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Editorial

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Factors Predicting Resistance to Intravenous Immunoglobulin and Coronary Complications in Kawasaki Disease: IVIG Resistance in Kawasaki Disease

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▸ See the article "Factors Predicting Resistance to Intravenous Immunoglobulin Treatment and Coronary Artery Lesion in Patients with Kawasaki Disease: Analysis of the Korean Nationwide Multicenter Survey from 2012 to 2014" in volume 48 on page 71.

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Downie et al.[1] defined intravenous immunoglobulin (IVIG) resistance in patients with Kawasaki disease (KD) as any patient who receives a second dose of IVIG and had a fever (body temperature [BT] >38.0°C) since finishing the first IVIG dose (2 g/kg). In addition, patients who do not respond to IVIG (BT ≥37.5°C more than 24 hours after the end of IVIG infusion) seem to develop coronary artery lesions (CALs).

Many factors that can affect IVIG resistance have recently been discovered and are outlined below.

Platelets, C-reactive protein (CRP), and aspartate aminotransferase (AST):
Shin et al.[2] reported the levels of platelets, CRP, and AST were independent predictors of IVIG resistance.

Levels of AST and lactate dehydrogenase and percent of neutrophils:
patients with abnormal levels of liver markers (AST and lactic dehydrogenase [LDH]) and neutrophils have a high risk for IVIG resistance.[3]

Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR):
Takeshita et al.[4] reported that the combination of NLR and PLR is a novel and useful predictor of IVIG resistance. And high NLR and PLR ratios before receiving IVIG are useful predictors of IVIG resistance.

Fc gamma receptor II A (FcγRIIA)/FcγRIIB expression:
Chang et al.[5] reported that FcγRIIA/FcγRIIB expression is elevated in KD patients with IVIG resistance and CALs. FcγRIIA is also a valuable marker for predicting the effectiveness of treatment for KD.

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N-terminal-pro-brain natriuretic peptide (NT-proBNP) levels and percent of polymorphonuclear neutrophils (PMNs):
patients resistant to IVIG have significantly higher serum levels of NT-proBNP and a percentage of PMNs compared to IVIG responders.[6]

Other factors:
the other factors involved in IVIG resistance are high levels of alanine aminotransferase (ALT), total bilirubin, gamma-glutamyl transferase (GGT),[7] and low levels of hemoglobin, albumin, sodium.[8] In this study, authors[9] found that PMN percentage and serum levels of NT-proBNP, CRP, AST, and ALT were significantly higher in KD patients with IVIG resistance.

The Japanese Ministry of Health classifies coronary arteries as abnormal if the internal lumen diameter is >3 mm in children <5 years old or >4 mm in children ≥5 years old, if the internal diameter of a segment measures ≥1.5 times that of an adjacent segment, or if the coronary lumen is clearly irregular.[10] Recent studies have investigated factors for predicting CALs in patients with KD, but the results are inconclusive. Cho and Kang[8] found that PMN percentage, CRP levels, and NT-proBNP levels were predictive factors for developing CALs. Other factors associated with CALs in KD patients include male sex and fever duration. In this study, authors[9] also found that serum levels of CRP were higher in KD patients with CAL.

This study is valuable due to the fact that the data were taken nationwide, the large number of cases, and the data were analyzed well by the Korean Society of Kawasaki Disease. However, there are several limitations, including its retrospective nature, partially incomplete data collection, different sampling times and reference ranges at each institution, and different cutoff values used between laboratories. Therefore, we will consider future studies with a prospective design, complete data collection, and standardized collection times, ranges, and cutoff values.

Early diagnosis and prompt IVIG infusion are the best ways to prevent CALs in KD. However, IVIG resistance can develop during or after the first IVIG treatment. Fast detection of IVIG resistance and subsequent administration of adjunctive therapies (IVIG, corticosteroids, tumor necrosis factor α blockade) can prevent CALs. Therefore, pediatricians must recognize changes in laboratory findings as soon as possible to detect IVIG resistance and prevent CALs.

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