

The prevalence of allergy in Kawasaki disease

KAWASAKI disease (KD) is an acute febrile illness of unknown cause which occurs primarily during infancy and early childhood (1). Coronary artery dilation or aneurysm develops in approximately 15–25% of affected children, and this may lead to myocardial infarction and sudden death.

It has been reported that there is an association between KD and atopic dermatitis (2). We have reported three siblings with KD who developed primary or recurrent illness (3). All the siblings in this family had allergic diseases including bronchial asthma and atopic dermatitis. Moreover, Japanese patients with a history of KD have been reported to have a greater tendency to develop allergic disease than a control population (4). Therefore, we carried out a detailed retrospective investigation of the prevalence of allergic diseases among children who had acquired KD and their parents.

■ We obtained data from the medical records of KD patients who had been admitted to our hospitals. There were 512 children, 296 boys (58%) and 216 girls, aged between 1 month and 8 years (mean 2 years) admitted to Juntendo University Hospital (Japan) and its branch hospitals during an 11-year period from January 1982 to March 1993. All patients met the criteria for KD. Allergic diseases were defined as follows:

- bronchial asthma: three or more separate episodes of coughing and wheezing
- atopic dermatitis: noninfectious, chronic or chronically relapsing, itchy dermatitis lasting at least 3 months with characteristic features and distribution
- allergic rhinitis: recurrent nasal discharge or blockage with attacks of sneezing
- drug allergy: urticaria, angioedema, or anaphylaxis attributed to ingestion of a drug.

■ Statistical analysis was performed with the chi-square test among groups.

■ As shown in Table 1, 194 KD patients (37.9%) had at least one allergic disease, 85 (16.6%) had a mother with a history of at least one allergic disease, and 49 (9.6%) had a father with a history of at least one allergic disease. We divided all KD patients into four groups by age: patients younger than 1 year old, those between 1 and 2 years old,

Table 1. Prevalence of allergic diseases

	Patient	Mother	Father
Allergic diseases*	194 (37.9)	85 (16.6)	49 (9.6)
Bronchial asthma	102 (19.9)	20 (3.9)	14 (2.7)
Allergic rhinitis	2 (0.4)	49 (9.6)	30 (5.9)
Atopic dermatitis	108 (21.1)	15 (2.9)	8 (1.6)
Urticaria	7 (1.4)	11 (2.1)	10 (2.0)
Drug allergy	3 (0.6)	5 (1.0)	4 (0.8)

*Total number of patients who had at least one allergic disease; (): %.

those between 2 and 3 years old, and those older than 3 years. Among the KD patients who were younger than 1 year old, 65 (39.8%) had mothers with a history of allergy. This was the highest prevalence among the groups ($P < 0.05$). However, there were no significant differences among the patient groups with regard to history of allergic disease in the fathers.

Sixty-nine patients (13.4%) had coronary artery lesions detected by two-dimensional echocardiography, and 17 patients (3.3%) had recurrent episodes of KD. There were eight families in which siblings were affected by KD. However, there were no significant differences in the incidence of allergic diseases among these groups.

■ We found in this study that the incidence of allergic disease in KD patients was as high as 37.9%. It has been reported that the incidences of

Kawasaki disease patients maternally inherit some aspect of the immune response which is also present in patients with atopic conditions.

allergic diseases in healthy Japanese children aged 1 year and 2 years are 20.1% and 26.1%, respectively (5). We also found that a majority of KD patients who were younger than 1 year old had mothers with a history of allergy. It has been reported that Japa-

nese and American patients with a history of KD have had a greater tendency to develop allergic diseases than a control population (2, 3). We have also demonstrated that serum levels of IgE are elevated in patients with acute KD (6). Thus, there appears to be some relationship between KD and allergic diseases.

Recently, segregation analysis has consistently suggested the presence of a major gene that influences atopy and IgE levels, and that the risk of

atopy is higher for children of atopic mothers than for those of atopic fathers (7). A major gene regulating serum IgE has previously been mapped to chromosome 5q31-q33 (8).

Although the cause of KD remains unknown, the presence of an infectious agent has been suggested by the epidemiologic and clinical features of the illness (9). Recently, it has been reported that T helper (Th)1 and Th2 subsets are implicated in the regulation of many immune responses. Some infectious agent might influence Th1 and Th2 balance, leading to the development of allergic diseases.

Previous studies have found no consistent association between HLA antigens and KD, but some reports of sibling cases (3) and two-generation cases (10) suggest the presence of a yet unidentified genetic basis for disease susceptibility. Younger children are thought to be influenced more by the genetic factor than by the infectious agent. KD patients might maternally inherit some aspect of the immune response that is also shared by patients with atopic conditions. Further work is necessary to clarify the actual relationship of KD to allergy.

Key words: allergic disease; Kawasaki disease.

T. MATSUBARA*, Y. FUJITA, T. SATO, K. SASAI, S. FURUKAWA

*Department of Pediatrics

Yamaguchi University School of Medicine

1144 Kogushi

Ube, Yamaguchi 755

Japan

Tel. 81-836-22-2258

Fax: 81-836-22-2257

E-mail: tmatsu@po.cc.yamaguchi-u.ac.jp

Accepted for publication 23 March 1998

Copyright © Munksgaard 1998

ALLERGY 1998;53:815-816

REFERENCES

1. Kawasaki T, Kosaki F, Osawa S, Shigematsu I, Yanagawa S. A new infantile acute febrile mucocutaneous lymph node syndrome (MLNS) prevailing in Japan. *Pediatrics* 1974;54:271-6.
2. Brousseau CL, Newburger JW, Burns JC, et al. Increased prevalence of atopic dermatitis in Kawasaki disease. *Pediatr Infect Dis J* 1988;7:863-6.
3. Matsubara T, Furukawa S, Ino T, et al. A sibship with recurrent Kawasaki disease and coronary artery lesion. *Acta Paediatr* 1994;83:1002-4.
4. Matsuoka S, Tataru K, Nakagawa R, Mori K, Kuroda Y. Tendency toward atopy in Kawasaki disease. *Eur J Pediatr* 1997;156:30-2.
5. Arita M, Mikawa H, Shirataka M, Takahashi K, Hayasawa H, Tomita M. Epidemiological research on incidence of atopic disease in infants and children in relation to their nutrition in infancy [in Japanese]. *Arerugi* 1997;46:354-69.
6. Furukawa S, Matsubara T, Motohashi T, et al. Increased expression of Fc ϵ R2/CD23 on peripheral blood B lymphocytes and serum IgE in Kawasaki disease. *Int Arch Allergy Appl Immunol* 1991;95:7-12.
7. Cookson WOCM, Young RP, Sandford AJ, et al. Maternal inheritance of atopic IgE responsiveness on chromosome 11q. *Lancet* 1992;340:381-4.
8. Marsh DG, Neely JD, Breazeale DR, et al. Linkage analysis of IL-4 and other chromosome 5q31.1 markers and total serum immunoglobulin E concentrations. *Science* 1994;264:1152-6.

9. Yanagawa H, Nakamura Y, Yashiro M, et al. A nationwide incidence survey of Kawasaki disease in 1985-1986 in Japan. *J Infect Dis* 1988;158:1296-1301.

10. Iwata F, Hanawa Y, Takashima H, Shimoura K, Nishibayashi Y. Kawasaki disease in a father and son. *Acta Paediatr Jpn* 1992;34:84-6.

A strange case of "tuna allergy"

A 19-YEAR-OLD boy presented at this allergy department in September 1997 with a clinical history of several episodes of angioedema of the penis and scrotum from the age of 4 to the age of 8 years; all these episodes took place about 2 h after the ingestion of different brands of tuna canned in olive oil. The patient had tolerated this food well from the age of 8 up to the age of 17 years, when intolerance of canned tuna in olive oil reappeared; in the last months, such food induced several episodes of angioedema of the lips, hands, and/or penis/scrotum. The patient never experienced similar episodes after the ingestion of other foods, and he tolerated all other fish (sole, cod, trout, etc.) well. He did not suffer from respiratory allergy, as shown by negative clinical history and negative skin prick test (SPT) with commercial extracts of the most common airborne allergens present in this geographic area. Moreover, he did not report any drug-induced adverse reaction.

The patient underwent SPT with a large panel of commercial food extracts (Bayer), which included tuna, cod, salmon, and olive oil; no reactivity was observed. After informed consent was obtained, an open oral challenge with increasing doses of fresh cooked tuna was carried out; the boy

A patient with suspected tuna allergy was found to have tartrazine intolerance.

tolerated up to 80 g of tuna without consequence. In view of these findings, double-blind, placebo-controlled, peroral challenges with a large spectrum of food additives were carried out (sub-

stances and doses are summarized in Table 1). Challenges were performed by established procedures (1-3) with some modifications. Increasing doses of each food additive (or placebo) were given at 1-h intervals up to the maximum scheduled dose unless a positive response was obtained. Consecutive substances were tested 1 week apart. All preparations were given in identical opaque capsules prepared by the local hospital pharmacy. At each provocation session, the patient spent at least