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Kawasaki Disease: A Retrospective Study

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Objective: The aim of this study was to appraise/review the criteria of diagnosis of Kawasaki Disease (KD), cardiac status and the management.

Design: A cross-sectional, retrospective and descriptive study.

Setting: Pediatric Department, Salmaniya Medical Complex.

Method: A retrospective review of children with diagnosis of KD between June 1992 and August 2002.

Result: Medical records of 34 children were reviewed. The median age at diagnosis was 31 ± 22.2 months. Male to Female ratio was 1.8:1. Thirty children were Bahraini while the rest were: two Indians, one Pakistani and one Filipino. All patients fulfilled the criteria for diagnosis of KD. Heart complications were recorded in sixteen patients (47%). One child presented with myocarditis but fifteen patients showed coronary artery dilatation (CAD). Children with CAD received aspirin therapy. The majority of the patients (33/34) received IVIG; seventeen patients (51%) had intravenous immune globulin (IVIG) as a single infusion.

Conclusion: All children fulfilled the criteria for diagnosing KD. Fifteen patients (44%) presented with CAD but none of them had aneurysm. Aspirin and IVIG were the main treatment. The majority of the patients with KD had resolution of CAD in less than six months, no patient had a relapse or developed heart complications in the follow up period.

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Kawasaki published the first few cases of KD in Japan in 1967[1]. Since it's original description KD has now been reported world-wide in children of all ethnic origins.

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Kawasaki believed that KD is a self-limited disease; however Tanaka disagreed with Kawasaki's beliefs because he discovered cardiac complications in autopsies of patients who died because of KD[2] .Thereafter in 1970, a Japanese nationwide survey of KD documented 10 autopsies cases of sudden cardiac death after KD[2,3,4]. In 1974, the link between KD and coronary artery aneurysm was established by Kawasaki in the first English language publication[5].

The Japanese ministry of health's criteria classify coronary arteries as abnormal if the internal diameter of a segment measures is equal or more than 3 mm in children less than five years old or greater than 4 mm in children more than five years old; if the internal diameter of a segment measures more than 1.5 times that of an adjacent segment; or if coronary lumen is clearly irregular[6]. The American heart association (AHA) classify aneurysm as small when internal diameter is less than 5 mm, medium if internal diameter is between 5 to 8 mm or large (giant) if internal diameter is more than 8 mm[7,8].

The aim of this study was to appraise/review the criteria of diagnosis of Kawasaki disease (KD), cardiac status and the management.

METHOD

All the records of the hospitalized patients diagnosed as KD were reviewed. The data collected included: the age at presentation, sex and nationality.

Inclusion and exclusion criteria:

Inclusion criteria

a. Children fulfilled the criteria of KD.
b. Children with atypical presentation of KD.

Exclusion criteria

a. Children with viral illness resembling picture of KD but laboratory results confirm viral infection.
b. Children with the features of KD and positive blood culture or CSF culture which is suggestive of bacterial meningitis or septicemia.
c. Children with clinical manifestations of KD and underlying systemic disease.

All the criteria for diagnosing KD were reviewed; duration of fever, presence of conjunctivitis, cervical lymphadenopathy, oral cavity changes or appearance of skin rashes. The review included the blood investigations such as ESR, WBC, Platelet counts on admission and one week after admission if available. We looked for gall bladder hydrops on ultrasonography. Furthermore the study reviewed the heart status considering ECG changes and two dimension-echocardiography findings; site and the size of coronary artery and the presence of any aneurysm.

Moreover the study looked for any heart complication that could have occurred during or after the treatment. Systemic or cardiac relapses were recorded.

We had reviewed the aspirin doses during and after the acute stage, Finally Intravenous immunoglobulin (IVIG) and the number of doses were assessed.

RESULT

A total of forty files with clinical impression of KD were reviewed. In six patients the diagnosis of KD was ruled out. Thirty four children were corresponding with the diagnosis of Kawasaki disease. The median age at presentation was 31 $\pm$ 22.2 months. Five of the children (14.7%) were more than five years of age. Male to female ratio was 1.8:1. Thirty of these children were Bahraini while the rest were: two Indians, one Pakistani and one Filipino.

All patients presented with fever, which lasted between 2 and 30 days with a median of 10.9 $\pm$ 5.6 days. The other five criteria of KD (cervical lymphadenopathy, rash, changes in extremeties, oral changes and conjunctivitis) were reviewed. Twenty- six patients (76.4%) had cervical lymphadenopathy. Twenty-nine patients (85.3%) had conjunctivitis and 25 patients (73.5%) had polymorphic rashes. Twenty-eight patients (82.3%) had oral changes and equal percentage was noticed to have erythema of palms and soles. However, only five patients (14.7%) of the patients developed peeling of hands, soles and perianal regions during hospitalization. The mean duration of peeling was 15 ±2 days from the start of illness.

Two female patients revealed atypical presentation of KD, one is six years old presented with fever for 19 days and evidence of myocarditis. She also had cervical lymphadenopathy and conjunctivitis. Her inflammatory markers showed ESR of 80 mm/hr and abdominal ultrasonography revealed gall bladder hydrops. The second patient is twenty one months old presented with fever, rash and erythema in the palms and soles. On echocardiography there was significant dilatation of right and left coronary arteries. The two patients were treated as KD and on follow up the first had no cardiac sequel, while the second patient did not show up after discharge.

Sixteen patients (47%) had abnormalities on echocardiography (Table I). One patient developed myocarditis, others had coronary artery dilatation (CAD). Twenty-three patients had electro-cardiogram (ECG) and eight of them showed ischemic changes; prolongation of PR interval and non-specific ST and T wave changes; three of these had no associated echocardiography abnormalities on admission or follow up (Table I). Echocardiography was done for all patients and the results showed that fifteen children (44%) had coronary artery dilatation while one patient presented with myocarditis. Seventeen patients (50%) with CAD had left CAD while the other seventeen patients had right and left CAD.

Table I

Echo findings in the 8 patients with significant ECG findings

Pts No.	ECG changes	Echo findings
1	T-wave changes	Normal
2	Low voltage QRS	CAD: Lt 0.55 cm
3	T wave changes	Normal
4	Left axis deviation (LAD)	CAD: Lt 0.40 cm, Rt : 0.30 cm
5	Low voltage, RSR pattern	FS: 23%, EF 48%, suggestive of myocarditis
6	Deep Q in lead III, ST changes in V_1, V_6	Normal
7	LAD, ST changes in V_1, V_6	CAD, Lt: 0.20 cm, Rt: 0.35 cm
8	Rt. axis deviation, T waves changes	CAD, Lt: 0.23 cm, Rt: 0.23 cm

In this study coronary artery dilatation (CAD) was seen without aneurysm. Children more than five years of age had CAD measuring more than 4 mm on left side. Children below five years of age, there left coronary artery ranged between 3 mm and 5.5 mm with a median of 3.8 mm while the range of right coronary artery was between 3.1 mm and 4.8 mm with a median of 3.5 mm. Fifteen patients (44%) had CAD but none had aneurysm.

Two patients with CAD their records did not show a clear period. Thirteen children required between one and 115 weeks with a median of 11.8 weeks for the CA dilatation to return to normal.

Acute phase reactant such as ESR was raised, median value 72 $\pm$ 27 mm/hour. WBC and platelets count was also raised: median WBC count was 13.8±4.6 × 10/L, median platelets count was 380 ± 155 ×10/L and 453± 273.3 × 10/L in the first and the second week respectively. Blood and urine cultures of all patients were sterile[9].

All patients except two received aspirin therapy. The doses of aspirin were <10 mg/kg/day in four patients and 30–35 mg/kg/day in two other patients. These children continued with the same dose until complete resolution of CAD as appeared on echocardiography; twenty-six patients had aspirin 90-100mg/kg/day at diagnosis. This high dose of aspirin was given for a mean period of 20 $\pm$ 18 days while the anticoagulant median dose was 7.5 mg/kg for a mean duration of 6 $\pm$ 4.5 months. Serum salicylates levels were measured in 11 patients only and found to be within the therapeutic level.

The patient with myocarditis was digitalized and remained on anti-failure treatment for some time and on the follow-up, this patient showed no abnormality on echocardiography.

Apart from one child, all patients had been commenced on intravenous immunoglobulin (IVIG), a total dose of 2 gram/kg. This child had all features of KD and high ESR.

However this patient showed neither abnormal echocardiography findings on admission nor follow up complications in the next three months.

More than half of our patients had IVIG as a single infusion. One patient had persistent CA dilatation after 2 gram/kg of IVIG and she therefore received a third dose. Those who were followed in the clinic showed no persistent CA abnormalities after discharge and none had systemic relapses.

We couldn't find any correlation between duration of fever, ESR status and the presence of coronary artery abnormality (P value: 0.668 and 0.226 respectively).

Abdominal ultrasonography was done on 27 patients, nine of whom were found to have gall bladder hydrops (33%).

No serious complications or relapses were found in our patients.

Eight patients developed sterile pyurea and one child had prolonged diarrhea but no organism isolated; Diarrhea resolved after KD treatment.

The duration of hospitalization was between 4 and 28 days and the median was 10 days.

DISCUSSION

Kawasaki Disease (KD) is an acute multisystem vasculitic syndrome of unknown etiology affecting infants and children. The most serious complication of KD is coronary artery aneurysm, which may lead to myocardial infarction and sudden death[4,9].

This study showed that fifteen patients (44%) had CAD, in a study done between 1986 and 1997 in one center in Kuwait, Abushaban et al reported 10 out of 135 (7.4%) of children with KD having coronary artery dilatation[10]. On the other hand, in a small descriptive study of Saudi children with KD, Muzaffer et al observed that 30% of children with KD had CAD and unusual complications[11].

In our study, two cases showed atypical presentation with prolonged fever and 2/5 of other criteria. The first case 6 years old girl had fever for more than two weeks, cervical lymphadenopathy, conjunctivitis and myocarditis and the second one twenty one months old girl with fever, rash, erythema of palm and soles and peeling. This girl had significant CAD. Levy et al described 17 cases of atypical KD with CA abnormalities but who did not fulfill 4/5 criteria to diagnose KD[12].

All children in this study underwent echocardiography on diagnosis. Children with CAD had at least weekly echocardiography in the acute stage, to monitor the size of coronary artery dilatation. After resolution of the CAD echocardiography was done every 3-6 months. Tizard and Brogan recommended echocardiography monitoring every 6-12 months while patients on anticoagulant dose (5-10 mg/kg/day) of aspirin[13,14]. Aspirin was

discontinued when the dilatation resolved on echocardiography. This study showed the mean of CAD is 3 mm. Apart from one patient who continued aspirin for 27 months; thirty-one patients had it up to a maximum of 11 months.

In our study six patients received less than 35 mg/kg of aspirin after they had been diagnosed as KD. However, these children were noticed to have neither persistent CA dilatation nor recurrence of fever.

Masaru et al revealed that prevalence of coronary abnormalities was inversely related to the total dose of IVIG and was independent of the aspirin dose[15]. Saulsbury compared high dose and low dose aspirin plus IVIG in the treatment of Kawasaki syndrome; twenty-four patients were started on high dose (80 – 100 mg/kg) which was given for a period of 6.1 $\pm$ 0.9 days then switched to low dose[16]. Forty-six children were started on low dose (3 – 5 mg/kg) of aspirin at the time of diagnosis and remained on this dose for the duration of treatment. The result of this study showed that none of the children who had no CA dilatation at time of diagnosis developed CA abnormalities after treatment with IVIG and either high or low dose aspirin.

Durongpisitkul et al have shown that single infusion of IVIG (2gr/kg) is superior to divided lower doses of IVIG (400 mg/kg/day for four consecutive days) in preventing CAD[17].

Thirty-four cases of KD in Bahrain during one decade leads one to state that KD had replaced rheumatic heart disease as the commonest cause of acquired heart disease in children similar to the situation in the USA and Japan[18].

This study showed that none of our patients had myocardial infarction or congestive cardiac failure. In our study no consistent relationship between ECG abnormalities and the presence of coronary artery dilatation, which may indicate a poor correlation between ECG changes, echocardiography findings and severity of disease. However the number of patients with ECG abnormality is small to make valid statistical analysis or draw meaningful conclusions in this regard.

Incidence of hydrops as shown in a study done by Madigal was 1/23 patients with KD and 8/250 in the Falcini review[19,9]. As we observed the incidence was much less than what we reported in our study.

CONCLUSION

All children fulfilled the criteria for diagnosing KD. Sixteen patients (47%) had heart complications (CAD and myocarditis). Aspirin and IVIG were the main treatment. Coronary artery dilatation resolved in the majority of these patients within six months and no further cardiac complications or mortality was reported. A future prospective study may give us a more realistic picture of the KD in Bahrain.

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