Kawasaki Disease in Central Area of Northeast Thailand

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Kawasaki disease (KD) is a leading cause of acquired heart disease of childhood. The authors retrospectively reviewed cases of KD in major referral centers of central Northeast Thailand from July 1991 to June 2003. Seventy-three episodes occurring in 72 patients were diagnosed with KD by the American Heart Association criteria with a mean age of presentation of 27 ± 19 months. The annual incidence was 2.2 per 100,000 children < 5 years of age. Coronary artery abnormalities (CAA) were found in 15 (20.5%) children. Nine patients (18%) who were diagnosed before 10 days were not treated with intravenous immunoglobulin (IVIG). Two (13%) of the 15 patients still had coronary lesions at the end of the follow-up period of 35.5 ± 13.4 months. Index of suspicious should be maintained in children who had clinical signs of KD for early diagnosis and prompt treatment with IVIG.

Keywords : *Kawasaki disease, Incidence, Coronary artery*

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Kawasaki disease (KD) is an acute febrile illness, which predominantly affects children under the age of 5 years[1-3]. The etiology remains unknown despite advances in research[4]. KD is now the most common cause of acquired heart disease in North American and Japanese children[2-4].

The cardiac sequelae are the most clinically important and potentially life- threatening problems[2-6]. The most serious cardiac complications are coronary artery abnormalities (CAA), which can occur in up to 20% of untreated patients[2-6]. Early treatment with intravenous immunoglobulin (IVIG) within the first 10 days of illness decreases the prevalence of coronary abnormalities to 2-5 %[5,6]. KD has been reported throughout the world but only a few epidemiologic studies have been cited from developing countries [2-4,7,8]. KD has been recognized in Thailand since early 1982[9,10]. However, there have been no scientific reports documenting its incidence. The authors report here the incidence and pattern of KD in the central area of Northeast Thailand during a 12-year period.

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Material and Method

Khon Kaen, Kalasin and Mahasarakham provinces are in the geographical heart of Thailand's northeast plateau with a population of 3.6 million. The population is predominantly Thai (99.8%). The following hospitals serve as the major centers for pediatric referrals: Khon Kaen University (Srinagarind) Hospital, Khon Kaen Hospital and Khon Kaen Ram Hospital.

A retrospective review of the medical records of all cases with KD was done in these 3 referral centers, covering the 12-year period between July 1991 and June 2003. In addition, the echo-cardiographic findings at the Khon Kaen University Hospital, Khon Kaen Hospital and Khon Kaen Ram Hospital were reviewed to validate the hospital records and to increase the likelihood of case identification. The authors also contacted all 56 pediatricians in this

area to ascertain that all cases with KD in this area had been referred to these three hospitals either for evaluation or treatment. Typical KD was diagnosed by the presence of fever for at least 5 days with at least four of five criteria, or fever plus three criteria if a coronary artery aneurysm was recognized by echocardiography[11]. Demographic, clinical, echocardiographic, treatment and follow-up data were extracted from each medical record.

Clinical data included fever, conjunctival injection, oral changes, extremity changes, cervical lymphadenopathy, skin changes, and other complications. Laboratory data included complete blood count, erythrocyte sedimentation rate, chest roentgenograms, electrocardiograms and two-dimensional echocardiograms. Two-dimensional echocardiograms were performed in all patients by one of the authors at least once. By echocardiography, a coronary artery was defined as abnormal if the diameter of the internal lumen was at least 3 mm; if the internal diameter of a segment was at least one and one-half times that of an adjacent segment, or if the lumen was clearly irregular[6]. Patients whose echocardiogram showed an internal coronary diameter $\geq$ 8 mm were considered to have a giant coronary artery aneurysm, those $\geq$ 4 to < 8 mm moderate in size, and those < 4 mm as dilatation lesions[12]. Treatment with aspirin and with intravenous immunoglobulin (IVIG) were identified. Follow up echocardiographic data included resolutions of cardiac complications and the development of new complications. Patients having coronary artery lesions in the acute phase were followed every 1-2 months for the first year and then every year. Patients with no coronary artery lesions were examined every 3 months for the first year and then every year thereafter. The principal investigator reviewed all information. The data were analyzed with a computer using SPSS program for Window version 9 (SPSS Inc, Chicago). Continuous data were expressed as the mean $\pm$ SD and the median. Categorical data were compared using either the χ^2 test or the Fisher's exact test when appropriate. A p-value of less than 0.05 was considered statistically significant.

Results

Demographic features

A total of 73 episodes of KD occurring in 72 patients were identified. The annual census reports from the Thai Bureau of Census were used for denominators to calculate the annual incidence rates.

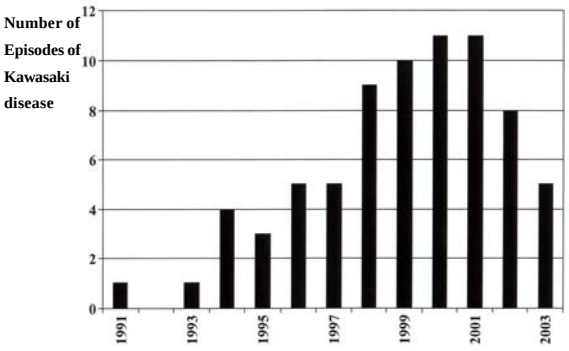

Fig. 1 Yearly number of episodes of Kawasaki disease

An estimated population of children less than 5 years old was 282,841 according to the 1997 Thai census. The number of cases annually is shown in Fig. 1 and the average minimum annual incidence was 2.2 (range, 0-3.9) per 100,000 children less than 5 years old. The average age at presentation was 27 $\pm$ 19 months (range, 3-102, median, 23) months. Ninety-five per cent of patients were under 5 years old, and 18 % of patients were under 1 year of age at the time of diagnosis. Fifty patients (68%) were male and the male to female ratio was 2.2:1.

Initial clinical findings

The mean duration of time from the onset of illness to diagnosis was 7.9 $\pm$ 3.3 days. Most patients presented with conjunctivitis (98%), skin rashes (93%), oral changes (100%) and extremity changes (92%). Cervical lymph node enlargement was found in only 53 (73%) episodes. Other clinical findings included irritability in 40 (55%) episodes, gastroenteritis in 16 (22%) episodes, febrile convulsion in 3 (4%) episodes, cough in 3 (4%) episodes, sepsis in 2 (3%), pulmonary infiltration on chest roentgenograms in 2 (3%) episodes, abdominal distention in 1 (1%) episode, and hepatitis in 1 (1%) episode. Fifteen (20.5%) of these episodes had echocardiographic changes in the acute phase. The echocardiographic changes included coronary artery dilatations (9 cases), coronary artery aneurysms (5 cases), giant coronary artery aneurysms (1 case) (Table 1). Two of 15 patients who had coronary artery involvements also had pericardial effusion (1 case) and mitral valve regurgitation (1 case). A boy had initial Kawasaki disease at the age of 29 months and had one recurrent episode at 6 years of age. This patient did not demonstrate cardiovascular complication during both the initial and the recurrent episodes.

Table 1. Age at onset of Kawasaki disease and development of coronary artery lesions

	Age at onset of Kawasaki disease	
	Age < 1 year (n=15)	Age ≥ 1 year (n=58)
No coronary artery lesions	8 (53%)*	50 (86%)*
Coronary artery lesions	7 (47%)	8 (14%)
Dilatation	3 (20%)	6 (10%)
Aneurysms	3 (20%)	2 (4%)
Giant aneurysms	1 (7%)	0 (0%)

* $p < 0.01$

The median initial hemoglobin level was 9.8 ± 1.7 g/dL in 44 of 73 episodes (range, 6.1-14.1 g/dL). The median white blood cell count on admission was 15.8×10^9/L (range, 2.1-33.7 $\times 10^9$/L) and the median maximum platelet count was 572×10^9/L (range, 130-1138 $\times 10^9$/L) in 53 episodes. The median maximum erythrocyte sedimentation rate in 47 episodes was 57 mm/h (range, 15-120 mm/h).

Treatment

Aspirin at 80 mg/kg/day was used in 48 (67%) episodes during the acute phase and low dose aspirin (3-5 mg/kg/day) was continued in all patients during the sub-acute and convalescent phases.

Forty-seven patients having 48 episodes of KD received IVIG. The average duration between onset of illness and initial IVIG treatment was 7.1 ± 2.7 (range, 5-16) days. IVIG were given as a single-dose (2 g/kg) in 43 patients. In the remainder, varying regimens were used, including a dose of 0.4 g/kg/day $\times$ 3 days (1 case), one dose of 1 g/kg (3 cases) and two doses of 2 g/kg (1 case).

Of the 49 children who had the diagnosis made in less than 10 days from onset of fever, 40 (82%) had received IVIG and the other 9 patients did not receive IVIG due to its high cost.

Follow up

Of the 58 patients who had no coronary artery lesion during the acute phase, 43 (74%) had echocardiographic studies at 3-months follow-up and coronary artery dilatations were found in two patients. These had resolved by the one-year echocardiographic studies.

Of the 15 patients who had coronary artery lesions during the acute phase, 11 (73%) still had coronary artery lesions and the other 4 patients had resolved at 3-months follow-up. Of the 11 patients who had coronary artery lesions at 3 months, 5 patients still had coronary lesions, whereas the other 6 patients had resolved at 6 months follow-up. At 1-year follow-up, only 3 of 5 patients still had coronary artery abnormalities.

Twenty patients had follow-up care for more than 1 year. These included the 3 with persistent coronary artery lesions. The mean duration of time of follow-up in these 20 patients was 35.5 ± 13.4 (range, 15-60) months. Two of the 3 patients who had coronary artery lesions at one-year follow-up, still had coronary lesions at the end of follow-up. There was no report of death.

Discussion

There has been no previous report of the estimation of annual incidence rate of KD in Thai children. A survey of all pediatricians in the study area confirmed that all cases with KD in this area had been referred to these three hospitals either for evaluation or treatment. The authors' estimation of the annual incidence of KD in this area is likely to be accurate. The minimum annual incidence from this study was 2.2 (range, 0-3.9) per 100,000 children less than 5 years old. It is the only available annual incidence of Kawasaki disease for Thailand to date and is similar to the figure reported in Jamaica (2.7/100,000)[7] which is also a developing country. However, the annual incidence of KD in this area of Thailand is less than that reported from the US (9.5/100,000)[13], British Isles (3.6/100,000)[14], and Japan (90/100,000)[15]. The incidence of KD among Northeast Thai children may have truly risen (Fig.1) as it has in many parts of the world[2-4,7,8,15]. A survey of this type has potential limitations and cannot be considered all children with Kawasaki disease in the study area during the study period.

The initial clinical findings in the presented patients were similar to the profiles of reports from other countries[4,9]. Of the five main clinical features, lymphadenopathy is the least common and oral changes were found in all patients.

Children less than 1 year old appeared to be at particularly high risk for the development of CAA (7/15, or 47%). This group of patients needs close monitoring of CAA, early treatment of IVIG to prevent the development of CAA and therapy, such as low-dose aspirin to prevent thrombosis in those who have developed CAA[12,13].

Although current recommendations that all patients with KD should receive IVIG within 10 days of onset of the illness[4-6], the authors are concerned that 18% of the presented patients diagnosed within 10 days did not receive this medication. The high cost of the IVIG contributed to the limited use of this drug in the presented patients.

The present results confirmed previous studies that more than 80% of mild to moderate coronary artery lesions healed within 5 years[12]. A multi-center, randomized study in the United States reported that IVIG treatment could significantly reduce the incidence of CAA and inflammation of the myocardium.[6] Awareness of this disease and the cost-benefit of using IVIG in the prevention of coronary lesion in Thailand and also in other developing countries need to be implemented.

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โรคคาวาซากิในบริเวณตอนกลางภาคตะวันออกเฉียงเหนือของประเทศไทย

มนัส ปะนะมณฑา, อรรฆิศา ไชกิจภิญโญ, กฤตย์วิกรม ดุรงค์พิสิษฏ์กุล, สุพัตรา สมจิตต์, เศรษฐสิริ เพชรรัตน์, ยุทธพงศ์ วงศ์สวัสดิวัฒน์, ภพ โกศลารักษ์, ผกากรอง ลุมพิกานนท์

โรคคาวาซากิ เป็นสาเหตุที่สำคัญของโรคหัวใจในเด็ก ได้ศึกษาย้อนหลังผู้ป่วยในโรงพยาบาลใหญ่ในภาคตะวันออกเฉียงเหนือของประเทศไทย ตั้งแต่เดือนกรกฎาคม 2534 ถึงเดือนมิถุนายน 2546 พบว่ามีผู้ป่วยเด็กจำนวน 72 ราย ป่วยเป็นโรคคาวาซากิ 73 ครั้ง อายุโดยเฉลี่ย 27 ± 19 เดือน อุบัติการณ์รายปี 2.2 ต่อแสนของเด็กที่อายุน้อยกว่า 5 ปี ความผิดปกติของหลอดเลือดแดงโคโรนารี่ พบ 15 ราย (ร้อยละ 20.5) ผู้ป่วยที่ได้รับการวินิจฉัยใน 10 วันแรกตั้งแต่เริ่มมีอาการจำนวน 49 รายซึ่งมี 9 ราย (ร้อยละ 18) ที่ไม่ได้รับการรักษาด้วย Intravenous immunoglobulin (IVIG) จากการติดตามผู้ป่วย 15 ราย เป็นเวลา 35.5 ± 13.4 เดือน พบว่าผู้ป่วย 2 ราย (ร้อยละ 13) ยังมีความผิดปกติของหลอดเลือดแดงโคโรนารี่ การเฝ้าระวังโรคและการศึกษาความคุ้มค่าของการใช้ยา IVIG เป็นสิ่งที่ควรดำเนินการในประเทศไทยและประเทศกำลังพัฒนา