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Early Compared to Late Presentation of Kawasaki Disease

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Background/Objective: Kawasaki disease (KD) is vasculitis of unknown etiology that occurs predominantly in young children. The diagnosis is clinical and the most serious complication is coronary artery changes. Early recognition may reduce morbidity and mortality.

The aim of this study is to evaluate the diagnostic criteria and the incidence of coronary artery complications in KD diagnosed either early or late and to compare the incidence of KD with other forms of acquired heart disease and vasculitis.

Design: Retrospective Study.

Setting: Pediatric Department, BDF hospital, Kingdom of Bahrain.

Method: All patients diagnosed with Kawasaki disease from July 1997 to July 2002 were reviewed.

Result: The study was performed for five years, from July 1997 to July 2002. During that period twenty-three patients were admitted with Henoch Schonlein purpura; only one patient with acute rheumatic carditis was admitted.

Sixteen patients with KD were diagnosed. The age ranged from 5 to 63 months (mean = 9 months). The male to female ratio was (9:7). Six patients presented early (<7days) and 10 late (>7 days). All patients fulfilled the clinical criteria for KD. Fever and irritability were the commonest clinical findings in both groups and all had raised ESR and C-reactive proteins. Thrombocytosis was more common in the late diagnosis group. Coronary artery abnormalities) were similarly more common in the late diagnostic group. Five early (83%) versus six late (60%) responded to a single dose Intravenous gamma globulins (IVIG). At four years follow up period, there was no difference in coronary artery changes between the early and late presentation.

Conclusion: In this study, Kawasaki disease is the leading cause of acquired heart disease in the Kingdom of Bahrain. The diagnosis is clinical and early recognition and treatment reduces short-term morbidity. The long-term effect of Kawasaki disease on coronary artery disease remains unclear.

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Kawasaki disease (KD) is a self-limiting vasculitis of unknown etiology, which occurs predominantly in infants and young children; Tomisaku Kawasaki first described it in 1976[1]. The diagnosis is clinical and in 1990 the American Heart Association committee on rheumatic fever, endocarditis and Kawasaki disease gave the case definitions that are now generally accepted, see Table 1[2].

Table 1: Diagnostic Criteria for Kawasaki Disease

No	Criteria	Description
1.	Fever	Duration of 5 days or more
2.	Conjunctivitis	Bilateral, bulbar, non-suppurative
3.	Lymphadenopathy	Cervical > 1, 5cm
4.	Rash	Polymorphous, no vesicles or crusts
5.	Changes of lips or oral mucosa	Red cracked lips, "strawberry" tongue, or diffuse erythema of oropharynx
6.	Changes of Extremities	Initial stage: Erythema and oedema of Palms and soles Convalescent stage: Peeling of skin from finger tips

*Fever plus other four criteria fulfill the requirement for the diagnosis of KD in the absence of any other disease. Kawasaki Disease could be diagnosed with fewer than four of these features if coronary artery aneurysms are detected.

The most common complication is coronary artery aneurysm (CAA) and coronary artery dilatation that occurs 1-8 weeks after the onset of the disease. The prevalence of CAA in untreated children is 18-23%[3]. The risk of death from coronary thrombosis and myocardial infarction is greatest within the first 60 days[4]. Mortality improves due to earlier and better recognition and treatment[5].

Early diagnosis and treatment of KD is vital to reduce morbidity and mortality. Intravenous gamma globulins (IVIG) are the cornerstone of treatment and the Cochrane review of 2003 showed significant benefits with IVIG treatment[6].

The aim of this study is threefold. First is to evaluate the diagnostic criteria of KD[2]. Second is to evaluate the complications of the coronary arteries, early or late presentation. Third is to compare the incidence of KD with other forms of acquired heart disease and vasculitis during the study period.

METHOD

A retrospective study was performed using a computerized database to identify all patients admitted to Bahrain Defense hospital with a diagnosis of KD during five years, from July 1997 to July 2002. The charts were studied to evaluate the diagnostic criteria and the incidence of coronary artery complications of KD patients presenting either early or late. Data are shown as frequencies and means where appropriate.

RESULT

During five years period, from July 1997 to July 2002, sixteen patients with KD were diagnosed during the study period. Their ages ranged from 5 to 63 months (mean = 9 months), male to female ratio was 9:7. Six patients presented early (<7days) and 10 were late presenters (>7

days). All the patients fulfilled the clinical examination and laboratory diagnostic criteria for KD, see Table 2. All the sixteen patients had the following investigations: FBC, ESR, C-reactive protein and liver function tests, blood and throat swab cultures, as well as, urine microscopy and culture. Echocardiography was performed within 24 hours of admission and clinical diagnosis.

Table 2: Clinical Criteria for KD

Diagnostic Criteria	**Patients with early Diagnosis (n = 6)**		**Patients with late Diagnosis(n = 10)**	
	No	Percentage	No	Percentage
Fever	6	100%	10	100%
Skin rash	3	50%	4	40%
Conjunctivitis	2	33.3%	5	50%
Lymphadenopathy	1	16.7	3	30%
Change of lips or oral mucosa	4	66.7	4	40%
Changes of extremities	3	50%	6	60%
Irritability	6	100%	10	100%

Table 3: Thrombocytosis and Coronary Artery Abnormalities in KD

Diagnostic Criteria	**Patients with early Diagnosis (n = 6)**		**Patients with late Diagnosis(n = 10)**	
	No	Percentage	No	Percentage
Thrombocytosis	1	16.7%	4	40%
Coronary abnormalities	1	16.7%	4	40%

All patients had raised ESR and C-reactive protein. Thrombocytosis, defined as peripheral platelet count >500 x 10^9/L, was more common in the late diagnosis group, see Table 3. Coronary artery abnormalities, defined as coronary artery aneurysm (CAA) and/or coronary artery dilatation, compared to normal size cornary artery for the same age, see Table 3.

Patients received aspirin 30-50mg/kg/day until the fever subsided. A single dose of IVIG 2gm/kg during 10-12 hours was also administered immediately on making the clinical diagnosis. Five (83.3%) of the early diagnosis group compared 6 (60%) of the late group responded to the single dose IVIG. Patients who did not respond to the initial IVIG dose were given a second similar dose.

All patients were discharged after clinical improvement. Those with coronary abnormalities were discharged on aspirin 5 mg/kg/day for a minimum of 6 weeks. None of them had any significant residual coronary dilatation or aneurysms, all well at 4 year follow up.

During five years period, from July 1997 to July 2002, 23 patients were admitted with vasculitis due to Henoch Schönlein purpura and one patient was admitted with acute rheumatic carditis. During the same period, sixteen Kawasaki patients were admitted.

DISCUSSION

In this study, Kawasaki Disease is the commonest form of acquired heart disease and the second commonest cause of vasculitis in children in The Kingdom of Bahrain. In this study, the age at presentation of KD and male to female ratio is similar to other published studies in the region (Table 4). There is no significant difference in the clinical presentation of patients, whether they are presenting early or late; fever and irritability is the commonest symptoms in both groups. Thrombocytosis and coronary abnormalities were more common in late presentation (16% compared to 40%). Early presentation responded more favorably to a single dose of IVIG.

Table 4: Other Gulf studies of Kawasaki Disease

	Iran[7] 2006	Iran[8] 2005	Oman[9] 2003	Iran[10] 2001	Kuwait[11] 1999	KS[12] 1998	Kuwait[13] 1997	Israel[14] 1983	Kuwait[15] 1978
No.	113	25	39	50	135	29	5	13	2
M:F	2.1:1	M>F		2.2:1	1.54:1		1.5:1		
Age	<5yrs	(3.5-80) months	(6-30) Months	(18) months	(3 months-13yrs)		(5-36) months		

The difference in complications and response to IVIG in the early compared to late presentations appears to have no effect on medium to long-term follow up. This is in contradiction to other studiesthat have shown that patients treated earlier with IVIG had a better cardiac outcome, statistically less coronary changes at one year follow-up than those treated later[16]. The reason for this discrepancy is unclear. Whether there will be any future implications, accelerated coronary artery disease remains an interesting question because abnormal coronary physiology in patients with KD even in the absence of echocardiographic changes had been documented[17]. At present invasive testing cannot be recommended in the absence of echocardiographic coronary abnormalities.

Sometimes Kawasaki disease is resistant to IVIG and aspirin treatment; therefore, steroids are used in these cases[18,19]. None of the cases reported in this study was resistant to IVIG.

CONCLUSION

In this study, Kawasaki Disease is the leading cause of acquired heart disease. The diagnosis is clinical and early recognition and treatment is vital to reduce short-term morbidity and mortality. Long-term effect on coronary artery disease is unclear, but close observation is recommended.

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