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


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– Introduction

• Approximately 10% of patients with Kawasaki disease (KD) are unresponsive to high-dose intravenous immunoglobulin (IVIG) therapy, and these patients have increased risks of developing coronary artery lesions (CALs).
• We focused on Tenasin-C (TN-C), an extracellular matrix molecule which is upregulated during inflammation and tissue remodeling.
• Our aim in this study was to determine whether the serum TN-C level can be a marker for predicting a resistance to IVIG and may have a high risk of developing CAL.

– Tenasin C

• TN-C is an extracellular matrix glycoprotein that is sparsely detected in normal but specifically and transiently expressed closely associated with inflammation and tissue remodeling.
• In adult, TN-C is a predicting biomarker for left ventricular dilatation and remodeling in patients with acute myocardial infarction and dilated cardiomyopathy.
• In acute phase of KD, TN-C was deposited in vascular wall and connective tissue surrounding coronary artery.

– Methods

< Study design >
Retrospective cohort study

< Subjects >
• 107 with KD whose blood samples were obtained at the 4 collaborative institutions
• 35 febrile child controls

< Diagnosis of KD >
All patients with KD fulfilled the Criteria for Diagnostic Guideline for Kawasaki Disease (5th revision).

< Treatment >
All patients with KD received 2g/kg of IVIG over 24 hours and 30 – 50 mg/kg/day of aspirin or 3 -5mg/kg/day of flurbiprofen until they became afebrile.

< TN-C measurement >
We measured serum TN-C levels at the following 3 point; (1) before IVIG, (2) day 9 – 15 of illness and (3) convalescent stage (day 30 – 40 of illness). Serum TN-C levels were analyzed using the Human TN-C Large (FN-C) Assay Kit (Immunno-Biological Laboratories Co., Gunma, Japan).

– Results

< Patient profile >

<table>
<thead>
<tr>
<th>KD patients</th>
<th>n = 107</th>
<th>FC group</th>
<th>n = 35</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, months</td>
<td>Median 24 [2 – 84]</td>
<td>15 [2 – 67]</td>
<td>0.005</td>
<td></td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>62/45</td>
<td>13/22</td>
<td>0.046</td>
<td></td>
</tr>
<tr>
<td>TN-C levels at IVIG, ng/mL (range)</td>
<td>76.3 (28.3 – 264.4)</td>
<td>75.5 (25.4 – 152.9)</td>
<td>0.512</td>
<td></td>
</tr>
<tr>
<td>TN-C levels at 9th day, ng/mL (range)</td>
<td>60.1 (25.2 – 180.5)</td>
<td>61.7 (20.6 – 150.2)</td>
<td>0.657</td>
<td></td>
</tr>
<tr>
<td>TN-C levels at 15th day, ng/mL (range)</td>
<td>50.7 (20.7 – 106.1)</td>
<td>53.5 (20.6 – 103.2)</td>
<td>0.683</td>
<td></td>
</tr>
</tbody>
</table>

< The chronological changes of the TN-C levels (n = 53) >

< The correlation between serum TN-C and the other laboratory data >

< TN levels before IVIG in each groups >

< The prediction of IVIG unresponsiveness by TN-C level before IVIG >

n = 87

< Serum TN-C level among patients with CAL >

< Future tasks >

• We conduct the prospective study to clarify high levels of TN-C are associated with IVIG unresponsiveness.
• Is TN-C harmful or beneficial for CAL formation?
• Which cells produce TN-C in KD patients?