Kawasaki disease shock syndrome: three cases

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Introduction

Kawasaki disease (KD) is a disease of unknown aetiology affecting medium sized blood vessels[1]. It is the commonest type of acquired heart disease in children and 15-25% of patients have coronary artery involvement[2]. Kawasaki disease shock syndrome (KDSS) is a rare haemodynamically unstable phenomenon in the acute stages of KD which was first described by Kenagaye et al in 2009[1]. Possible causes for the haemodynamic instability are vasculitis with capillary leak, myocardial dysfunction and cytokine dysregulation[1]. KDSS may be misdiagnosed as it mimics other causes of shock[3]. It is important to have a high index of suspicion for KD in any child with prolonged fever of unknown origin and to refer to a paediatric facility promptly, as timely treatment reduces coronary artery damage[3]. We report three cases of KDSS seen over a period of one year needing care in the high dependency and intensive care units.

Case 1

A 10-year-old girl presented with a history of fever for 2 days and an episode of vomiting. On examination, she was febrile with tachycardia and signs of circulatory collapse (hypotension with poor peripheral perfusion). There were no changes in the mucous membranes, no rashes, no cervical lymphadenopathy and no inflamed BCG scar. Differential diagnoses considered were dengue, leptospirosis, sepsis, myocarditis and KD. The white blood cell (WBC) count was 5,600/cu mm, the platelet count 42,000/cu mm, the C-reactive protein (CRP) 177mg/dl and the erythrocyte sedimentation rate (ESR) 70mm in the first hour.

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Her liver function tests were abnormal with aspartate aminotransferase (AST) 2066U/L and alanine aminotransferase (ALT) 1427U/L. Blood culture was negative. The electrocardiogram (ECG) showed sinus tachycardia with no ischaemic changes, and serum troponin I was within normal range (0.019ng/ml). Dengue antibody was negative. She was treated with intravenous (IV) cefotaxime, normal saline boluses and maintenance IV fluid. The 2D-echocardiogram, done on day 3 of admission, showed uniformly dilated right and left coronary arteries, with an ejection fraction of 55%. (Figure 1).

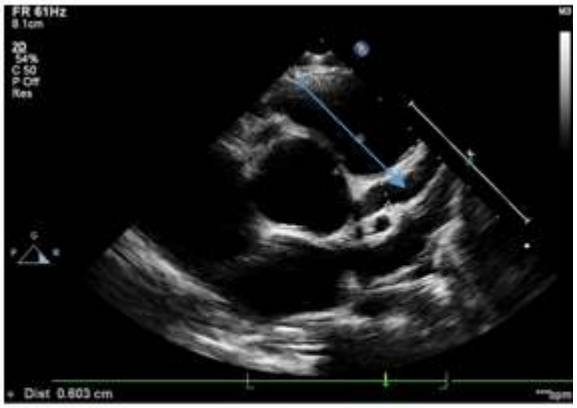

Figure 1: ***2D-echocardiogram showing dilated left anterior descending coronary artery***

The ultrasound scan (USS) of the abdomen was normal. Blood picture excluded microangiopathic haemolytic anaemia and disseminated intravascular coagulation (DIC). She was treated with IV human immunoglobulin 2g/kg. Anti-platelet dose of aspirin was commenced when the platelet count rose to more than 400,000/cu mm. She developed peeling of skin during the 2nd week of illness. Coronary angiogram also showed dilated coronaries. She is currently on regular follow up with 2D-echocardiograms.

Case 2

An 11-year-old boy, with a history of fever and throat pain of 4 days duration, presented in shock with unrecordable blood pressure. He had cervical lymphadenopathy, redness and swelling of lips and peeling of skin in the hands and feet. The WBC count was 10,000/cu mm and the platelet count 14,000/cu

mm. The CRP and ESR were high. Troponin I was normal and dengue antibody was negative. There was no ischaemic change in ECG. 2D-echocardiogram showed dilated left anterior descending and right coronary artery, a thin rim of pericardial effusion and an ejection fraction of 50%. He was managed with IV human immunoglobulin 2g/kg and anti-platelet doses of aspirin and clopidogrel, when the risk of bleeding was excluded. Follow up echocardiogram and coronary angiogram showed progressive dilatation of left anterior descending artery. The 6 month follow-up also showed persistence of the dilated coronaries.

Case 3

A 4 year-old boy was admitted with a 6 day history of high grade fever and generalized erythematous rash. He also had bilateral non purulent conjunctivitis and right submandibular lymphadenopathy. He was haemodynamically stable on admission but went into circulatory collapse on the second day of admission. There was a 4 cm tender hepatomegaly. The haemoglobin level was 10.6 g/dl, the WBC count 10,390/cu mm, the platelet count 65,000/cu mm, packed cell volume (PCV) 29.4%, ESR 70mm in first hour, CRP 160.5mg/L, sodium 134mEq/l, potassium 3.9mEq/l, blood urea 8.9mmol/l, aspartate transaminase (AST) 55U/L and gamma glutamyl transferase (GGT) 80U/l. The dengue antigen and antibody were negative and troponin I was 0.11 µg/l. Blood picture showed a reactive white cell picture and mild thrombocytopenia. Ultrasound scan of the abdomen and neck revealed hepatosplenomegaly and mild ascites and lymphadenitis respectively. Echocardiography revealed mildly reduced left ventricular function, thin rim of pericardial effusion, uniformly dilated right (4mm) and left (4mm) coronary arteries and no aneurysms of the coronaries (Figure 2).

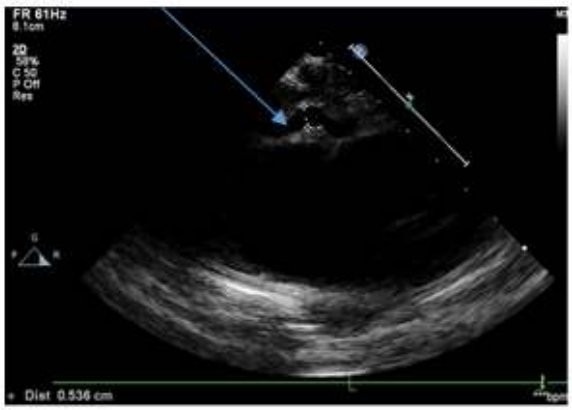

Figure 2: ***2D-echocardiogram showing dilated right coronary artery***

He was managed in the intensive care unit with inotropic support and IV immunoglobulin. Antiplatelet treatment was started when the platelet count rose to 500,000/cu mm. As the family lives abroad, details of follow up are not known.

Discussion

Literature shows the disease is predominant in the 3-3.5 year age group but the cases reported here are older children[3]. Males have shown a preponderance and the clinical feature of erythematous rash was prominent[2]. KDSS can also present without any of the typical features of KD[3]. Detecting and suspecting KDSS is difficult as it clearly mimics dengue shock syndrome, toxic shock and septic shock[2]. The presence of high inflammatory markers with deranged liver function test can mislead the clinician. Performing 2D echocardiography early in the disease and having a suspicion of KDSS can help the clinician to pick this disease early[3]. The persistent nature of tachycardia prompted the clinicians to perform 2D Echocardiography in all three cases we report.

One published research article showed that compared with patients with KD, patients with KDSS had a higher CRP concentration, and lower haemoglobin concentrations and platelet counts[3]. Evidence of consumptive coagulopathy was common in KDSS[4]. Patients with KDSS more often had impaired left ventricular systolic function, mitral regurgitation and coronary artery abnormalities[2]. All three patients had high inflammatory markers, and low platelet levels with impaired left ventricular systolic function and coronary artery abnormalities.

The coronary artery abnormalities were seen during acute, convalescent and chronic phases of the disease more prominently in KDSS when compared to KD[5]. All the cases reported here also show the persistent nature of the coronary artery abnormalities even after timely diagnosis and timely administration of IVIG therapy. It is also shown that IVIG can be resistant in KDSS[4]. This may be the reason for the persistence of the coronary artery disease. More prominent inflammatory markers are found in these patients. We suppose more severe inflammation may make them more likely to be IVIG resistant.

It is recommended that refractory disease is first treated with a second dose of IVIG 2 g/kg, though there are a number of other therapeutic options, including IV corticosteroid pulse therapy, anti-TNF-alpha antibodies, and cytotoxic agents[2,5]. In the presence of coronary artery disease, the children

should be on aspirin and clopidogrel to prevent thrombotic events.

Patients with KDSS may have an uneven clinical course and may be misdiagnosed when they are first examined. They may have more prominent inflammatory markers and result in shock and hypotension, which require critical care support at an early stage. They have a greater risk of coronary artery abnormalities, which may become coronary artery disease. These patients frequently fail to fulfil the full spectra of KD in the early phase, so delay in IVIG treatment may occur. They are also likely to be IVIG resistant because of more severe inflammation. Early recognition of KDSS and provision of adequate therapy are very important.

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