Assessment and follow-up of coronary abnormalities in Turkish children with Kawasaki disease

Kawasaki hastalığı olan Türk çocuklarında koroner arter anomalilerinin saptanması ve izlemi

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Kawasaki disease (KD) is an acute self-limited febrile systemic vasculitis complicated by coronary and peripheral arterial aneurysms in 20-35% of untreated patients (1, 2). The diagnosis of the disease is based on a combination of symptoms and laboratory data (3). Children with incomplete KD and children with a variety of unusual or atypical complications are also at high risk for the development of coronary artery aneurysms (4). In this report, we describe the clinical features, and follow-up of eight patients with incomplete Kawasaki disease complicated with coronary artery abnormalities.

Patients with persisting fever at five days and coronary artery involvement are diagnosed as incomplete KD if they do not fulfill the criteria of the disease (2). We performed echocardiography in all patients after routine laboratory evaluation with electrocardiography, complete blood count, acute phase reactants, serum biochemistry and urinanalysis. Computerized tomography angiography is performed in children with coronary abnormalities. Conventional coronary angiography is performed 6 months after the diagnosis if coronary abnormalities persisted. Patient characteristics, demographic features, clinical presentation, diagnostic criteria, and treatment modalities are demonstrated in Table 1. All of our patients were treated with other diagnosis for several times and there was a mean of 16.4±2.8 days (range 7-40 days, median 14 days) delay between the start of symptoms and the diagnosis of KD (Table 1). The first cardiac manifestation was pericardial effusion in two patients (patients 1, 2) and mitral insufficiency in one patient (patient 4) (Table 2). We detected 22 coronary artery aneurysms at the time of diagnosis. After a mean follow-up time of 4.0±3.9 years total number of aneurysms decreased to 11. Coronary artery calcification was present in two patients (patient 1 and 3). We observed coronary artery stenosis and ectasia in patient 3 (Video 1. See corresponding video/movie images at www.anakarder.com). There was left ventricular aneurysm in patient 1. Myocardial perfusion imaging was normal in all patients. Upon these findings, successful coronary bypass surgery was performed in patient 3 at the age of 12 years (this child was treated beyond 10 days) and we decided to perform coronary surgery in patient 1 who was not treated at time of diagnosis. Other patients are observed clinically.

Kawasaki disease is a childhood vasculitis involving small and medium-sized arteries (4). There is no any specific tool for definite diagnosis of KD. For this reason diagnostic criteria depending on clinical features and nonspecific laboratory data for KD were developed. In any individual child, all the criteria need not be present at the same time. They may appear sequentially. Furthermore, not all children with KD develop the complete picture before coronary involvement is recognized. Also, patients with atypical onset KD may not develop the typical features for a long time, thus risking delay in diagnosis (5). Incomplete KD should be considered in all children with unexplained fever for ≥5 days associated with two or three of the principal clinical features of KD (2, 6). It is more common in young infants, making accurate diagnosis and timely treatment especially important in these young patients who are at substantial risk of developing coronary abnormalities (2). The diagnosis was incomplete KD in all of our patients and they were treated with other diagnosis for several times. There was a mean of 16.4±2.8 days (range 7-40 days, median 14 days) delay between the start of symptoms and the diagnosis of KD. In case of incomplete KD there may be a delay in diagnosis and treatment. The result is prolonged hospitalization, unnecessary use of antibiotics, anxiety, and loss of workdays for the parents. In addition to that, there is definite increase in morbidity with delay in treatment like development of coronary aneurysms and myocardial complications. Early detection and treatment would have prevented all such complications. We can conclude that KD should be suspected in any young child with persistent unexplained high fever that is associated with any of the principal clinical features of KD to prevent time delay in treatment and finally formation of coronary complications.

The long-term prognosis for children with KD depends on the specific nature of coronary artery or other cardiovascular involvement (3). Coronary artery lesions resulting from KD change dynamically with time (7, 8). Angiographic resolution 1 to 2 years after the onset of the disease has been observed in 50–67% of vessels with coronary aneurysms (2). In our study total number of coronary aneurysms decreased from 22 to 11 in number after a median follow-up time of 2.8 years (50%). Whereas aneurysm size tends to diminish with time, stenotic lesions that are

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Table 1. Clinical and demographic features of patients

Patient no	Gender	Age, years	Age at diagnosis	Clinical presentation	Previous diagnosis	Delay of diagnosis, days	Criteria of the disease other than fever	IVIG	Steroid	Salicylate therapy
1	M	5	2 years	Fever, LAP	Viral pancarditis	40	1	-	-	+
2	M	8.5	6 years	Fever, jaundice, LAP	Lymphadenitis, hepatitis, EBV infection	15	3	+	-	+
3	M	12	2 months	Fever, LAP	FUO	10	3	+	-	+
4	M	15	8 years	Fever, LAP, diarrhea	Lymphadenitis	7	3	+	-	+
5	M	6	1 year	Fever, eye injection	AGE, meningitis	20	2	+	-	+
6	M	2	1 year	Fever, rash	Scarlet fever	15	3	+	-	+
7	M	2	1 year	Fever, diarrhea	FUO, hepatitis	13	1	+	-	+
8	F	6	5 years	Fever, arthritis	ARF	11	2	+	+	+
		7±4.5 years	3±3 years			16±10 (median 14)	2±1 (median 2.5)			

AGE - acute gastroenteritis, ARF - acute rheumatoid fever, EBV - Ebstein-Barr virus, F- female, FUO - fever of unknown origin, IVIG - intravenous immunoglobulin, LAP - lymphadenopathy, M - male

Table 2. Details of cardiologic manifestations

	CA involvement at time of diagnosis	Cardiac manifestation at time of diagnosis	Giant aneurysm	Follow-up			
				Echocardiography	Coronary CT angiography	Conventional coronary angiography	Perfusion scintigraphy
1	-	Pancarditis	2	LAD aneurysm, IVS-apical hypokinesia	LAD-Cx aneurysm	LAD-LCA-Cx aneurysm, LV apicobasal hypokinesia	Normal
2	+	Pericarditis	None	LAD dilatation	LAD dilatation, LAD aneurysm	LAD dilatation	Normal
3	+	Coronary artery		Normal	RCA aneurysm, LAD calcification, RCA stenosis	LAD stenosis, RCA dilatation	Normal
4	-	Mitral insufficiency	None	-	RCA; LAD aneurysm	LAD, RCA, Cx aneurysm	Normal
5	+	CA dilatation, aneurysm	1	LAD dilatation	LAD dilatation, calcification, RCA dilatation	LAD aneurysm	Normal
6	+	CA dilatation	None	LAD dilatation	LAD dilatation	LAD dilatation	Normal
7	+	CA dilatation	1	LAD dilatation	LAD dilatation	LAD dilatation	Normal
8	+	CA dilatation	1	LAD dilatation	LAD, RCA, Cx aneurysm	LAD, RCA aneurysm	Normal

CA- coronary artery, CT- computerized tomography, Cx- circumflex artery, IVS- interventricular septum, LAD- left anterior descending artery, LV- left ventricle, RCA- right coronary artery

secondary to marked myointimal proliferation are frequently progressive. The prevalence of stenosis continues to rise almost linearly over time (9). The highest rate of progression to stenosis occurs among patients whose aneurysms are large (9). In our study, we observed coronary stenosis in only one patient (12.5%). This patient's aneurysm was not a giant one. Since the number of cases was limited we could not make a risk analysis and an interpretation about risk factors of resolution of aneurysms and stenotic lesions. However, we can conclude that coronary aneurysm number may decrease in time.

In conclusion, Kawasaki Disease should be strongly considered in children presenting with fever for more than one week even they do not fulfill classic criteria for the diagnosis of KD, coronary artery lesions change dynamically in time. Since coronary artery aneurysms produce the most serious sequelae of Kawasaki disease all patients must be observed carefully for coronary artery lesions.

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