Bahrain Medical Bulletin, Volume 17, Number 2, June 1995

Case Report

KAWASAKI DISEASE: REPORT OF THREE CASES

Joshua A Owa* Naem Ahmad* Hussain A Abusrair*
Salwa H Shawfey*

Kawasaki disease is a common cause of acquired heart disease in children. Three cases of Kawasaki disease with involvement of the coronary arteries in two cases are presented. All the three were given immunoglobulin. There was a complete regression of the coronary artery lesion in one patient and this encouraged us to give immunoglobulin to the third patient even though the coronary was already involved on admission. We conclude that although Kawasaki disease is increasingly being diagnosed, cases are often being missed due to lack of high index of clinical suspicion. It should be excluded in all children with unexplained fever of more than one week duration. Echocardiogram should be done in all suspected cases and immunoglobulin given even in patients with coronary artery lesion, since such lesions may be reversible.

Since the first description of Kawasaki disease (KD) in Japan 20 years ago, the disease has emerged as an important childhood disorder with a worldwide distribution1. It is now well recognised as a leading cause of acquired heart disease[1-12]. In the Arabian Gulf region cases from Saudi Arabia and Kuwait have been reported[2,13,14].

The aetiology is unknown[5]. The clinical features of acute self limiting febrile illness, rash, mucous membrane involvement, lymphadenopathy, leucocytosis and epidemic nature of the disease suggest an infectious aetiology. Suspected causative agents include house dust mites, bacterial agent like Propionibacterium acnes or their toxins and retrovirus, but conventional microbiological and serological investigations have failed to identify a causative agent5. Racial predisposition has also been suspected on the basis of high incidence in Japan, and among American children of Japanese descent, as well as among children of Japanese families living in the United Kingdom[1-5].

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* Department of Paediatric Medicine
Qateef Central Hospital
Qateef, Saudi Arabia

Three patients of Kawasaki disease with coronary artery involvement in two are reported here. Attempt to determine the aetiology was unrewarding.

THE CASES

Case 1: AMS, an 18 months old Egyptian male child was admitted on 7 January 1993 with fever, poor feeding and irritability of one week duration. His parents were healthy. His immunisation was complete and up to date and he had not received any vaccination prior to admission. On examination he was very irritable with a temperature of 38.8oC and weighed 10.4 kg. Systemic examination was unremarkable except for congested oral and throat mucosa and a few bilateral palpable upper cervical lymph nodes. His growth parameters were around the 50th percentile.

Laboratory investigations showed haemoglobin (Hb) of 9 gm/dL, total white blood cell (WBC) count of 20.6 x 109/L, platelets count of 1028 x 109/L, erythrocyte sedimentation rate (ESR) of 80 mm in the first hour, SGOT of 78 U/L (normal 15-37 U/L), SGPT of 123 U/L (normal 30-65 U/L). Other blood chemistry results were

normal. Blood, urine and throat swab cultures were negative. Tests for infectious mononucleosis were also negative and serology for enteric fever was negative. The findings on chest X-ray were within normal limits.

During his hospital stay, he developed macular rash over the chest, neck and nappy area. He also developed swelling of both hands and feet and cracked lips (Fig 1). Kawasaki disease was suspected at this stage and an echocardiogram on 11 January 1993 revealed a beaded appearance of both coronary arteries. These dilatations were more marked in the right coronary artery. One week after admission, peeling of the skin of palms, soles and nail beds started (Fig 2). He was treated with aspirin at 100 mg/kg/day from 9 January 1993 and intravenous immunoglobulin at the dose of 2 gm/kg given once over 10 hours on 13 January 1993. He improved dramatically after this and he was discharged 10 days after admission on low dose aspirin. A follow-up echocardiogram three months later showed some regression of the coronary artery dilatations and the last echocardiogram done on 14 November 1993 showed complete regression of coronary dilatations.

Case 2: YAF, a 10 months old Egyptian male child was admitted on 30 December 1993 with the diagnosis of Kawasaki disease by one of us (HAA). At the time he was seen in our unit he had been ill for about 21 days. He had fever and cough for 21 days. His father who is a medical doctor also gave a history of enlarged cervical lymph nodes at the onset of illness. His immunisation was up to date. He weighed 10 kg and his growth parameters were normal for his age. His temperature was 37oC. His eyes and throat were congested. There was minimal swelling of the dorsum of all the limbs and desquamating rash on the back and chest wall. There was desquamation of the nail bed. He had several blood cultures done and all were negative. His blood counts on 8 December 1993 showed Hb of 11.2 gm/dL, WBC of 20.9 x 109/L, platelets of 577 x 109/L, and ESR of 93/hour. Serology tests for enteric fever and infectious mononucleosis were negative. The liver and renal function tests were normal. Echocardiograms done on 24 December 1993 and 1st January 1994 were normal. He had been started on aspirin at 5 mg/kg/day. He was given immunoglobulin at 2 gm/kg single dose over 10 hours on 31 December 1993. He was discharged on 3 January 1994 in good condition. He is being followed in the Paediatric Cardiology and General Paediatric Clinics.

Case 3: HMBG, an 11 months old Egyptian male infant, was admitted on 15 January 1994 with three days history of fever, diarrhoea and vomiting, and convulsion lasting about 15 minutes along with excessive crying on the day of admission. His immunisation was up to date. He had been well before the onset of current illness. He was a product of full term pregnancy and normal delivery. He had been on breast feeding since birth. He was very irritable with a temperature of 38.5oC. He was well hydrated. His eyes, oral and throat mucosa were mildly congested. He had discrete non-tender cervical lymphadenopathy. He was started on paracetamol and ampicillin on admission. At this level Kawasaki disease was suspected because of the persistance of fever and irritability, and the development on the third day of admission of erythematous macular rash on the upper chest and neck along with swelling of dorsum of hands and feet. The antibiotics were changed to cefotaxime. Echocardiogram done on 22 January 1994 showed right coronary artery aneurysm. The myocardial function was normal. The ECG showed depressed ST segment. His blood, cerebrospinal fluid, urine and throat swab cultures were all negative. Rotavirus was isolated from the stool.

Investigations for infectious mononucleosis and enteric fever were all negative. The blood counts on admission on 15 January 1994 showed Hb of 9.9 gm/dL, WBC of 27.6 x 109/L and platelets of 591 x 109/L. The platelets rose to 1155 x 109/L on 25 January 1994. It was not possible to give immunoglobulin because it was not immediately available. The patient was discharged on 27 January 1994 and was readmitted on 31 January 1994 for the immunoglobulin therapy which was given as single dose of 2 gm/kg over 10 hours. He was discharged the following day in

good condition. He was last seen on 15 February 1994 and was clinically well. His blood counts showed WBC 16 x 10^9/L, Hb 10.9/dL, and platelets 657 x 10^9/L.

Table 1 show the summary of the major clinical features in the three patients.

Table 1
Major clinical features in the three patients with Kawasaki disease

Patients	Number 1	Number 2	Number 3
Age (months)	18	10	11
Sex	male	male	male
Nationality	Egyptian	Egyptian	Egyptian
Month of admission	January	December	January
Duration of fever	18 days	21 days	9 days
Conjunctivitis	++	++	++
Changes in the mucous membranes	++	++	++
Changes in extremities	++	++	++
Skin rash	++	++	++
Cervical lymphadenopathy	++	++	++
Coronary artery involvement	++	--	++
Maximum platelet count	1156	832	1155
Maximum ESR	135	70	73

ESR = Erythrocyte sedimentation rate ++ = Present, -- = Absent

DISCUSSION

Kawasaki disease is now one of the common causes of acquired heart disease in children world wide[1-12]. In a nation-wide Japanese survey, it was noted to be more common in male infants and in the age group above five years old4. All our patients were males.

Kawasaki disease which was initially thought to be a benign, self-limiting febrile illness is now known to be associated with sudden death in about one percent of affected children[2,3]. Most deaths are due to acute coronary vasculitis which occurs in up to 30% of children with the disease[3]. Though about 80% of those who have cardiac involvement have myocarditis, the majority of deaths are due to myocardial infarction secondary to thrombus formation in the affected vessels. Two of our three patients had coronary artery involvement.

Electrocardiography is abnormal in one third of children with KD, showing decreased R wave voltage, ST segment depression and T wave flattening or inversion. Myocardial inflammation may cause slow conduction resulting in prolonged PR or QT intervals or both[5].

Coronary artery abnormalities develop in approximately 20% of children with untreated KD and are the most common cause of short and long term morbidity and mortality. These include ectasia or aneurysms that may be fusiform or saccular. Aneurysms have been detected within three days of onset of illness but more commonly occur 10 days to four weeks after the onset of symptoms. This was the case in our third patient. The appearance of aneurysms more than six weeks after the onset of illness is uncommon. Patients with giant aneurysms (internal diameter at least 8 mm) have the worst prognosis and are at the greatest risk of developing coronary thrombosis, stenosis and myocardial infarction. Giant

aneurysms generally do not resolve[5]. Mortality from myocardial infarction has been reported to be approximately 25%6.

When possible, patients with KD should be treated within 10 days of illness with immunoglobulin and high dose aspirin. A single infusion dose of 2 gm/kg of immunoglobulin with 100 mg/kg/day of aspirin are preferred[5]. If coronary artery abnormalities are detected 3-5 mg/kg/day of aspirin, for its antithrombotic effects should be given indefinitely.

All our patients were Egyptians although Egyptians form a minor proportion of our patient population. This is in favour of the suspicion that some racial groups are susceptible[5]. The present report and the report from Kuwait and Riyadh would suggest that the disease may not be uncommon in the Gulf area[2,13,14]. High index of suspicion will result in early diagnosis.

One of the challenges for the paediatricians and infectious diseases physicians in the 1990s is to identify the causative agent of the disease. With the view of a toxin acting as a superantigen in the causation of KD the role of group A streptococci is currently being investigated[7]. Similar observations had led to the belief that an infectious agent transmitted by a vector may be involved[5,11,12]. All our patients were seen during the winter raining season of December/ January.

Table 2
Diagnostic criteria for Kawasaki disease

A. Fever of five days duration or more
B. Presence of four of the following five conditions:
    1. Bilateral conjunctival injection
    2. Changes in the mucous membranes of the upper respiratory tract, such as injected pharynx, dry cracked lips, strawberry tongue*
    3. Changes of the peripheral extremities, including oedema, erythema, desquamation (may occur later)*
    4. Polymorphous rash
    5. Cervical lymphadenopathy

C. Exclusion of known clinical conditions with similar presentation: staphylococcal and streptococcal infections, measles, leptospirosis, infectious mononucleosis, rickettsial disease.

    * One of these is sufficient
Note: In the presence of coronary artery aneurysms detected by echocardiogram a fever of 5 days duration or more pluse three of the five criteria in B are diagnostic.

In the absence of specific diagnostic tests, clinical criteria (Table 2) have been established to assist the clinicians in making the diagnosis of KD[5,8,9,12]. Recent recognition of atypical cases however, makes high index of suspicion essential in any child with atypical febrile illness. Early diagnosis requires an awareness of the disorder since effective therapy with high dose immunoglobulin has to be instituted early in the course of the disease to reduce coronary artery complications particularly thrombosis[5]. There is general belief that giving immunoglobulin does not influence the course of the illness once there is a coronary artery involvement[5]. The response of our first patient favour giving immunoglobulin. This encouraged us to give immunoglobulin to our third patient. We recognise however that this could have been a spontaneous regression of the coronary artery lesion[5].

CONCLUSION

Kawasaki disease is not uncommon in the Arabian Gulf region. The diagnosis is made on clinical ground and it should be suspected and promptly investigated in any child with unexplained fever of more than one week duration. All suspected cases should have echocardiogram done and be treated with immunoglobulin even in the presence of coronary artery involvement since such lesions may be reversible.

ACKNOWLEDGEMENTS:

We would like to thank Dr S K Sanyal, Professor of paediatric Cardiology, King Faisal University, Al-Khobar, Saudi Arabia and Mrs. Sohail, Echocardiographer for their assistance in doing the echocardiogram.

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