infections, such as enterovirus, adenovirus, norovirus

These more common childhood conditions present with similar non-specific features, such as fever and rash.

TREATMENT

Intravenous immunoglobulin 2 g/kg (single dose) and high-dose aspirin 7.5 mg/kg every 6 hours were started prior to transfer to the cardiology centre. Methylprednisolone (20 mg/kg daily intravenously) and intravenous heparin (infusion titrated to achieve therapeutic anti-Xa levels) were initiated at the tertiary centre, and high-dose aspirin continued. The patient required a second dose of intravenous immunoglobulin 5 days after the initial dose for recrudescence of fever. She received a blood transfusion for anaemia. She was discharged on low-dose aspirin (5 mg/kg daily), subcutaneous enoxaparin, a weaning dose of prednisolone and ranitidine.

OUTCOME AND FOLLOW-UP

The patient was discharged 25 days after her initial presentation to hospital. PredischARGE echocardiogram showed good biventricular function, reducing pericardial effusion and no evidence of coronary thrombus. ECG showed no evidence of ischaemia. CRP had peaked 11 days after the onset of fever at 154 mg/L and fell to 7 mg/L 1 week after discharge. At clinic review 12 days after discharge, the patient was clinically well and gaining weight. Alongside regular clinical review, she is to be followed up with coronary angiography to document the full extent of coronary involvement.

DISCUSSION

The diagnostic challenge of this case stemmed largely from the fact that the patient, a Caucasian female infant aged just under 3 months, did not fit the typical KD patient profile. Only 1.6% of patients with recognised KD are younger than 3 months of age,¹¹ and the disease is most common in Asian male children. Furthermore, our patient presented with incomplete KD, with fever and rash—signs that more

commonly indicate viral infection in this age group—being the only features that fulfilled diagnostic criteria for KD. Nevertheless, she developed giant coronary aneurysms, demonstrating that the most severe sequelae can develop in patients with few of the typical symptoms. Abdominal ultrasound revealed hydrops of the gallbladder, also recognised as a manifestation of KD.¹²

Incomplete cases of KD present diagnostic difficulty for clinicians, particularly as echocardiography requires paediatric cardiology input. However, a 2013 survey found that 17% of UK district general hospitals that cared for children did not provide this service.¹³ In the present case, echocardiography was locally available and was instrumental in confirming the diagnosis of KD, highlighting the importance of having this service available to all children. We propose that echocardiography should routinely be considered for any child with persistent unexplained fever, and particularly in children aged under 6 months, to try and prevent the sequelae of unrecognised KD.

Patient's perspective

Written by the patient's mother and father

- ▶ Our daughter was 3 months old when she was admitted to hospital with sickness, diarrhoea and a high temperature. She had been unwell for 3–4 days by this stage but not admitted to hospital by her general practitioner as the illness was thought to be viral. There had been an initial rash but this disappeared after a few days in hospital.
- ▶ Initially she was treated for bacterial meningitis, then *Moraxella* and then herpes. Throughout her initial 10 days in hospital, she didn't present many of the classic symptoms of Kawasaki apart from the regular spikes in temperature. While obviously unwell she seemed clinically fine which probably delayed the diagnosis of Kawasaki. Her symptoms seemed to suggest a viral infection however the 'not knowing' what she had was difficult as parents.
- ▶ Throughout this time, we were worried that our daughter wasn't getting any better and that her case was puzzling the doctors. On day 9 postadmission, the team were beginning to think outside the box and mentioned a rare disease called Kawasaki, although they didn't think it was this. In hindsight this thinking outside the box may have saved her life. Once the echo was performed, the giant aneurysms in her coronary arteries were discovered and intravenous Ig was started within the hour and we were transferred to a specialist children's hospital.
- ▶ Once the diagnosis was made, we felt the treatment and care was fantastic and our daughter is now doing as well as she can be. The first 48 hours postdiagnosis were the worst time in our lives.
- ▶ We will never know whether an earlier diagnosis would have stopped the aneurysms growing to the size they are; however, we are delighted that our daughter's case is being published and hopefully the insight will help doctors 'think Kawasaki' earlier and diagnose cases to stop them developing into more serious Kawasaki cases.

Learning points

- ▶ Kawasaki disease (KD) can affect children younger than 3 months of age.
- ▶ Clinical suspicion is required to recognise KD in the youngest patients, as they are more likely to present with few features of KD.
- ▶ Consider KD in the differential diagnosis for any febrile infant who has no clear source of infection.
- ▶ Perform echocardiography where there is clinical suspicion of incomplete KD, but recognise that a normal echocardiogram does not exclude the diagnosis.
- ▶ Giant coronary artery aneurysms confer a significant risk of major adverse cardiac events. Early treatment with aspirin and intravenous immunoglobulin reduces the risk of these developing. Steroids are indicated in high-risk patients to minimise the progression of coronary artery lesions.

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