CASE REPORT

Prolonged profound abciximab associated immune thrombocytopenia complicated by transient multispecific platelet antibodies

J A G Lown, A S Hughes, P Cannell

Patients receiving abciximab occasionally develop transient severe thrombocytopenia within a few hours of receiving the drug. Thrombocytopenia has been reported to resolve within 10 days of abciximab administration, but in this case profound thrombocytopenia lasted 21 days before a slow spontaneous recovery. Management was complicated by the presence of HLA antibodies and the transient production of antibodies directed at major platelet glycoproteins IIb/IIIa, Ib/IX, and Ia/IIa. The patient remained refractory to platelet transfusion and two courses of intravenous gammaglobulin for the duration of her admission.

ABCIXIMAB is a widely used antiplatelet drug in interventional cardiology that exerts its effect by binding to receptor sites on glycoprotein IIb/IIIa. About 1% of patients receiving abciximab develop transient severe thrombocytopenia within a few days of infusion. For patients receiving a second exposure, the incidence of profound thrombocytopenia is about 4% and more likely to arise within a few hours of drug administration.

Recently, antibodies directed at sequences in the drug structure have been discovered and suggested as a possible cause of the thrombocytopenia. For cases published so far, the thrombocytopenia has resolved within 10 days of abciximab administration. Platelet transfusion has been used as supportive treatment during the thrombocytopenic phase. There have been no reports of cases complicated by the coincident production of drug unrelated platelet antibodies.

This report outlines a case of prolonged, profound thrombocytopenia associated with abciximab administration and the development of multispecific platelet antibodies directed at three major platelet glycoproteins.

CASE REPORT

A 44 year old woman was admitted to hospital in October 2002 with a six year history of ischaemic heart disease and coronary artery stenosis. She had received a stent in February 1999, at which time abciximab at a dose of 4.5 mg/250 ml was given uneventfully. Further stent insertions were required and abciximab at a dose of 4.5 mg/250 ml was administered but ceased after < 3 hours. She received in total 0.79 mg, when the platelet count dropped from 280 x 10^9/L to 83 x 10^9/L. Within 24 hours the platelet count was 25 x 10^9/L. Platelets were transfused but no increment resulted in more than a transient (< 24 hours) platelet increment. Platelets from seven ABO compatible siblings were tested and found to be incompatible by platelet cross match. On day 9 antibodies directed at glycoproteins IIb/IIIa, Ib/IX, and Ia/IIa, in addition to HLA antibodies to both the A and B loci, were detected (table 2). A further course of intravenous gammaglobulin was given on days 10–12 but the patient maintained platelet counts < 10 x 10^9/L without further intervention until day 21. During this time the patient experienced episodes of bleeding with haematemesis, epistaxis, and per vaginal bleeding for which she was transfused on three occasions over two weeks with a total of 5 U of red cells. From day 21 the platelet count increased spontaneously but slowly from 4 x 10^9/L to 47 x 10^9/L over five days, at which time the patient was discharged. At a follow up visit seven weeks later only the HLA antibodies were detectable (table 2).

DISCUSSION

Thrombocytopenia is a recognised complication of abciximab administration. However, in most cases the cytopenia is

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**Table 1** Results of serological investigation

| Sample                  | Platelet panel tested by SPRCA
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Patient’s serum day 2</td>
<td>0</td>
</tr>
<tr>
<td>Patient’s serum+ abciximab</td>
<td>3</td>
</tr>
<tr>
<td>Patient’s sample day 8</td>
<td>3</td>
</tr>
</tbody>
</table>

0, negative; 2, moderately positive; 3, strongly positive; NT, not tested; SPRCA, solid phase red cell adherence.

*Titre of abciximab antibody 1:128.

**Table 2** Glycoprotein specificity of platelet antibodies

<table>
<thead>
<tr>
<th>Sample date</th>
<th>IIb/IIIa</th>
<th>Ib/IX</th>
<th>Ia/IIa</th>
<th>HLA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 2</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
</tr>
<tr>
<td>Day 8</td>
<td>Pos</td>
<td>Pos</td>
<td>Pos</td>
<td>Pos</td>
</tr>
<tr>
<td>Day 27</td>
<td>Pos</td>
<td>Pos</td>
<td>Neg</td>
<td>Pos</td>
</tr>
<tr>
<td>Day 77</td>
<td>Neg</td>
<td>Neg</td>
<td>Neg</td>
<td>Pos</td>
</tr>
</tbody>
</table>

Neg, negative; Pos, positive.
transient and, once the drug is stopped, the platelet count usually resolves spontaneously within five days. Occasionally, with profound thrombocytopenia, and especially if bleeding occurs, platelet transfusion may be necessary.

The case reported here is exceptional for the prolonged period of thrombocytopenia before spontaneous recovery (21 days). The additional complication of pre-existing HLA antibodies and the development of antibodies to the major platelet glycoproteins resulted in ineffective platelet support, which was abandoned after day 11. Initial platelet transfusions appeared to stimulate the production of multispecific HLA antibodies, which precluded acquisition of compatible platelets. In retrospect, perseverance with platelet transfusion in this situation may have exacerbated the situation.

Two courses of intravenous gammaglobulin were also ineffective in ameliorating the thrombocytopenia.

Previous reports have been published of bleeding associated with abciximab-related thrombocytopenia. This patient also experienced episodes of bleeding requiring red cell transfusion.

This case illustrates an exceptional prolongation of abciximab-associated thrombocytopenia and the management difficulties aggravated by the development of multispecific platelet antibodies.

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