Letter to the Editor

Critical role of platelets in the production of thymus and activation-regulated chemokine in children: A case series study

Dear Editor,

Thymus and activation-regulated chemokine (TARC), a member of the CC chemokine family, is a ligand for CC chemokine receptor 4 that is expressed on Th2 lymphocytes. TARC plays important roles in Th2-type immune response by selectively recruiting CC chemokine receptor 4+ Th2-polarized memory/effector T cells into inflamed tissues. Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by pruritic eczema associated with predominant infiltration of Th2 cells in the lesional skin. A serum TARC level serves as a reliable biomarker of AD disease severity in clinical practice. It is reported that serum levels of TARC are significantly higher in infants and children than adults even in the absence of AD. TARC is produced by thymus, epidermal keratinocytes, endothelial cells, bronchial epithelial cells, dendritic cells (DCs), and platelets. TARC is also reported to be expressed in dermal vessels of the noninflamed skin. However, the source of serum TARC in AD remains controversial. We, first, found that a serum TARC level was undetectable in a boy with acute immune thrombocytopenia (ITP) despite the complication of AD (case 1), suggesting that a serum TARC level is dependent on platelet counts. In all cases, serum TARC levels correlated with platelet counts but not with eosinophil count or serum lactate dehydrogenase levels. Serum levels of TARC in AD are reported to reflect its over-production in the skin lesions. On the other hand, a rapid decrease in serum TARC level (3308 pg/ml to <100 pg/ml) in only seven days in case 5 corresponded exactly with that of platelet counts (212 × 10^9/L to 10 × 10^9/L) (Table 1), a recent report has demonstrated that serum levels of TARC are low in a child with AD complicated by mild thrombocytopenia. Our results support this observation and strongly suggest a critical role of platelet in the production of TARC.

Platelets are abundant components of the blood and mediate immune responses by various mechanisms, e.g. recruitment of leukocytes via expression of P-selection, on activation. Patients with AD show elevated levels of β-thromboglobulin and platelet factor 4. Furthermore, these markers correlated with the severity of AD, indicating that platelets are activated in AD. As well, platelets from AD patients express higher TARC levels than control. Platelet counts recovered following intravenous IgG treatment. His eczema responded well to topical glucocorticoid treatment. Unfortunately, some cases of AD, particularly those with severe disease, may be resistant to conventional therapy. Therefore, new treatments that specifically target the Th2 Type immune response by selectively recruiting CC chemokine receptor 4+ Th2-polarized memory/effector T cells into inflamed tissues are needed.

In conclusion, our findings suggest that platelets play important roles in the pathology of AD. In this regard, the rapid response of eczema to topical glucocorticoid treatment in these patients may be due to the inhibition of TARC production by platelets. Further studies are needed to elucidate the exact role of platelets in AD and to develop novel therapeutic strategies targeting platelet function.

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treatment in case 1 might have reflected a low level of TARC expression associated with thrombocytopenia.

There are several limitations in this study. First, we have included only a small number of children with ITP. Second, we did not evaluate the levels of serum TARC in adult patients. In addition, pathological roles of TARC in the development of AD are still unclear. Nevertheless, our results indicate that platelets are main cellular sources or potential inducers of TARC, and suggest a possible role of platelet in the pathology of AD.

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Conflict of interest

The authors have no conflict of interest to declare.

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References


Table 1

Clinical profiles of six patients with ITP.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age at onset</th>
<th>Sex</th>
<th>Platelets (x 10^9/L)</th>
<th>TARC (pg/ml)</th>
<th>PA-IgG (ng/10^9 platelets)</th>
<th>Eosinophils (/µL)</th>
<th>LDH (U/L)</th>
<th>Skin rash</th>
<th>Treatment</th>
<th>Remission</th>
<th>ITP Dx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1</td>
<td>11 months</td>
<td>Male</td>
<td>2</td>
<td>&lt;100</td>
<td>31.8</td>
<td>416</td>
<td>305</td>
<td>AD (mild)</td>
<td>IVIG</td>
<td>Remission</td>
<td>IVIG Dx</td>
</tr>
<tr>
<td>Case 2</td>
<td>5 years</td>
<td>Male</td>
<td>4</td>
<td>&lt;100</td>
<td>982</td>
<td>450</td>
<td>265</td>
<td>AD (mild)</td>
<td>GC for 2 months</td>
<td>Remission</td>
<td>GC for 1 month</td>
</tr>
<tr>
<td>Case 3</td>
<td>5 years</td>
<td>Female</td>
<td>192</td>
<td>&lt;100</td>
<td>201</td>
<td>0</td>
<td>56</td>
<td>no</td>
<td>GC for 2 months</td>
<td>Remission</td>
<td>GC for 1 month</td>
</tr>
<tr>
<td>Case 4</td>
<td>1 year</td>
<td>Female</td>
<td>139</td>
<td>&lt;100</td>
<td>210</td>
<td>0</td>
<td>0</td>
<td>no</td>
<td>IVIG followed by GC for 2 months</td>
<td>Remission</td>
<td>GC for 2 months</td>
</tr>
<tr>
<td>Case 5</td>
<td>4 years</td>
<td>Male</td>
<td>15</td>
<td>&lt;100</td>
<td>20.3</td>
<td>180</td>
<td>96</td>
<td>no</td>
<td>ND</td>
<td>2 months</td>
<td>ND</td>
</tr>
<tr>
<td>Case 6</td>
<td>8 years</td>
<td>Male</td>
<td>148</td>
<td>&lt;251</td>
<td>12.7</td>
<td>96</td>
<td>383</td>
<td>no</td>
<td>ND</td>
<td>10</td>
<td>ND</td>
</tr>
</tbody>
</table>

ITP, immune thrombocytopenia; Dx, diagnosis; TARC, thymus and activation-regulated chemokine; PA-IgG, platelet-associated IgG; IVIG, intravenous IgG; GC, glucocorticoid; ND, not done; LDH, lactate dehydrogenase.

TARC normal range: 6–12 months, <1367 pg/ml; 1–2 years, <998 pg/ml; >2 years, <743 pg/ml; adults, <450 pg/ml.

PA-IgG normal range: 0–27.5 ng/10^9 platelets.