Mucocutaneous Lymph Node Syndrome (Kawasaki Disease)

A Report of 2 Cases

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SUMMARY

Two cases of Kawasaki disease, both with cardiac involvement, are reported in South African children and the diagnostic problems are discussed. In patient 1 an ECG showed the development of an inferior myocardial infarction, and in patient 2 an aneurysm of the left coronary artery was found at postmortem examination.

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During 1960 a 'new disease' was discovered in Japan, and in 1967 Kawasaki described 50 cases of this disease, also referred to as the mucocutaneous lymph node syndrome (MLNS).[1,2] The main features of MLNS are pyrexia of long duration, bilateral conjunctival congestion, changes in the lips and oral cavity, changes in the peripheral extremities, polymorphic exanthema of the body, without vesicles, and acute non-purulent cervical lymph gland enlargement (Tables I and II).[1-4]

TABLE I. MAJOR DIAGNOSTIC CRITERIA OF THE JAPANESE MLNS RESEARCH COMMITTEE

Most common symptoms	Case 1	Case 2
Temperature for ⩾5 d, in spite of antibiotic treatment*	+	+
Bilateral conjunctival congestion	+	−
Changes in extremities peripherally		
Indurative oedema, initial stage	+	−
Erythema of palms and soles	+	+
Membranous desquamation of fingertips	+	+
Changes in lips and mouth		
Dryness, redness and fissuring of lips	+	+
'Strawberry'-like swelling of tongue papillae	+	?
Diffuse reddening of oral and pharyngeal mucosa	+	?
Polymorphic exanthema of torso, without vesicles or crusts	+	+

* Must be present as well as 3 of the other 4 remaining most common symptoms.

+ = present; − = absent; ? = information not available.

TABLE II. MINOR DIAGNOSTIC CRITERIA OF THE JAPANESE MLNS RESEARCH COMMITTEE

Important symptoms	Case 1	Case 2
Acute, non-purulent swelling of cervical lymph nodes of 1,5 cm or more in diameter	+	−
Diarrhoea	+	?
Arthralgia or arthritis	+	?
Proteinuria and increase of leucocytes in urine sediment	−	−
Haematological abnormalities		
Leucocytosis with nuclear shift to the left	+	+
Increased ESR (40 mm/h) (Westergren)	+	+
Positive C-reactive protein test	+	−
Changes occasionally observed		
Aseptic meningitis	−	−
Mild jaundice or slight increase in serum glutamic oxalo-acetic transaminase level	−	−
Carditis and myocarditis	+	+
Other important features		
Most prevalent in children under 5 years	+	+
Usually favourable prognosis, but sometimes fatal due to coronary thrombosis	+	+
No familial occurrence	+	+

+ = present; − = absent; ? = information not available.

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The most serious anomaly is an arteritis involving all arteries, in particular the coronary arteries.[4] The incidence of the disease is unknown, but more than 10 000 cases have been reported in Japan.[4] We wish to document 2 cases.

CASE REPORTS

Case 1

During March 1979 an 18-month-old Coloured boy was admitted to Tygerberg Hospital with a history of

pyrexia, conjunctival congestion, an erythematous body rash which became macular and spread to the extremities, and erythema of the palms and soles, followed by scaling, swelling of the hands and feet, cervical lymph node enlargement, diarrhoea and a non-productive cough.

His general practitioner diagnosed measles, gastroenteritis and upper respiratory tract infection. Antibiotics were administered, but had no effect. On admission he was well-fed but acutely sick, with a temperature of 38,9°C, bilateral conjunctival congestion, scabs on his lips, a red tongue and pharynx, enlarged red tonsils without an exudate, no Koplik spots, enlarged cervical lymph glands, a macular rash on his body and extremities, erythema of the feet and hands, arthralgia of the knee and hip joints, sinus tachycardia and tachypnoea. No hepatosplenomegaly was found. The haemoglobin value was 12 g/dl, examination of the urine was negative, and the ECG was normal (Fig. 1a).

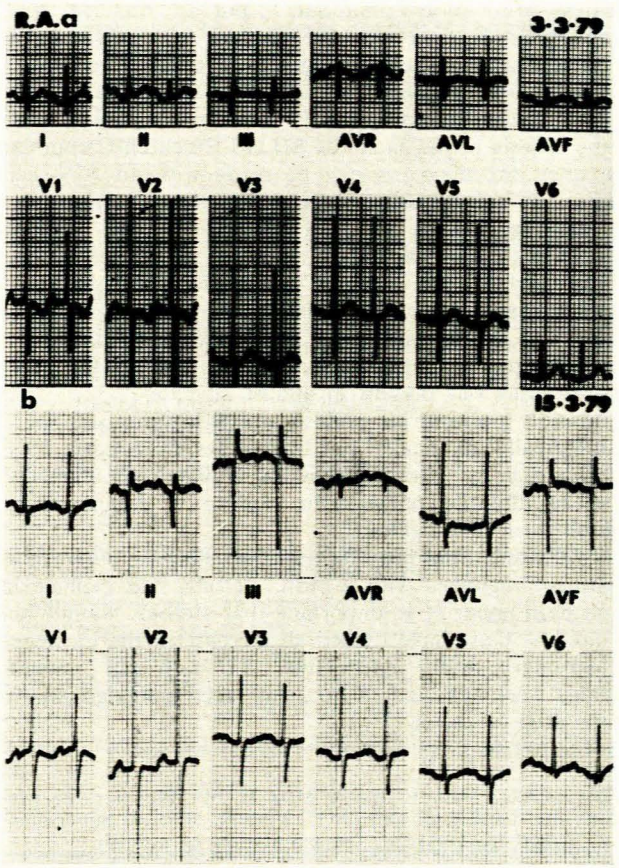

Fig. 1 a — normal ECG; and b — Q waves in inferior leads indicative of an inferior myocardial infarction.

A preliminary differential diagnosis of streptococcaemia, infective mononucleosis or Kawasaki disease was made.

The haemoglobin value was 7,7 g/dl, the white cell count 13 700/μl, the differential count 64% neutrophils, 33% lymphocytes, 2% monocytes, and 1% eosinophils, and the erythrocyte sedimentation rate (ESR) 97 mm/1st h (Westergren). No organisms could be cultured from either throat swabs, urine, faeces or blood samples. Bone marrow cultures were not done. The Mantoux test (1st strength), and viral studies were negative. The cerebrospinal fluid (CSF) was normal. Chest radiographs (Fig. 2) showed cardiomegaly, while the skeletal films were normal. The ECG (Fig. 1) showed inferior myocardial infarction. A liver and spleen scintigram showed an enlarged liver, but liver function tests were negative. The C-reactive protein test was positive. The following serological tests were negative: antistreptolysin 0 titre, Widal, Weil-Felix, *Brucella*, Paul-Bunnell, Wassermann, and rheumatoid factor.

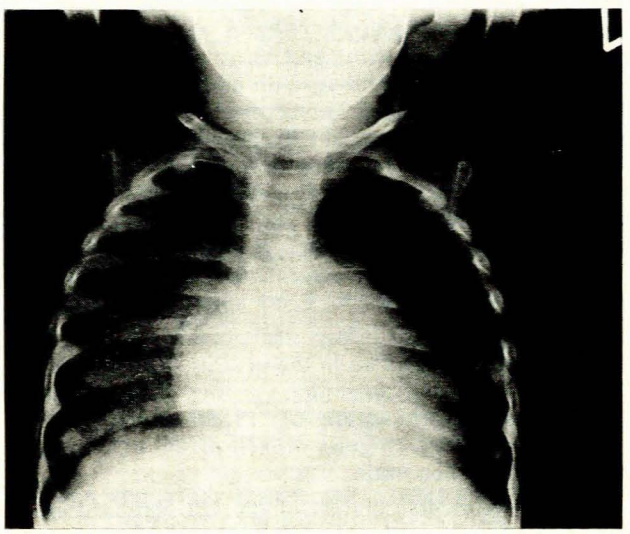

Fig. 2. Anteroposterior view of chest radiograph showing cardiomegaly with lung congestion.

Fourteen days after admission the patient developed acute congestive cardiac failure. The ECG showed Q waves in the inferior leads, indicative of an inferior myocardial infarction (Fig. 1,b). Chest radiographs showed cardiomegaly with lung congestion (Fig. 2), and bidimensional echocardiography showed akinesis of the inferior wall. Cardiac catheterization was planned for 1 month after the infarction, but 3 weeks after the infarction the patient was allowed to go home for a weekend and died suddenly. No postmortem examination was performed.

Case 2

A 2-year-old White boy was admitted to the Emergency Unit at Tygerberg Hospital during October 1979 with a cardiopulmonary arrest, but attempts at resuscitation were unsuccessful. According to his history he had been pyrexial, with a maculopapular body rash 10 months before admission. The rash later spread to the extremities and lips, and antibiotic treatment was ineffective. He was admitted to the Red Cross War Memorial Children's Hospital with a low-grade temperature, a maculopapular

rash of the body and extremities, scaling at the skin-fingertip junction, cheilosis and pitting oedema of the extremities, but lymphadenopathy was not noticeable. The liver was palpable 2 cm below the costal margin, but the spleen could not be felt. A sinus tachycardia of 180 and a gallop rhythm were present. A short ejection systolic murmur was considered to be functional. No satisfactory explanation for the disease process could be given and the symptoms disappeared over a period of 3 weeks, after which the patient became asymptomatic.

The results of special investigations 10 months before his death were as follows: haemoglobin level 9,1 g/dl, white cell count 19 800/μl, differential count 68% neutrophils, 24% lymphocytes, 7% monocytes, and 1% eosinophils and ESR 52 mm/1st h (Westergren). No organisms could be cultured from throat swabs, urine, faeces or blood samples. Bone marrow cultures were negative. The Mantoux test (1st strength) and virus studies were negative (the CSF was not investigated), and chest and skeletal radiographs were normal. Liver and spleen scintigrams showed an enlarged liver, but liver function was normal. The serum globulin level was normal and the albumin level slightly reduced. The C-reactive protein test was not available. The following serological tests were all negative: Widal, Weil-Felix, *Brucella*, Paul-Bunnell, Wassermann, rheumatoid factor, and LE cells. The anti-streptolysin O-titre was 200 Todd units.

Permission for an autopsy was obtained. Postmortem examination revealed foam in the nostrils, bilateral pleural effusions (±50 ml), congestion of the lungs, a small amount of ascites, thickening of 1,5 cm of the proximal section of the interventricular branch of the left coronary artery, and a swollen brain.

The interventricular branch of the left coronary artery showed features of aneurysm formation, namely extensive destruction of the internal elastic lamina and media with fibrous replacement of the destroyed tissues. A patchy and slightly mixed inflammatory cell exudate and focal dystrophic calcification were present. No fibrinoid necrosis was seen. Sections taken from the distal portion of the same blood vessel showed focal thickening of the media or prominent intimal thickening, with or without evidence of thrombosis, organization and recanalization. Large arteries in the salivary gland and kidney had undergone similar changes, but to a lesser extent. The lungs showed evidence of bronchopneumonia, pulmonary oedema, fresh intra-alveolar haemorrhages and lymphoid hyperplasia.

DISCUSSION

Both patients were under 2 years of age and presented with pyrexia of unknown origin and a rash involving the hands and mouth. An infective cause could not be found and neither patient reacted to antibiotic treatment. Both had cardiac involvement; patient 1 had an abnormal ECG (Fig. 1) and in case 2 the postmortem findings were abnormal. These symptoms and signs were in keeping with those of Kawasaki disease (Tables I and II).[3] Since Kawasaki's description of the disease, many reports have emanated from other parts of the world.[4]

The disease is commonest in children under the age of 5 years, the majority of patients being younger than 2 years.[2,5] The most common symptom is a low-grade pyrexia lasting longer than 1 week, accompanied by conjunctival congestion, and redness of the lips and oral cavity, with excessive enlargement of the tongue papillae. Three to four days after the onset of the disease a maculopapular rash develops on the extremities and spreads to the body, followed by induration of the skin, with scaling, particularly of the fingers and toes. There is usually non-purulent enlargement of the neck lymph nodes.[2,5]

The course of the disease is usually uncomplicated, but carditis, aseptic meningitis and arthritis may occur.[5] Antibiotics have no effect on the disease.[3-5]

Special investigations show an increase in all non-specific reagents,[5] but all examinations and tests for a specific organism or cause have so far been negative. Several researchers have isolated Rickettsia-related particles from biopsy material,[2,4,6] but an infective cause is questionable since the disease does not appear to be associated with particular geographical areas or seasons of the year and because no infective agents have been isolated. The diagnosis of MLNS is thus a clinical one.[3] If the criteria of the Japanese MLNS Research Committee are used, the diagnosis can be made with an 85% certainty.[4] Pyrexia must be present before a diagnosis can be made, as well as any 3 of the other 4 most common symptoms (Tables I and II).[3]

The mortality rate is 1 - 2%[6] and most deaths are due to cardiac complications, especially coronary artery aneurysms and thromboses.[3-5] At postmortem examination it has been found that aneurysmal dilatation of the coronary arteries was present in almost all cases.[3]

Infantile polyarteritis nodosa and MLNS appear to be histologically identical,[3,4] but both differ from adult polyarteritis nodosa.[4] Kawasaki disease is diagnosed clinically, whereas infantile polyarteritis nodosa is diagnosed by pathological investigation.[3]

No treatment has been found to be effective, but various treatment regimens with aspirin, steroids and cephalexin have been used. It is important that steroids should not be used as these have caused an increase in the incidence of coronary artery aneurysms.[7] In both our patients steroids were not used. Kato *et al.*[7] recommended aspirin as the drug of choice.

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