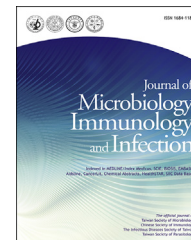


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ORIGINAL ARTICLE

Characteristics of children with Kawasaki disease requiring intensive care: 10 years' experience at a tertiary pediatric hospital

Ching-Chia Kuo^a, Yu-Shin Lee^a, Ming-Ru Lin, Shao-Hsuan Hsia, Chih-Jung Chen, Cheng-Hsun Chiu, Mao-Sheng Hwang*, Yhu-Chering Huang*

Department of Pediatrics, Chang Gung Children's Hospital and Chang Gung Memorial Hospital, Chang Gung University College of Medicine, Taoyuan, Taiwan

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Abstract *Background/Purpose:* Kawasaki disease (KD) is a febrile systemic vasculitis, and some patients may develop serious complications requiring intensive care. We aim to ascertain the clinical presentations and outcomes of these patients.

Methods: From October 2004 to October 2014, children with KD who had stayed in the pediatric intensive care unit (ICU) for acute stage treatment were defined as case patients; for each case, three age/sex-matched patients with KD but without ICU stay, if identified, were selected as control patients. Clinical data were retrospectively collected and analyzed.

Results: Among the total of 1065 KD patients, we identified 26 case patients and 71 controls for statistical analysis. ICU patients had a longer fever duration, and tended to have hemoglobin level < 10 g/dL, platelet count $< 150 \times 10^9$ /L, band cell percentage $> 10\%$, peak serum C-reactive protein level > 200 mg/L, serum albumin value < 3 g/dL, and often presented with multiorgan system involvement. Time from symptom onset to the diagnosis of KD was similar between the two groups, but ICU patients were less likely to have KD as a leading admission diagnosis. Shock (73.1%, $n = 19$) was the most common reason for ICU admission. ICU patients were more likely to receive antibiotics, albumin infusion, and require a second dose of intravenous immunoglobulin or steroid therapy. No in-hospital mortality was observed.

* Corresponding authors. Department of Pediatrics, Chang Gung Children's Hospital and Chang Gung Memorial Hospital, Number 5, Fuxing Street, Guishan District, Taoyuan City 333, Taiwan.

E-mail addresses: hms3013@cgmh.org.tw (M.-S. Hwang), ychuang@cgmh.org.tw (Y.-C. Huang).

^a These two authors equally contributed to this manuscript.

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Conclusion: Patients with KD requiring ICU admission are significantly associated with multi-organ involvement, abnormal hematological and biochemistry biomarkers, KD recognition difficulty at the time of admission, and intravenous immunoglobulin-refractory KD.

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Introduction

Kawasaki disease (KD) is an acute febrile vasculitis that mainly affects medium-sized vessels at the systemic level; its etiology remains unclear. Intravenous immunoglobulin (IVIG) and aspirin are the treatment of choice to lower the risk of coronary artery lesion (CAL) formation. If left untreated, KD may result in coronary artery aneurysms in 15–25% of patients,¹ and, although rarely, might further develop into fatal myocardial infarction. The reported case-fatality rate is low,² and most deaths occur within 1–2 months of onset.^{3,4} Several studies have reported the features of KD shock syndrome (KDSS) over the past few years in North America and Taiwan,^{5–8} which included difficulty for early recognition, delay of treatment, and increased need for IVIG retreatment. In addition to KDSS, we encountered a group of children with KD who did not develop hemodynamic instability in the acute stage but still required intensive care in the critical care settings. Therefore, we conducted a case–control study to delineate the characteristics of children with KD requiring intensive care.

Methods

Hospitalized pediatric patients with Kawasaki disease were selected by discharge code in charts (International Classification of Diseases, 9th Revision, Clinical Modification code 446.1) from October 1, 2004 to October 1, 2014 at the Chang Gung Children's Hospital, Linkou, Taiwan. Demographic data and clinical characteristics were collected via retrospective electronic medical records reviewed independently by two pediatric infectious disease specialists.

Those who had been admitted to the intensive care unit (ICU) during their hospital stay were categorized as ICU case patients. Patients were excluded if any of the following conditions was met: underlying primary immunodeficiency diseases receiving immunoglobulin therapy; conditions requiring systemic corticosteroid administration for more than 4 weeks; evidence of bacterial growth from sterile sites; concomitant illness with a diagnosis other than Kawasaki disease during the same hospitalization; or ICU admission resulting from conditions other than the acute, direct impacts of Kawasaki disease. Conditions requiring ICU admission were categorized by the Guidelines for Developing Admission and Discharge Policies for the Pediatric Intensive Care Unit. Controls were selected from patients who had a discharge diagnosis of Kawasaki disease but were not admitted to the ICU. Three control patients, if achievable, were identified for each case patient matched by sex and age (within 3 months of range).

Electronic medical records of enrolled ICU cases and control patients were reviewed retrospectively to collect the following data: demographic data (age, sex, admission season, and days of fever prior to admission); laboratory test results (white blood cell count, hemoglobin, platelet count, percentage of neutrophil, percentage and count of band cell, C-reactive protein, aspartate aminotransferase, alanine transaminase, blood urea nitrogen, creatinine, and albumin); clinical information (overall duration of fever, days of hospitalization, tentative diagnosis at presentation, time to documented diagnosis of Kawasaki disease, and time to IVIG therapy); treatments (empiric antibiotics, aspirin, IVIG, adjuvant corticosteroids, albumin transfusion, and inotropic agents), and echocardiogram findings (measurements of coronary artery lesions and time to recovery from coronary artery lesions). The day of fever onset was defined as Day 0. Spring months were defined as February–April, summer months were defined as May–July, and so on. Diagnosis of complete or incomplete Kawasaki disease was classified based on the published standard clinical criteria. Measurements of CALs were performed by pediatric cardiologists according to the standard of the Japanese Ministry of Health criteria. Acute stage was defined as 0–10 days after disease onset, subacute stage as 11–21 days, convalescent stage as 22–90 days, and chronic stage as 91–365 days. For patients admitted after July 2014 and who were applied with Z-score calculation according to the department policy, we retrospectively reassessed CALs based on documented coronary artery diameter measurements of the time because the height records for Z-score calculation were not documented in some of the earlier patients.

We conducted Student *t* tests to compare means of continuous variables and Chi-square analysis for proportional differences. Mann–Whitney *U* test was used for comparing medians in skewed continuous variables. Data analyses were performed using SPSS software version 20.0 (SPSS Inc., Chicago, IL, USA). A *p* value < 0.05 was considered statistically significant. This retrospective study was approved by the Institutional Review Board of Chang Gung Medical Foundation, Taoyuan, Taiwan (reference number: 103-5514B).

Results

During a 10-year period from October 1, 2004 to October 1, 2014, a total of 1065 patients were admitted to the Linkou Chang Gung Children's Hospital with a discharge diagnosis of Kawasaki disease, and 30 (2.82%) of these patients had been admitted to the ICU. The annual rate of hospitalized KD patient requiring intensive care in these 10 study years (defined from October to September of the next year) ranged from 0.93% to 4.44%.

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