Incomplete Kawasaki Disease in a 44-day-old baby

Nor Azizah Abu, MRCPCH[1], Siew Peng Thong, MRCPCH[2], Hung Liang Choo, MRCP Paeds[3]

[1]Faculty of Medicine, Sungai Buloh Campus, Universiti Teknologi MARA (UiTM), Selangor, Malaysia, [2]Department of Paediatrics, Hospital Selayang, Selangor, Malaysia, [3]Department of Paediatrics, Institute of Paediatrics, Hospital Kuala Lumpur, Kuala Lumpur, Malaysia.

SUMMARY

Kawasaki disease (KD) is an acute systemic vasculitis usually affecting children <5 years old. We report a 44-day-old baby who had persistent fever despite being on antibiotics for presumed sepsis. Erythema of Bacillus Calmette-Guerin (BCG) scar and thrombocytosis were noted on day-2 of illness. Diagnosis of incomplete KD was made on the 10th day of illness. Her fever resolved with intravenous immunoglobulin, but echocardiogram revealed coronary artery aneurysm. High index of suspicion is required to diagnose KD in infants ≤3 months since it is rare and commonly presents with incomplete clinical features. The presence of unexplained fever for ≥5 days with erythema of BCG scar or thrombocytosis in infants should alert the clinicians of KD.

INTRODUCTION

Kawasaki disease (KD) is an acute febrile systemic vasculitis of unknown origin, affecting children below 5 years of age. Cases are seen in all races, but it has higher incidence among Asians. The first case was described by Dr Tomikasu Kawasaki in 1967. Nowadays, KD is one of the leading causes of acquired heart disease in children in developed countries. Despite extensive research, the aetiology of KD remains unknown. Diagnosis is still based on clinical criteria described by Dr Kawasaki five decades ago. The diagnostic criteria are fever for at least five days with at least four out of five of the following features, in the absence of other known diseases: 1) bilateral bulbar conjunctival injection without exudate; 2) erythema and cracking of lips, strawberry tongue, and/or erythema of oral and pharyngeal mucosa; 3) changes in extremities such as oedema or erythema of hands or feet, desquamation of fingers or toes; 4) maculopapular, diffuse erythroderma, or erythema multiforme-like rash; 5) cervical lymphadenopathy (≥1.5 cm diameter), usually unilateral.[1]

Incomplete KD can be diagnosed in patients who do not fulfil the clinical criteria as stated above, but have the following: C-reactive protein (CRP) ≥3mg/dL or erythrocyte sedimentation rate (ESR) ≥40mm/hr, supplemented by ≥ 3 laboratory criteria: a) serum albumin ≤3g/dL; b) anaemia for age; c) elevation of alanine aminotransferase (ALT); d) platelets ≥450000/mm^3 after the 7th day of fever; e) white cell ≥15000/mm^3; f) urine ≥10 white cells/high-power field; or echocardiographic findings which fulfil the criteria for coronary artery dilatation or aneurysm.[1]

Neurological, gastrointestinal, renal, musculoskeletal, ocular and pulmonary involvements have been described. These include aseptic meningitis, hepatitis, diarrhoea, vomiting, abdominal pain, gallbladder hydrops, urethritis, hydrocele, arthralgia, arthritis, anterior uveitis and infiltrates on chest radiography.[1]

If left untreated, 15 to 25% of patients with KD develop coronary artery aneurysms, which may lead to myocardial infarction and death.[1]

CASE REPORT

We report a 44-day-old "Orang Asli" girl, who was referred to our centre from a peripheral hospital with suspected meningitis. She had history of fever associated with mild cough, runny nose and reduced oral intake for one day. There were no other systemic symptoms. Her perinatal, past medical and family histories were unremarkable. On examination, her temperature was 38°C, respiratory rate was 34 breaths per minute, SpO_2 was 100% in room air and blood pressure was 104/71 mmHg. She was irritable but consolable. Her anterior fontanelle was normal. Her lips were red and cracked, and the Bacillus Calmette-Guerin (BCG) vaccination scar was mildly erythematous. Other systemic examination was normal. Initial laboratory tests showed thrombocytosis, elevated CRP and mildly elevated ALT. Other results were normal (Table I). She was treated as suspected sepsis with intravenous cloxacillin and gentamicin. In view of her irritability, lumbar puncture was performed the following day and the antibiotics were changed to benzylpenicillin and cefotaxime.

On the 4th day of illness, she developed transient maculopapular rash and non-purulent conjunctivitis which resolved within 48 hours. At this juncture, KD was suspected but considered unlikely because of her age. Subsequently her urine, blood and cerebrospinal fluid cultures did not grow any organism. In view of her persistent fever, the antibiotics were escalated to imipenem and erythromycin. Other investigations including chest x-ray, echocardiography and abdominal ultrasound were normal.

On the 10th day of illness, her symptoms and serial investigations were reviewed and diagnosis of incomplete KD was made in view of her fever of more than five days, red cracked lips, maculopapular rash and non-purulent conjunctivitis, supported by raised inflammatory markers of both ESR and CRP, anaemia for age, leucocytosis,

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Corresponding Author: Nor Azizah Abu
Email: azizahdublin@gmail.com

Table I: Laboratory findings of the patient

Day of illness	Haemoglobin (g/dL)	White blood cells (/mm3)	Platelet (/mm3)	CRP (mg/dL)	ESR (mm/hr)	Albumin (g/dL)	ALT (U/L)
2	12.5	11,820	585,000	8.57		3.7	56
5	10.0	16,300	515,000	17.62	45	2.8	23
9	9.4	17,160	719,000	14.71		2.9	12
13	10.2	11,530	895,000	1.59		2.8	50
28	10.9	10,540	614,000	<0.5	40	3.7	32
135	13.0	12,300	525,000		18		

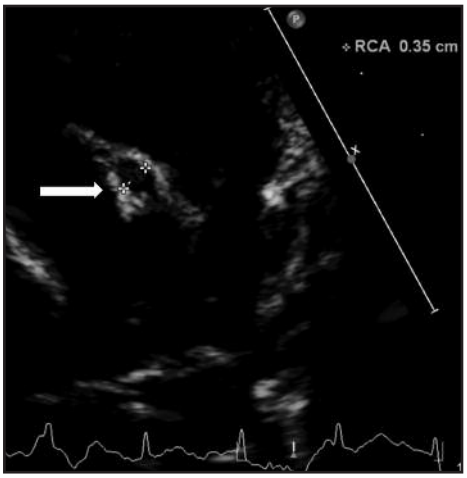

Fig. 1a: Echocardiogram in parasternal short axis view showing fusiform aneurysm of the proximal right coronary artery (RCA) measured 3.5mm (Z-score +7.75) (white arrow).

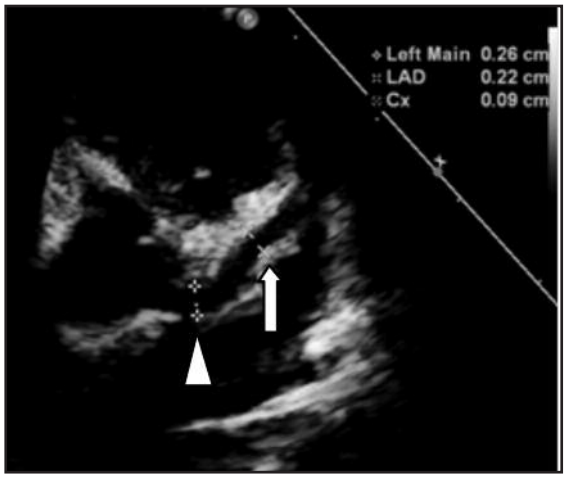

Fig. 1b: Echocardiogram in parasternal short axis view showing ectasia of the left main coronary artery (LMCA) measured 2.6 mm (z-score +4.17) (white arrowhead) and the left anterior descending (LAD) artery measured 2.2mm (z-score +4.14) (white arrow). The circumflex artery was normal, measuring 0.9mm (z-score -0.09).

*z score is calculated based on body surface area.[2]

thrombocytosis, elevated ALT, hypoalbuminaemia and sterile pyuria. In addition, she also had erythema at the BCG inoculation site. Hence IVIG 2g/kg infusion over 12 hours and aspirin 50mg/kg/day in four divided doses were commenced. Echocardiography on the 11th day of illness showed fusiform aneurysm of the proximal right coronary artery (Figure 1(a)), ectasia of the left main coronary and left anterior descending arteries (Figure 1(b)). The left circumflex artery was normal. Clopidogrel 0.2mg/kg/day was commenced in view of the dilated coronary arteries.

Her fever settled within 36 hours after completion of IVIG infusion and she was discharged on the 15th day of illness with aspirin 5mg/kg/day and clopidogrel. On follow-up at outpatient clinic, she was asymptomatic with no signs of cardiac failure. Her inflammatory markers and platelet count gradually normalised. Serial echocardiograms showed reduction in the size of coronary artery aneurysms, with no evidence of stenosis or thrombosis. Her echocardiogram eight months after the illness showed normal calibre coronary arteries. Subsequent serial echocardiograms remained normal.

DISCUSSION

High index of suspicion is required to diagnose KD in infants ≤3 months since it is rare among infants of this age (1.7 to 2.2%) and is usually associated with incomplete clinical features.[3]

Thrombocytosis in KD usually occurs in the second week of illness and is rarely seen during the first week.[1] Our patient had platelet count of 585,000/mm^3 on the second day of illness and later rose to 895,000/mm^3 during the second week of illness. This finding is consistent with report by Nigrovic LE et al., that the presence of unexplained prolonged fever and extreme thrombocytosis in infants should alert the clinician regarding the possibility of KD.[4]

She also developed erythema of her BCG scar as early as day 2 of illness. A systematic review by Mohammad SR et al., showed that erythema at the BCG inoculation site was present in 49.87% of 15,955 KD patients overall. It was present in all patients with incomplete KD. It was also noted to be more common than rash and cervical lymphadenopathy in incomplete KD.[5]

This patient received single dose of IVIG 2g/kg given as infusion over 12 hours, which is the recommended treatment of KD and has been shown to decrease coronary artery abnormalities.[1]

She also received oral aspirin which is the standard treatment in KD together with IVIG. Aspirin is usually given at moderate dose, 30 to 50mg/kg/day or high dose, 80 to 100mg/kg/day for its anti-inflammatory action until the patient is afebrile for 48 to 72 hours. Subsequently it is continued at antiplatelet dose of 3 to 5mg/kg/day for 6 to 8 weeks from the onset of illness if the patients do not have coronary abnormality or indefinitely for those who do. This aims to reduce thrombosis in the coronary artery aneurysms.[1]

Clopidogrel is used as thromboprophylaxis together with aspirin for patients with severe or complex coronary artery aneurysms due to high risk of thrombosis.[1] It was prescribed as additional anti-platelet agent in our patient as she had multiple coronary artery abnormalities.

CONCLUSION

The fact that the possibility of KD was dismissed initially indicates the need to increase awareness among paediatricians regarding the possibility of KD occurring in young infants just beyond the neonatal period. The diagnosis of KD should especially be considered in young infants who have unexplained fever for more than five days with erythema of BCG scar or thrombocytosis. Timely diagnosis is crucial as administration of intravenous immunoglobulin within ten days of illness reduces the incidence of coronary artery aneurysm.[1]

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