Six cases of autoimmune acquired coagulation factor VIII deficiency: Single center experience in Japan

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Abstract
We report six cases of autoimmune acquired coagulation factor VIII deficiency, which is a rare bleeding disorder. It is an autoimmune disease, however, there are various causes. We experienced cases with malignancy, co-exist with another autoimmune disease, pregnancy, and unknown epidemiology with repeated bleeding episode. All patients were controlled the acute bleeding phase and they have been under treatment with immunosuppression.

Case Reports
Patients with malignancy
Six individuals with Autoimmune Acquired Coagulation Factor Deficiency (AiFD) attended Kansai Medical University Hospital (Table 1). Three of them had histories of malignant disease. Patients 1 and 2 had histories of colon cancer more than three years before with no current evidence of active disease.

Patient 1 presented with a hematoma on the buttocks of rapid onset and was found to have a prolonged activated partial thromboplastin time (aPTT) (113.8 seconds). Factor VIII was under 1% and inhibitor against FVIII was 2070 BU/mL. She was diagnosed as having AiFD. When the dose of PSL was increased (1 mg/kg/day), her symptoms resolved. Patient 5 had a prior diagnosis of Rheumatoid Arthritis (RA), for which she was receiving no medication. She had recently been pregnant and was diagnosed in the third trimester as having placenta previa. She accordingly underwent cesarean section. Control of bleeding during the operation was good; however, she noticed hematuria a few days after the operation. She was found to have a prolonged aPTT (104.5 seconds). Factor VIII was under 1% and inhibitor against FVIII was 174.6 BU/mL. She was negative for lupus anticoagulant. She was diagnosed as having AiFD. Her hematuria was slow to improve. She was therefore started on PSL (1 mg/kg/day), which achieved good control of her symptoms.

Patient with repeated episodes of bleeding
Patient 6 had a long history of bleeding episodes, the first of which had occurred 22 years ago, at which time he had been diagnosed as having ‘AiFD for factor IX’ (supporting data unavailable). He had received PSL and CSA. He stopped attending for follow-up and 6 years later again presented with bleeding episodes. This time the diagnosis was ‘AiFD for factor IX and VIII’. He received PSL pulse therapy and again stopped attending for follow-up. Three years later, he again presented with bleeding, for which he received rFVIIa and PSL pulse therapy. Eleven years later, he again presented with bleeding. On this occasion, his aPTT was prolonged (66.9 seconds), factor VIII was 24% and factor IX 17%. The concentration of inhibitor of factor VIII was 0.7 BU/mL and of inhibitor of factor IX 1.0 BU/mL. He was negative for lupus anticoagulant. Although the concentrations of inhibitor were low, his history of repeated bleeding prompted restarting treatment with PSL. His aPTT returned to within the normal range and factor VIII and IX activities increased in parallel with decreases in inhibitor concentrations.

Discussion
AiFD is a rare bleeding disorder, its incidence being 1.5/million/year. It is characterized by development of immune-mediated antibodies to coagulation factors, resulting in bleeding episodes of sudden onset, especially in older individuals with no history of bleeding disorder. Although it is possible to create antibodies to any coagulation factor, the most commonly targeted coagulation factor is VIII, followed...
Table 1. Patients’ characteristics.

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Sex</th>
<th>Past history</th>
<th>Symptom</th>
<th>aPTT (sec)</th>
<th>FVIII (%)</th>
<th>Inhibitor against FVIII (BU/mL)</th>
<th>Treatment treatment</th>
<th>Current Coagulant</th>
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<tbody>
<tr>
<td>1</td>
<td>75</td>
<td>Female</td>
<td>Colon cancer</td>
<td>Hematoma</td>
<td>113.8</td>
<td>&lt;1</td>
<td>2070</td>
<td>rFVIIa/PSL/CSA/Rituximab</td>
<td>PSL</td>
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<tr>
<td>2</td>
<td>80</td>
<td>Male</td>
<td>Colon cancer</td>
<td>Subcutaneous bleeding</td>
<td>82</td>
<td>&lt;1</td>
<td>1587</td>
<td>PSL</td>
<td>PSL/CSA</td>
</tr>
<tr>
<td>3</td>
<td>66</td>
<td>Female</td>
<td>Breast cancer</td>
<td>No symptom</td>
<td>62.3</td>
<td>26</td>
<td>-</td>
<td>PSL</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>63</td>
<td>Female</td>
<td>Scleroderma</td>
<td>Subcutaneous bleeding</td>
<td>113.3</td>
<td>&lt;1</td>
<td>36.7</td>
<td>PSL</td>
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<tr>
<td>5</td>
<td>34</td>
<td>Female</td>
<td>RA/pregnancy/placenta previa</td>
<td>Hematuria</td>
<td>104.5</td>
<td>&lt;1</td>
<td>174</td>
<td>PSL</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>48</td>
<td>Male</td>
<td>Prior bleeding episode</td>
<td>Hematoma</td>
<td>66.9</td>
<td>24</td>
<td>0.7</td>
<td>rFVIIa/PSL</td>
<td></td>
</tr>
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</table>


References