

Letter to the Editor

Patient characteristics and intravenous immunoglobulin product may affect eosinophils in Kawasaki disease

Editor

Khan et al. showed that both patients' phenotype and choice of intravenous immunoglobulin (IVIG) product may explain our finding of dynamic eosinophil changes in the acute stage of Kawasaki disease (KD) and the association with IVIG response (1). From the literature review, they found that polymorphisms in the platelet-activating factor acetylhydrolase (PAF-AH) gene associated with IVIG resistance in KD and anti-sialic acid binding immunoglobulin-like lectin-8 (Siglec-8) autoantibodies in IVIG preparations can lead to spontaneous apoptosis of eosinophils. We agree that such eosinophil-reducing factors should be considered before assuming that a low eosinophil count is an indicator of IVIG resistance. Further studies focusing on the relationships between PAF-AH genotype and eosinophils in different stage of KD and IVIG treatment response are needed to clarify the role of eosinophils in KD and IVIG treatment response.

There are many factors that can affect the distribution of eosinophils in KD including genotype of the PAF-AH gene, IVIG product, disease course, aspirin, other prescribed medicines, etc. The naturally occurring anti-Siglec-8 autoantibodies in IVIG preparation may be an important factor that can influence eosinophil distribution in acute KD. If apoptosis were induced by anti-Siglec-8 autoantibodies of IVIG, we should observe a decrease, rather than an increase, in eosinophils after IVIG treatment. From our data, we showed a marked increase in eosinophils in the acute stage before IVIG treatment. After IVIG treatment, eosinophils were significantly increased and higher than that before IVIG treatment. Tsai et al. also showed that IVIG, prepared with beta-propiolactone, was most significantly associated with resistance, coronary artery aneurysm at convalescence, and

giant aneurysm in KD (2). From 1999 to 2006, we have recorded four different brands of IVIG prescribed in different years for 75 KD patients. The absolute eosinophil counts after IVIG treatment in different brands were as follows: Bayer Gamimune N ($295.5 \pm 50.1/\text{mm}^3$, $n = 19$), Do ($443.7 \pm 73.6/\text{mm}^3$, $n = 30$), Biotest Intraglobin F ($411.1 \pm 76.3/\text{mm}^3$, $n = 20$) and E-com ($448.8 \pm 101.1/\text{mm}^3$, $n = 6$). There were no significant difference in absolute eosinophil counts between different brands of IVIG ($p = 0.6$, one-way ANOVA by SPSS 12.0 for Windows XP; SPSS Inc., Chicago, IL, USA).

Kawasaki et al. first observed that 11 of 50 KD patients (22%) had eosinophilia in peripheral blood (3). Terai et al. found accumulation of eosinophils in the coronary micro-vessel lesions and eosinophilia in peripheral blood and postulated the involvement of eosinophils in the pathogenesis of KD vasculitis (4). We have recently shown that eosinophils were significantly elevated in KD both before and after IVIG treatment, and eosinophilia after IVIG treatment had an inverse correlation to KD patients with IVIG resistance (1). Brosius et al. reported that the incidence of atopic dermatitis among children with KD was nine times greater than that of controls (5). Serum immunoglobulin E and interleukin-4 levels were also significantly higher in KD patients than in age-matched children (6). Patients with KD among these studies, including those not only without IVIG treatment but also those using different brands of IVIG in different countries, were toward an eosinophilia and Th2 regulation. The dynamic changes in eosinophils observed may be not affected primarily by IVIG product.

Our previous results showed an inverse correlation of eosinophilia with the IVIG-resistant rate. Indeed, further investigation is needed to clarify the role of eosinophils through eosinophil

activation markers and/or T helper 2-related cytokines in the immunopathogenesis of KD.

*Ho-Chang Kuo,
Chih-Lu Wang,
Lin Wang,
Hong-Ren Yu and
Kuender D. Yang*

*Division of Pediatric Allergy and Immunology,
Department of Pediatrics, Chang Gung Memorial
Hospital-Kaohsiung Medical Center; Graduate
Institute of Clinical Medical Sciences, Chang Gung
University College of Medicine, Kaohsiung, Taiwan.
123 Ta-Pei Rd., Niao-Sung
Hsiang, Kaohsiung County,
Taiwan 833.
E-mail: erickuo48@yahoo.com.tw*

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