

Case Report

Kawasaki Disease in a Kuwaiti Family

Maha Bourusly, Naheda Jawad

Department of Pediatrics, Al-Amiri Hospital, Ministry of Health, State of Kuwait

Kuwait Medical Journal 2005, 37 (2): 110-112

ABSTRACT

Kawasaki disease (KD) is one of the most common vasculitis of childhood. We describe the occurrence of Kawasaki disease in five children belonging to the same family, within a period of four months. Between the months of October 2000 and January 2001, five Kuwaiti children, belonging to the same extended family, were diagnosed with Kawasaki disease. All children fulfilled at least four of the five additional criteria for the diagnosis of Kawasaki disease. They received intravenous immunoglobulins commencing within the first 24 hours of admission in addition to salicylates. The duration of fever ranged between one and eight days. Most patients reported to have marked irritability and one had signs of meningeal irritation. Another child had

severe genital erythema and peeling which subsided one day after the initiation of treatment. The laboratory findings showed raised platelet count after the first week in most patients. All throat swab cultures yielded -hemolytic *Streptococcus* group A organisms. However, the ASOT titer was not raised. They all received intravenous immunoglobulins and salicylates and made a good clinical recovery. One child had a relapse ten months later and developed dilatation of the left descending coronary artery but no aneurysm. The cause of Kawasaki disease remains unclear after thirty years of research. The results emphasize the possibility of both genetic predisposition and environmental factors in the etiology of Kawasaki disease.

KEYWORDS: -hemolytic *Streptococcus*, Kawasaki disease, relapse, vasculitis**INTRODUCTION**

Kawasaki disease (KD) is one of the most common vasculitis of childhood. It is characterized by prolonged fever, diffuse mucosal inflammation, edema of the hands and feet, skin rash, non-purulent conjunctivitis and cervical lymphadenopathy^[1]. It is now being recognized as a leading cause of acquired heart disease in children in North America and Japan^[2]. In this short report, we describe the occurrence of Kawasaki disease in five children belonging to the same family, within a period of four months. This emphasizes the possibility of both genetic predisposition and environmental factors in the etiology of Kawasaki disease.

CASE REPORT

Between the months of October 2000 and January 2001, five Kuwaiti children, belonging to the same extended family and living in the same household, were diagnosed as having Kawasaki disease according to the diagnostic criteria of the Center for Disease Control (Table 1). The pedigree of this family is shown in Fig. 1. Three girls and a boy presented in October 2000 with fever for at least four days and were initially diagnosed as having scarlet fever. They were therefore, prescribed antibiotics with no clinical improvement. All four children fulfilled at least four out of the five additional criteria essential for the diagnosis of

Kawasaki disease.

The fifth patient presented three months later in January 2001, with fever and also fulfilled four of the five additional criteria. All five children were admitted to the hospital and blood samples were collected for the following: complete blood count (CBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), liver function test (LFT), anti-streptolysin O titer (ASOT), virology study, and blood culture. Throat swab culture, urinalysis and urine culture were also taken. An Electrocardiogram (ECG) and a chest X-ray were also done followed later, by an echocardiograph at two weeks and two months from the onset of the first symptoms to detect any coronary artery lesion. All patients received intravenous immunoglobulins (IVIG) in a dose of 2 grams/kg commencing within the first 24 hours of admission in addition to salicylates in a dose of 30 mg/kg initially, which was then reduced to 5 mg/kg, once the fever subsided.

RESULTS

Table 2 summarizes the clinical features and laboratory findings in all the five children. The duration of fever before admission ranged between one and eight days and cases 2 and 3 had the longest duration of fever. All patients were reported to have marked irritability except case 4.

Address correspondence to:

Dr. Maha Bourusly, DCH, MRCPCH (Kuwait Board of Pediatrics) Al-Sabah Hospital, Pediatric Department NBK, PO Box 13041 - Safat - 4078. Kuwait. Tel: 4818219 - 4835826, E-mail: m_bourusly@yahoo.com

Table 1
Diagnostic Criteria for Kawasaki Disease

- A. Fever of five or more days' duration.
- B. Presence of four of the following five conditions:
- (1) Bilateral non-purulent conjunctivitis
 - (2) Mucosal inflammation including sore/cracked lips, injected pharynx, or strawberry tongue
 - (3) Changes in the peripheral extremities: erythema of the palms and soles, desquamation of the fingers and toes, and peripheral non-pitting edema
 - (4) Polymorphous rash
 - (5) Cervical lymphadenopathy
- C. Exclusion of streptococcal and staphylococcal infection

Case 1, in addition, showed signs of meningeal irritation. Case 4 had severe genital erythema and peeling, which subsided one day after the initiation of IVIG treatment.

The laboratory findings showed the highest ESR in case 1. The platelet count was raised above $448 \times 10^9/L$ after the first week in hospital in all the patients except in case 5, where it was only raised to $314 \times 10^9/L$. All throat swab cultures yielded -hemolytic *Streptococcus* group A organisms but the ASOT titer was not raised.

All the children made a good clinical recovery. There were no ECG or echocardiographic abnormalities detected in any of the patients.

Case 5 had a relapse of KD in August 2001, nearly 10 months after the first episode. He received IVIG treatment again within the first 10 days of fever but unfortunately his baseline Echocardiograph, done within two weeks from the onset, showed dilatation of the left descending coronary artery but no aneurysm. Currently he is on salicylates at a dose of 5 mg/kg once daily.

DISCUSSION

The cause of KD still remains unclear after thirty years of research. The epidemiological studies performed on patients with KD have always suggested an infectious agent although this could not be confirmed or substantiated by the isolation of a specific organism^[3,4].

In our patients, the simultaneous occurrence of KD in four patients living in the same household strongly suggests exposure to a common environmental factor, which might be infective, dietary, or even environmental pollution^[5]. In the previous reports of KD in families, the disease developed within 10 days after the onset in the index case, which suggested that the siblings could have been exposed to an unknown etiological factor at the same time^[6,7]. The recurrence of Kawasaki disease in Case 5, which was associated with coronary artery lesion, further supports the diagnosis of Kawasaki disease in the family^[8,9].

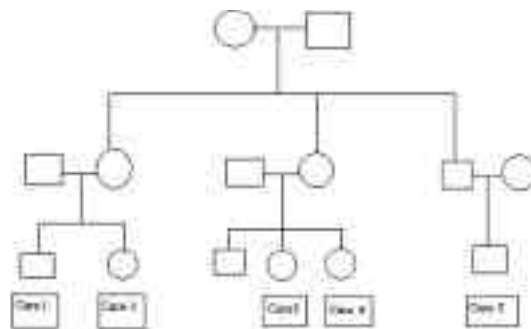


Fig. 1: Family pedigree indicating the relationship between the five patients with Kawasaki disease

In our report, four out of five patients presented at the same time and the fifth child presented 2-3 months later, which might suggest a remarkable susceptibility to KD, most probably due to genetic factors. Genetic influences on the nature and magnitude of the immune response in individuals may underlie the susceptibility to KD. Kato *et al* evaluated HLA antigens in KD in a Japanese population and found HLA-BW22 to be statistically more common in patients with KD as compared to control subjects^[10]. Of interest are the clinical, pathological and immunological similarities between KD and streptococcal infections such as scarlet fever and staphylococcal toxic shock syndrome^[11].

All our patients had positive throat swab cultures for -hemolytic *Streptococcus* group A. This supports the widely debated theory of the presence of super antigens, which trigger the cascade of events leading to KD. Anderson *et al*, reported members of the same family who presented with clinical and laboratory features of KD and also had evidence of streptococcal infection and concluded that KD could be precipitated by streptococcal infection^[12].

CONCLUSION

Although the etiology of KD is still unknown, the epidemiological, immunological and clinical features of the disease suggest an infectious agent, which possibly triggers an immunologically mediated vasculitis in children with genetic susceptibility to KD.

The occurrence of a number of cases on the same day or within a few days of the onset of the first case suggests a co-primary infection due to an exposure to the same etiological factor. The role of streptococcal infection, as possible triggering infectious agent, needs further study.

The late development of KD in members of the same family, months from exposure to the first index case or relapse of KD in the same patient strongly indicates genetic susceptibility to the

Table 2

Clinical manifestations and laboratory parameters of the five patients with Kawasaki Disease

	Patient no. (Sex)				
	Case 1 (Female)	Case 2 (Female)	Case 3 (Female)	Case 4 (Male)	Case 5 (Male)
Date of presentation	Oct. 2000	Oct.2000	Oct.2000	Oct.2000	Jan.2001
Age at onset (Years)	4.5	7.1	5	3.5	4.6
Duration of fever on admission (days)	6	7	8	4	1
Clinical Manifestations:					
- Bilateral non-purulent conjunctivitis	+	+	+	+	+
- Changes in mucosa of oropharynx	+	+	+	+	+
- Edema of hands and feet	+	+	+	-	-
- Polymorphous rash	-	+	-	+	+
- Cervical lymphadenopathy	+	+	+	+	+
Laboratory Findings:					
WBC ($\times 10^9/L$)	10.7	9.7	9.5	10.9	6.9
Hemoglobin (g/dl)					
- initial Hb	11.2	13.6	12.0	12.6	13.0
- later Hb	11.7	12.6	12.9	12.0	10.6
Platelet count ($\times 10^9/l$)					
- initial platelets	411	411	242	252	119
- later platelets	448	510	510	542	314
Erythrocyte sedimentation rate (mm/hr)	52	42	31	45	32

disease. Therefore, a high index of suspicion is necessary when dealing with siblings or close relatives of children diagnosed with KD, who present with fever.

It is probably worthwhile to treat patients in whom it is difficult to distinguish between

streptococcal infection and KD to prevent the occurrence of late complications of coronary artery abnormalities.

REFERENCES

1. Kawasaki T, Kosakai F, Okawa S, Shigematsu I, Yanagawa H. A new infantile acute febrile mucocutaneous lymph node syndrome (MLNS) prevailing in Japan. *Pediatrics* 1974; 54:271-276.
2. Freeman AF, Shulman ST. Recent developments in Kawasaki disease. *Curr Opin Infect Dis* 2001; 14:357-361.
3. Levin M. Kawasaki disease: Recent advances. *Arch Dis Child in Childhood* 1991; 66:1369-1374.
4. Fatica NS, Ichida F, Engle MA, Lesser ML. Rug shampoo and Kawasaki disease. *Pediatrics* 1989; 84:231-234.
5. Ichida F, Fatica NS, O'Loughlin JE, *et al.* Epidemiologic Aspects of Kawasaki disease in a Manhattan Hospital. *Pediatrics* 1989; 84:235-241.
6. Fujita Y, Nakamura Y, Sakata K, *et al.* Kawasaki disease in families. *Pediatrics* 1989; 84:666-669.
7. Elamin A. Kawasaki disease in a Sudanese family. *Ann Trop Paediatr* 1993; 13:263-268.
8. Zhang T, Yanagawa H. Factors related to cardiac sequelae of Kawasaki disease. *Eur J Pediatr* 1999; 158:694-697.
9. Matsubara T, Furukawa S, Ino T, Tsuji A, Park I, Yabuta K. A sibship with recurrent Kawasaki disease and coronary artery lesion. *Acta Paediatr* 1994; 83:1002-1004.
10. Kato S, Kimura M, Tsuji K. HLA antigens in Kawasaki disease. *Pediatrics* 1978; 61:252-255.
11. Akiyama T, Osawa N. Possible role of streptococcus pyogenes in mucocutaneous lymph node syndrome XII. Variable responses of platelets in MCLS seem to be explainable by streptococcal pyrogenic exotoxin. *Acta Paediatr Jpn* 1991; 33:20-26.
12. Anderson DG, Warner G, Barlow E. Kawasaki disease associated with streptococcal infection within a family. *J Paediatr Child Health* 1995; 31:355-357.