Journal of the Formosan Medical Association (2015) 114, 72–76

Available online at www.sciencedirect.com

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journal homepage: www.jfma-online.com

ORIGINAL ARTICLE

Transmission of acute infectious illness among cases of Kawasaki disease and their household members

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Received 21 April 2014; received in revised form 10 July 2014; accepted 21 July 2014

KEYWORDS
household;
Kawasaki disease;
transmission

Background/purpose: Kawasaki disease (KD) is a disease of unknown cause and the causative agent is most likely to be infectious in nature. To investigate the household transmission pattern of infectious illness and etiology, we thus initiated a prospective case and household study.

Methods: We enrolled KD cases and their household members from February 2004 to September 2008. The KD cases and their household members accepted questionnaire-based interviews of the contact history, signs of infection, and symptoms to check whether clusters of infectious illness occurred.

Results: A total of 142 KD cases and 561 household members were enrolled. Among the 142 KD cases, 136 cases (96%) were typical KD, and six (4%) were atypical KD. Of the 561 household members, 17% were siblings, 46% were parents, 18% were grandparents, and the others were cousins or babysitters. Prior to the onset of their KD illness, 66% (94/142) KD cases had contact with ill household members. On the same day of the onset of KD cases' illness, 4% (6/142) KD cases had household members with illness. After KD cases' disease onset, 70% (100/142) KD cases had at least one other family member with illness. Overall, 61% (343/561) of all the household members had acute infectious illness during KD cases' acute stage, and 92% (130/142) of the families had clusters of infectious illness.

Conflicts of interest: The authors have no conflicts of interest relevant to this article.

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http://dx.doi.org/10.1016/j.jfma.2014.07.005

Conclusion: A total of 66% KD cases had positive contact with ill household members prior to their disease onset and 92% of families had clusters of infectious illness, so KD is strongly associated with infections.

Introduction

Kawasaki disease (KD) is an acute systemic febrile illness of unknown etiology, predominantly affecting children $<$ 5 years of age. Initially described in 1967 by Tomisaku Kawasaki,[1] it is now the most common cause of acquired heart diseases in children in the developed world, since rheumatic heart disease occurs much less frequently than before. KD is associated with a range of complications, the most important of which is the development of life-threatening coronary artery abnormalities.

There are reported incidence differences in different countries. Asian countries are reported to have higher incidences of KD (30—200/100,000 children $<$ 5 years of age) than Western countries (3.5—10/100,000 children $<$ 5 years of age).[2—10] We reported that KD has seasonal clustering, and usually the peak occurred in the summer, and the annual incidence was 50—70/100,000 children $<$ 5 years of age from 1996 to 2006.[11] The etiology of KD is still controversial and infectious etiology is considered to be one of the predisposing factors. The infectious evidence of KD includes temporal clustering and marked seasonality, geographic clustering, family clustering, high association between KD and infection disease surveillance,[11—13] and age distribution with the highest incidence among 6-month-old to 2-year-old children,[11] who have little maternal antibodies and are most susceptible to infection in general. We hypothesize that infection with certain microorganisms may trigger systemic inflammation, and then small and median sized vasculitis in certain hosts. The important susceptible genes for KD include the immunoglobulin G receptor gene *FCGR2A*, B-lymphoid tyrosine kinase (BLK) region at 8p22-23, the human leukocyte antigen (HLA) region at 6p21.3, and in the CD40 region at 20q13.[14—16] The microorganisms may be transmitted within households and the infected household members may have illness, but only children with certain host genetics develop KD. To confirm the above hypothesis, we did a prospective household and case study for KD to investigate the transmission pattern and the cluster rate of infectious illness among the household members of KD cases.

Patients and methods

KD case enrollment

At the National Taiwan University Hospital in Taipei City and the other collaborative hospitals including Taiwan Adventist Hospital in Taipei City, Far Eastern Memorial Hospital in Taipei County and Min-Sheng Hospital in Taoyuan County in Taiwan, we enrolled patients of KD and their household family members from February 2004 to September 2008. The Institutional Review Board of the National Taiwan University Hospital approved this study and informed consents were obtained from all participants or their parents.

The classic diagnosis of KD has been based on the presence of $\geq$ 5 days of fever and more than four of the five principal clinical features including neck lymphadenopathy, lip fissure and/or strawberry tongue, skin rash, nonpurulent bulbar conjunctivitis, palm/sole erythema and induration followed by desquamation.[17] Patients with fever for $\geq$ 5 days and less than four principal features can be diagnosed as having KD when coronary artery disease is detected by two-dimensional echocardiography or coronary angiography.[17] The onset of KD cases' illness was defined as the 1st day of fever onset.

After informed consent was obtained from the parents, a questionnaire interview was done to solicit clinical symptoms and preceding contact history with household members with infectious illness or with extra-household ill people. Their clinical laboratory data and coronary arterial lesions were collected.

Two-dimensional echocardiography was performed in all patients during hospitalization, and was repeated at convalescence, 8 weeks after discharge. Coronary arterial abnormality was defined as coronary arterial dilatation/ectasia, aneurysm, increased echogenicity or irregularity, and coronary artery aneurysm. A coronary artery aneurysm was defined as having a lumen diameter (inner border to inner border) of $\geq$ 3 mm in KD cases $<$ 5 years old and $\geq$ 4 mm in cases $>$ 5 years old,[14] and giant aneurysm was defined as a lumen diameter of $\geq$ 8 mm.[18,19]

Enrollment of household members

Household members were defined as people who lived with KD cases. People were defined as household members if they had stayed overnight in the same house with the KD patient for at least 1 night within 10 days prior to or after the onset of his or her symptoms. After informed consent was obtained, household members of KD cases were asked to a questionnaire-based interview including demographic data, and presence of current or recent signs and symptoms of infections 1—10 days prior to, on the same day of, or 1—10 days after the onset of the illness of their household KD case. We took throat swabs for vial isolation from the household members if they had infectious illness when KD patients were admitted to the hospitals in the acute stage. A household cluster of infectious illness was defined as at least one member having infectious illness in one family in addition to the KD case.