Brief Report

Clinical and Epidemiological Characteristics of Children with Kawasaki Disease in Turkey

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Summary

Background: Kawasaki disease (KD) is the leading cause of acquired heart disease in childhood in the developed countries. The objective of this study is to describe the clinical and epidemiological characteristics of children with KD in Turkey.
Methods: The medical records of 24 patients treated for KD between January 1994 and June 2009 at Ankara University Medical School, Turkey were reviewed.
Results: The male-to-female ratio was 1.4 : 1. The median age at diagnosis was 2 years (range: 6.5 months to 11 years). Conjunctivitis and changes in the lips and oral cavity were seen in 21/24 (87.5%), cervical lymphadenopathy 17/24 (70.8%), polymorphous rash 16/24 (66.7%) and peripheral changes in 12/24 (50%). Coronary artery abnormality (CAA) was observed in 8/24 (33.3%) cases. CAA was seen in both the complete and incomplete groups with similar frequency (31.3% vs. 37.5%, respectively).
Conclusions: KD must be kept in mind in the differential diagnosis of infants with prolonged fever.

Key words: children, Kawasaki disease, prolonged fever.

Introduction

Kawasaki disease (KD) is an acute systemic vasculitis of unknown cause that primarily affects children under the age of 5 years [1, 2]. Coronary artery aneurysms develop in 15–25% of untreated patients, and coronary artery abnormalities (CAAs) present a risk for coronary thrombosis and myocardial infarction [3, 4].

KD has an incidence of 90/100 000 in children below the age of 5 years in Japan, 8.9/100 000 in USA and 3.7/100 000 in Australia, and an increasing incidence over time has been observed in some countries [5–9]. From Turkey, there has been limited published data regarding KD such as case reports. We only have the knowledge about KD that it constitutes the 9% of the childhood vasculitides [10].

The aim of this article is to describe the epidemiology, clinical features, management and outcomes of KD and to increase awareness of it across Turkey, a developing country.

Methods

We reviewed the medical records of 24 patients treated for KD between January 1994 and June 2009 at the Department of Pediatric Infectious Disease in Ankara University Medical School, Ankara, Turkey. Our hospital is in the capital city of Turkey and it is one of the biggest children referral hospitals. So, our patients' features almost reflect our country's profile.

Diagnosis was reviewed with reference to the criteria of the American Heart Association (AHA) [11]. Classical KD was diagnosed when four or more criteria were present with at least 5 days of fever, others being classified as incomplete.

Results

All 24 patients with KD treated during the study period were included. Most of the patients (87.5%) were diagnosed between 2003 and 2009. The findings of this study are summarized in Tables 1–3.

The 22 cases (91.7%) treated with intravenous immunoglobulin (IVIG) at a dose of $2\,g\,kg^{-1}$ [2 children received only IVIG, 19 received high dose of acetylsalicylic acid (ASA) with IVIG and 1 child received IVIG, ASA and warfarin]. The only two cases treated with high-dose ASA without IVIG. Of the two patients who did not receive IVIG, one was the late presenter and the other had anaphylaxis at the beginning of the IVIG infusion. In 23 patients (95.8%), the fever was resolved in the first 48 h after

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therapy, but in 1/24 (4.2%) it took ≥72 h for the fever to subside, despite repeated doses of 2 g kg^{-1} IVIG.

CAA was observed in 8/24 (33.3%): six had ectasia in left coronary artery, one had aneurysms in left coronary artery and one had aneurysms in left and right coronary arteries with mitral valve regurgitation. CAA was seen in both the complete and incomplete groups with similar frequency (31.3% vs. 37.5%, respectively). Two of the eight (25%) patients whose disease type was complete had persistent CAA during the follow-up. All patients are still alive.

TABLE 1
Age and gender distribution of the patients

Variable	Complete ($n=16$)	Incomplete ($n=8$)	Total ($n=24$)
Sex, *n* (%)			
Male	11 (68.8)	3 (37.5)	14 (58.3)
Female	5 (31.2)	5 (62.5)	10 (41.7)
Age, *n* (%)			
< 1 year	2 (12.5)	2 (25)	4 (16.7)
> 5 years	4 (25)	1 (12.5)	5 (20.8)

TABLE 2
Clinical findings of the cases

Clinical findings	*n* (%)
Findings of diagnostic criteria	
Fever	24 (100)
Conjunctivitis	21 (87.5)
Changes in the lips and oral cavity	21 (87.5)
Cervical lymphadenopathy	17 (70.8)
Polymorphous rash	16 (66.7)
Extremity changes	12 (50)
Other findings	
Sterile pyuria	8 (33.3)
Elevated liver enzymes	8 (33.3)
Perineal desquamation	5 (20.8)
Jaundice	3 (12.5)
Gallbladder hydrops	3 (12.5)
Aseptic meningitis	1 (4.2)

Discussion

KD is an acute febrile vasculitis of unknown etiology, although an infectious or toxic triggering agent is suspected by some authors [12]. Although the real incidence of KD in Turkey is not known, KD perhaps is more common than it has been diagnosed and reported. There are only a few case reports from Turkey in the literature, so this report is important for being the first study of KD undertaken in Turkey [13–15].

The incidence of KD presents regional variations that oscillate between 90 and 108 in 100 000 children below the age of5 years in Japan and 10 in the USA [5, 16, 17]. Reports from the United Kingdom in 2002 indicate an incidence of 8.1 for children with KD under the age of 5 years, which is more than double the incidence of 3.4 identified in 1990 [9, 18]. Similarly, a rising incidence has been observed in Japan, from 73.8 in 1987 to 111.7 in 1998 [16]. In our study, 3/24 of the patients were diagnosed between 1994 and 2002 and 21/24 were between 2003 and 2009. These data show a real increase in incidence beyond increased physician awareness in Turkey like the other countries. However, it could be associated with the environmental components such as infectious and toxical factors, because its etiology is still unknown.

We observed a male predominance and similar age distribution resembling the previous studies [7–9]. The incomplete form of KD is varying from 15% to 56.6% in Taiwan, Australia, Canada and Korea [7, 19–21]. The percentage of incomplete KD increased from 6.7% to 17.9% from 1987 through 2000 [22]. In our report, the ratio of incomplete cases was 33.3% and 75% of those patients were diagnosed in last 4 years. The true reason for this increase remains unclear, but it may be associated with the increased awareness of the physicians. The median age of the patients with incomplete KD was less than the patients with complete KD, like the cases in previous studies [7, 22, 23].

Conjunctivitis and changes in the lips and oral cavity were the most common major clinical manifestations except fever in our patients similar to

TABLE 3
Laboratory findings of the cases

Variable[a]	Complete ($n=16$)	Incomplete ($n=8$)	Total ($n=24$)
Haemoglobin (g dl^{-1})	10.5 ± 1.14 (8.8–13.5)	10.4 ± 0.98 (8.9–11.9)	10.5 ± 1.07 (8.8–13.5)
White blood cell (× 10^9 l^{-1})	14.9 ± 6.45 (4.2–33.2)	19.0 ± 9.41 (7.4–29.3)	16.3 ± 7.62 (4.2–33.2)
Platelet count (× 10^9 l^{-1})	447 ± 130 (97–562)	454 ± 80 (275–500)	452 ± 114 (97–562)
ESR (mm h^{-1})	80 ± 37.25 (14–136)	71 ± 23.65 (46–110)	77 ± 13.1 (14–136)
CRP (mg dl^{-1})	13.1 ± 11.01 (0.6–27.1)	9.8 ± 8.83 (2–24.2)	12.1 ± 10.26 (0.6–43)

[a]Laboratory values are given as mean ± SD (minimum–maximum). ESR, erythrocyte sedimentation rate. CRP, C-reactive protein.

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the literature, but polymorphous rash and peripheral changes were observed less than the previous studies [6, 19, 24, 25]. The laboratory findings of our patients were similar to the patients in the other studies [7, 23, 24]. However, we found that the white blood cell counts were higher in patients with incomplete KD than with complete KD, and the platelet counts at admission and during convalescent period were higher in patients with CAA than without CAA. Yeo *et al*. [21] determined the relationship between CAA and high platelet and white blood counts and between CAA and incomplete KD. But, we did not find statistically significant relationship between CAA and high platelet and white blood counts.

In conclusion, the diagnosis of the disease in infants is usually difficult, since they are more likely to have incomplete presentation. This can lead to a delay in diagnosis and treatment of KD, which has been suggested to be a major contributor to the development of CAA. Therefore, KD must be kept in mind in the differential diagnosis of infants with prolonged fever.

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