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Editorial

Could Immunoglobulin Level Be a Prognostic Factor for Coronary Artery Lesions in Kawasaki Diseases?

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▸ See the article "IgA Levels Are Associated with Coronary Artery Lesions in Kawasaki Disease" in volume 51 on page 267.

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Although etiology of Kawasaki disease (KD) remains unknown, both epidemiologic and clinical characteristics strongly support an infectious etiology. So, most accepted hypothesis of KD pathogenesis is systemic vasculitis due to host immune responses resulting from ubiquitous agents causing infection in genetically predisposed children.[1] Studies supporting this hypothesis by Rowley et al.[2][3] showed that $CD8^+$ T cells, oligoclonal immunoglobulin (Ig) A, and upregulation of cytotoxic T cell and interferon pathway genes were observed in the coronary arteries in fatal KD patients. In addition, a study using a murine model with KD vasculitis by Noval Rivas et al.[4] also proved that intestinal barrier dysfunction causes secretory IgA leakage, IgA-C3 immune complex is deposited in the vascular tissue, and increased IgA production is a key role in vasculitis.

Without intravenous immunoglobulin (IVIG) use, Ig (IgG, IgA, IgM) has been reported to increase during 1 to 2 weeks of KD administration and then decrease to normal levels within 4 weeks.[5] In particular, Ohshio et al.[6] reported increased secretory IgA and serum total IgA, and Gupta et al.[7] also reported an increase in IgA anticardiolipin antibodies in KD patients, suggesting that the degree of increase in these immune antibodies reflects the degree of systemic inflammation. Based on these results, it is thought that serum Ig levels may be related to the occurrence of coronary complications, and thus may be used as a useful therapeutic index.

In this issue of *Korean Circulation Journal*, Kim et al.[8] reported results regarding the comparison between serum Ig levels (IgG, IgA, IgM, and IgE) during clinical courses and coronary artery lesions (CALs) in KD. They conducted a study using blood samples and clinical data from 241 KD patients collected from 11 hospitals. Through this study, they showed significantly higher Ig levels (IgG, IgA, IgM, and IgE) in the subacute phase compared to the reference Ig values. In particular, the IgA level of the CALs group was 2.2 times higher in the acute phase and 1.7 times higher in the subacute phase than those in the non-CAL group, and IgA levels sowed a strong correlation with CAL size. So, they suggested high IgA levels in patients with KD may have an increased risk of CALs. These results support the research findings that IgA plays an important key role in KD pathogenesis.[4]

However, these results are inconsistent with the results of previous studies. Yanagimoto et al.[9] reported that there was no significant differences between pretreatment levels for IgG,

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IgA or IgM in patients with or without CALs, but IVIG non-responders had significantly higher pretreatment IgG values. The results of Sawaji et al.[10] also suggested that the high IgG level before IVIG treatment was a risk factor for CAL, but IgA level was rather lower in the CAL group. Therefore, it is not yet possible to conclude that a specific Ig level is a definite predictor of clinical outcomes.

This study has some limitations. First, in the study subjects, Ig levels were not measured serially at each clinical stage of KD. Because the number of CAL patients was very small in the acute phase, it was not appropriate to accurately analyze the correlation between pretreatment Ig levels and clinical outcome. More detailed examinations during the all clinical phases of KD have the potential to refine these relationships. Another limitation is that they have no age-matched healthy control, because it is known that Ig levels increases with age except for the newborn period.

Therefore, to determine the usefulness of the Ig levels during the clinical course of KD in predicting the clinical outcomes, more studies are needed on the relationship of Ig levels and clinical outcomes.

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