Dear Sir,

ADAMTS13 (a disintegrin-like and metalloproteinase with thrombospondin type 1 motif 13) plays a major role in converting the ultralarge multimers of von Willebrand factor (VWF) into smaller fragments that are less reactive in mediating platelet adhesion (1). Congenital or acquired deficiency of ADAMTS13 activity has been recognized as the cause of thrombotic thrombocytopenic purpura (TTP) (2, 3). Also, reduced ADAMTS13 activity was found in idiopathic thrombocytopenic purpura (ITP) and systemic lupus erythematosus (SLE) (4). To investigate whether there is a different role of ADAMTS13 in TTP, ITP and SLE patients, we evaluated the activity and inhibitors of ADAMTS13, as well as antigen levels of ADAMTS13 and VWF in those patients.

Fifty-one patients were included in this study, which included eleven TTP patients aged between 18 and 64 years, twenty ITP patients with ages of 5 to 63 years, and twenty SLE patients aged 16 to 47 years. Twenty-six normal Chinese with ages 23 to 67 years were used as controls. For ADAMTS13 antigen assay, pooled plasma from 20 healthy Caucasians was used as standard. For other assays, pooled plasma from healthy Chinese donors was used as standard. ACD was used as anti-coagulant. Plasma was prepared and frozen for assays. ADAMTS13 activity and inhibitors were measured as previously described (5). Inhibitors in patients with ITP and SLE were tested only when their ADAMTS13 activities were below 50%. ADAMTS13 antigen assay was performed using a sandwich ELISA kit with anti-ADAMTS13 monoclonal antibodies (provided by Prof. Deckmyn, Leuven University, Belgium). The antigen of VWF was evaluated by using a kit established by our laboratory (6).

In our study, the mean of ADAMTS13 levels in normal Chinese (CN) was 0.60 ± 0.15 U/ml (n=26, mean ± SD) compared to the level set at 1 U/ml in pooled (n=20) normal human plasma from Caucasian origin. Since ADAMTS13 antigen levels in the Caucasian donors we tested were 0.95 ± 0.21 U/ml (vs. CN, p<0.01), which were similar with that in Rieger’s report (7), it was suggested that ADAMTS13 antigen may vary among different races (8). As shown in Table 1, our data revealed that ADAMTS13 antigen levels in idiopathic TTP patients before plasma infusion were severely deficient, and ADAMTS13 activity was reduced in parallel with ADAMTS13 antigen. Since inhibitors against ADAMTS13 were found in 9 of 11 idiopathic TTP patients in this study [according to Studt, et al. (9), those inhibitors against ADAMTS13 were anti-ADAMTS13 antibodies], it seems that the activity of ADAMTS13 was deficient due to both clearance and blocked function.

As in previous reports, highly increased VWF:Ag in ITP and SLE may be due to an instinctive response to diseases or increased releases from damaged vascular endothelial cells. But with such highly increased levels of VWF:Ag as observed in TTP, one may wonder why so few thrombi occur in those diseases compared to TTP? From our study, we can conclude that one of the answers may be that ADAMTS13 antigen rose after VWF:Ag. Though ADAMTS13 activity was mildly reduced (20% ~ 50%) in 7 patients with ITP and 6 with SLE, respectively, there was no statistically significant difference between normal controls and patients, and none of the inhibitor to ADAMTS13 was found in our study.

In summary, our data show that ADAMTS13 definitely plays different roles in diseases such as ITP, SLE and idiopathic TTP. ITP and SLE patients were associated with increased ADAMTS13 antigen levels, whereas idiopathic TTP patients presented a severely deficient level of ADAMTS13. Since no inhibitor was found, the mild decrease of ADAMTS13 activity in ITP and SLE may be a kind of relative reduction when ADAMTS13 did not increase as much as VWF did.

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Table 1: The activity, inhibitors and antigens of ADAMTS13 and VWF: Ag in plasma of patients with TTP, ITP and SLE (mean ± SD).

<table>
<thead>
<tr>
<th>Groups</th>
<th>ADAMTS13 activity (%)</th>
<th>ADAMTS13 Inhibitor (Num. +/ Num. tested)</th>
<th>ADAMTS13 antigen levels (U/ml)</th>
<th>vWF-Ag (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ITP (n=20)</td>
<td>63 ± 16</td>
<td>0/7</td>
<td>0.83 ± 0.23 +/−</td>
<td>317 ± 113 +/−</td>
</tr>
<tr>
<td>SLE (n=20)</td>
<td>70 ± 14</td>
<td>0/6</td>
<td>0.72 ± 0.20 +/−</td>
<td>436 ± 122 +/−</td>
</tr>
<tr>
<td>Idiopathic TTP (n=11)</td>
<td>22 ± 19 +/−</td>
<td>9/11</td>
<td>0.10 ± 0.08 +/−</td>
<td>444 ± 236 +/−</td>
</tr>
<tr>
<td>Normal controls (n=26)</td>
<td>75 ± 12</td>
<td>Not tested</td>
<td>0.60 ± 0.15</td>
<td>106 ± 39.6</td>
</tr>
</tbody>
</table>

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Alteration of ADAMTS13 antigen levels in patients with idiopathic thrombotic thrombocytopenic purpura, idiopathic thrombocytopenic purpura and systemic lupus erythematosus

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