Tenascin-C as a novel predictor of unresponsiveness to high-dose intravenous immunoglobulin and coronary artery lesions in patients with Kawasaki disease.


Department of Pediatrics, National Center for Global Health and Medicine, Tokyo, Japan (1); Department of Pathology and Matrix Biology, Mie University Graduate School of Medicine, Mie, Japan (2); Department of Cardiology, National Center for Global Health and Medicine, Tokyo, Japan (3); Department of Allergy and Immunology, National Research Institute for Child Health and Development, Tokyo, Japan (4); Department of Pediatrics, Faculty of Medicine, Toyama University, Toyama, Japan (5); Department of Pediatric Cardiology, National Cerebral and Cardiovascular Center, Osaka, Japan (6); Department of Pediatrics and Child Health, Faculty of Medicine, Kurume University School of Medicine, Fukuoka, Japan (7); Department of Pediatrics, Mie University Graduate School of Medicine, Mie, Japan (8); Department of Pediatrics, Faculty of Medicine, Fukuoka University, Fukuoka, Japan (9)

Introduction:
Tenascin-C (TN-C) is an extracellular matrix protein specifically upregulated in response to tissue injury and inflammation. Recent studies have shown that serum TN-C could be a useful biomarker for disease activity such as myocardial infarction or aortic aneurysm. Around 10% of Kawasaki disease (KD) patients are unresponsive to high-dose intravenous immunoglobulin (IVIG) therapy, and these patients have increased risks of developing coronary artery lesions (CALs). We report the usefulness of TN-C as a novel biomarker to predict IVIG unresponsiveness and CAL formation in patients with KD.

Methods:
Subjects consist of 108 patients with KD (6 patient with CAL) and 36 febrile child controls (FC group). We measured serum TN-C levels using ELISA and correlated with other laboratory data in KD patients. We compared the TN-C levels between KD and control as well as between the IVIG responder group (R group; n = 89) and the non-responder group (NR group; n= 19). In 51 KD patients, the chronological changes of the TN-C levels were evaluated; before IVIG treatment (pre TN-C), after IVIG at 9-15 days of the illness (post TN-C), and convalescent stages (late TN-C).

Results:
In KD, pre TN-C levels positively correlated with serum AST (r = 0.31, p = 0.01), ALT (r = 0.35, p = 0.004), and CRP levels (r = 0.25, p = 0.02). Pre TN-C levels demonstrated no statistical significance between patients with KD and FC group (mean 86.2 vs. 76.9 ng/mL, p = 0.57, respectively). However, pre TN-C were significantly higher in NR group than those in R group or FC group (mean 106.1 vs. 69.6 and 76.9 ng/mL, p = 0.029). In addition, TN-C levels significantly decreased after IVIG administration (pre TN-C mean 69.5 vs. post TN-C 56.1 vs. late TN-C 38.8 ng/mL, p < 0.01). When pre TN-C was used to predict IVIG unresponsiveness, sensitivity, specificity and AUC were 63%, 76%, and 0.66 respectively. The increased TN-C levels were observed between 9-15 days of illness among CAL positive patients.

Conclusions:
The TN-C level reflects not only inflammation but also tissue remodeling and may be a predictor of IVIG unresponsiveness and CAL formation.