Successful Management of Bleeding in a Patient With Factor V Inhibitor by Platelet Transfusions

By Juan Chediak, Julia B. Ashenhurst, Ivor Garlick, and Richard K. Desser

A 71-yr-old male was seen because of the development of severe bleeding diathesis secondary to an acquired factor V inhibitor. The lack of clinical and laboratory response to fresh frozen plasma prompted us to treat him with platelet transfusions during 4 separate bleeding episodes; on each occasion he received 10–15 U of homologous platelet concentrates. There was a remarkable clinical response associated with a marked correction of the prolonged prothrombin time, prolonged partial thromboplastin time, and prolonged Russell viper venom time; this correlated with higher factor V levels and complete neutralization of the inhibitor. The beneficial effect of platelet transfusion lasted 5–6 days. The inhibitor was of low titer, and it was precipitated by staphylococcal protein A. The in vivo response to platelet transfusion correlated with subsequently performed in vitro experiments. Nonwashed control platelet pellets mixed with inhibitor plasma partially corrected the prolonged PTT, whereas washed platelets or albumin density gradient separated samples did not. Similarly, nonwashed platelets from a patient with congenital factor V deficiency had no corrective effect. Likely mechanisms of the effect of transfused platelets might include: (A) factor V was provided by platelets; (B) the platelet surface provided receptor sites for the factor V inhibitor; or (C) platelet participated in local hemostasis. Treatment of this patient with immunosuppression (cyclophosphamide and prednisone) resulted in disappearance of the inhibitor. Thus, platelet transfusions could be an alternative therapy to fresh frozen plasma in the treatment of bleeding in patients with factor V inhibitors.

FOURTEEN PATIENTS with inhibitors directed against factor V have been previously reported. In one report, the patient was congenitally deficient in factor V and had received plasma transfusions. 1 In all the remaining cases, the patients had not previously been bleeders but had a variety of clinical conditions, such as systemic infections, tuberculosis, administration of aminoglycosides (streptomycin and gentamicin), or had received blood transfusions. 2–4 Bleeding manifestations in patients with inhibitors have ranged from mild to severe; in at least three instances, the presence of the inhibitor was associated with a fatal bleeding diathesis. 5–7 Immunoechemial characterization of factor V inhibitors have shown that the majority were immunoglobulins of the IgG type. Bleeding manifestations secondary to factor V inhibitors have usually been managed with factor V replacement in the form of fresh frozen plasma, plasmapheresis in order to decrease the titer of the inhibitor, and immunosuppressive drugs. In the majority of cases, the inhibitor disappeared spontaneously in less than 4–6 wk.

Recently, important discoveries have established the basis of a better understanding in the management of patients with fact V inhibitors. First, it has been shown by different groups of investigators that factor V is present within the human platelet and that different stimuli will activate, expose, or release it. 8,9 Second, Giddings et al. 10 have demonstrated that factor V antigen is present on the platelet surface. Finally, the activation of factor X at the platelet surface, and therefore thrombin formation, depends on the presence of factor V. 11

It is the purpose of this article to report the beneficial effects of platelet transfusions in a bleeding patient with a factor V inhibitor. Subsequent disappearance of this inhibitor occurred when cyclophosphamide and prednisone were administered.

MATERIALS AND METHODS

Case History

A 71-yr-old white retired salesman was first seen at our hospital on 2/5/79 with complaints of recurrent cutaneous ecchymoses for 6 mo, epistaxis requiring cauterization twice in the past 3 mo, and recurrent painless nontraumatic hematuria for 6 wk.

A month earlier he was hospitalized in another institution on two occasions because of hematuria. The physical examination was noncontributory, and laboratory tests showed an abnormally prolonged prothrombin time (PT) of 42.4 sec with a control of 11.2 sec, and a partial thromboplastin time (PTT) of greater than 100 sec with a control of 40 sec. Factor analysis disclosed a factor V of 4% of normal plasma. The remaining coagulation factors were normal as were chemical tests of liver and renal function. A complete blood count including the platelet count was also normal. Since he had had prior surgery without bleeding complications, it was thought that he had an acquired coagulopathy with a factor V inhibitor. The medical management at that hospital included frequent fresh plasma infusions, prothrombin complex concentrates, and azathioprine (Imuran) 150 mg daily in 3 divided doses. He had mild symptomatic improvement as manifested by a reduction in the severity of his hematuria.

When first seen at our institution, he gave a 20-yr history of mild
hypertension treated with a rauwolfia compound until 3 mo prior to admission when therapy was changed to methyldopa and a thiazide diuretic. An evaluation of an isolated lung lesion in 1976 was negative for infection or neoplasm. He denied exposure to tuberculosis or treatment with streptomycin. Physical examination was unremarkable except for numerous ecchymoses and a few petechiae on the buccal mucosa. There was a systolic ejection murmur attributed to aortic stenosis.

The results of coagulation studies are listed in Table 1. Family studies showed a factor V coagulant level of 54%, 46%, and 80% in his brother, daughter, and son, respectively. A search for lupus, collagen, tuberculosis, and collagen vascular disease was negative, and he was discharged to be followed as an outpatient.

He returned a month later with a vitreous hemorrhage of the left eye and microscopic hematuria. Cytoscopy revealed only punctate cystitis. Laboratory evaluation again showed a prolonged PT (greater than 120 sec) and a factor V level of 3%. Transfusion with fresh frozen plasma (700 ml) and prothrombin complex concentrate (2400 U) failed to correct the PT and PTT, but the vitreous hemorrhage stabilized and the patient was discharged on April 12 on azathioprine, 100 mg daily. On April 16 he developed a severe spontaneous left retroperitoneal hemorrhage. There was a significant drop in hemoglobin to 7 g/dl, the PT was 27.9 sec, PTT 247 sec, and factor V 3%. The calcium level in blood was within normal limits. Transfusion of 7 U of fresh frozen plasma, along with 5 U of packed red cells failed to correct the coagulopathy, and evidence of congestive heart failure (rales, distended jugular veins) developed. Plasmapheresis was contemplated, but it was decided to attempt platelet transfusions first. Transfusion of 15 U of platelets promptly resulted in a partial correction of the PT and PTT, and the factor V level rose to 8%. A prompt clinical response was evident, characterized by cessation of back pain and stabilization of vital signs. The PT and PTT remained partially corrected for the next 6 days and the hemorrhage resolved. The patient was discharged on May 2, on the same dose of azathioprine. He returned on May 17 with a large right thigh hematoma. The PT was 27.6 sec, the PTT was greater than 120, and the factor V was 4% of normal. Transfusions of 15 U of platelets again resulted in immediate partial correction of the PT and PTT. His factor V level rose to 8%-9%, and the hematoma resolved. Platelet transfusions were also successful in arresting gum bleeding after the vigorous use of dental floss. The fourth bleeding episode was a minor one, also treated with platelet transfusion. Laboratory data were obtained after the infusion of platelets.

On June 6, since the azathioprine administration showed no effect, it was discontinued and cyclophosphamide, 100 mg/day, and prednisone, 40 mg/day, were begun. Three weeks later, his factor V level rose to 26% and it was 27% on July 5. This partial correction of PT and PTT with increased factor V levels were unrelated to platelet transfusion. There was a significant drop of the factor V inhibitor titer. On July 28, the patient complained of mild fever. Cyclophosphamide was discontinued, prednisone was decreased, and he was readmitted on August 7 for investigation of fever of uncertain origin. Physical examination revealed only herpes labialis and a systolic ejection murmur. There were no ecchymoses or other signs of bleeding. The PT was 11 sec, PTT 49.9 sec, and factor V 60%. Multiple blood cultures and serologic investigations were negative. Liver enzyme elevation and liver biopsy were consistent with a posttransfusion hepatitis. The fever subsided and the patient was discharged on August 22, 1979. At the present time, he is doing well on antihypertensive medications alone without recurrence of bleeding, factor V inhibitor, or fever.

Figure 1 illustrates the main clinical events and factor V levels seen in response to therapy. The effect of platelet transfusion on the factor V levels were not included. The administration of either fresh frozen platelets or activated prothrombin complexes did not increase factor V levels.

**Laboratory Investigation**

**Blood Collection and Platelet Samples Preparation**

Blood was obtained from the patient, control subjects, and from another patient known to have congenital factor V deficiency (factor V level of 3%). Venous blood was drawn by the two-syringe technique through a 19-gauge scalp vein needle without the use of a tourniquet. Nine milliliters of blood were drawn into a plastic syringe and then transferred into a plastic tube containing 1 ml of 3.8% sodium citrate. The blood was centrifuged at room temperature at 250 g for 10 min to obtain platelet-rich plasma (PRP).

Further centrifugation at 4500 rpm yields platelet-poor plasma (PPP). The PRP was used either to assess platelet aggregation or in

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**Table 1. Coagulation and Platelet Function Studies in a Patient With Factor V Inhibitor**

<table>
<thead>
<tr>
<th>Study</th>
<th>Normal Values</th>
<th>Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prothrombin time (sec)</td>
<td>10–11</td>
<td>21*</td>
</tr>
<tr>
<td>Partial thromboplastin time (sec)</td>
<td>35–45</td>
<td>246*</td>
</tr>
<tr>
<td>Thrombin time (sec)</td>
<td>15–18</td>
<td>18</td>
</tr>
<tr>
<td>Russell viper venom time (sec)</td>
<td>5–6</td>
<td>65*</td>
</tr>
<tr>
<td>Bleeding time (min)</td>
<td>2–7</td>
<td>620*</td>
</tr>
<tr>
<td>Fibrinogen (mg/dl)</td>
<td>200–500</td>
<td>400</td>
</tr>
<tr>
<td>Platelet count (10^3/μl)</td>
<td>200–400</td>
<td>360</td>
</tr>
<tr>
<td>Factor II (%)</td>
<td>60–150</td>
<td>96</td>
</tr>
<tr>
<td>Factor V (%)</td>
<td>60–150</td>
<td>4*</td>
</tr>
<tr>
<td>Factor VII (%)</td>
<td>60–150</td>
<td>80</td>
</tr>
<tr>
<td>Factor X (%)</td>
<td>60–150</td>
<td>110</td>
</tr>
<tr>
<td>Factors IX, XI, XII (%)</td>
<td>60–150</td>
<td>152, 220, 91</td>
</tr>
<tr>
<td>Platelet factor 3 (sec)</td>
<td>47–54</td>
<td>51.9</td>
</tr>
<tr>
<td>Platelet aggregation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Collagen, epinephrine, ADP,</td>
<td></td>
<td></td>
</tr>
<tr>
<td>arachidonic acid (% change in light transmission)</td>
<td>60–80</td>
<td>Normal</td>
</tr>
<tr>
<td>Ristocetin-induced agglutination</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1.5 mg/ml, %)</td>
<td>70–80</td>
<td>Normal</td>
</tr>
<tr>
<td>Euglobulin lysis time (min)</td>
<td>&gt;120</td>
<td>120</td>
</tr>
</tbody>
</table>

*Average of at least four separate determinations.

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![Fig. 1. Main clinical events, factor V levels, and response to therapy in a patient with a factor V inhibitor. Three of these bleeding episodes were treated with platelet transfusions.](image-url)
the preparation of platelet pellets. The platelet count in PRP was adjusted to 350–400 × 10^3 platelets/μl for aggregation studies. In order to prepare platelet pellets with varying platelet counts, the PRP was divided in aliquots of 0.5, 1.0, 1.5, and 2.0 ml and then centrifuged at 250 rpm for 15 min. Platelet pellets used for in vitro experiments were washed twice in artificial media containing albumin as described. Another set of platelet pellets were not washed but a complete removal of the original plasma supernatant was attempted. Finally, a third set of platelet pellets was obtained by albumin density gradient separation (ADGS) according to the method of Walsh. These three types of platelet pellets were resuspended with 0.5 ml of either factor V deficient plasma or factor V inhibitor plasma by gentle agitation. Platelet counts were determined on the resuspended samples; the mixtures were then incubated at 37°C from 60 to 120 min. The samples were centrifuged at 4500 rpm to yield PPP. This plasma was used to assay factor V levels and to perform PT, PTT, and inhibitor titers.

**Coagulation Methods**

Routine tests such as PT, PTT, and thrombin time were performed by standard techniques. Russell viper venom time (RVTT) was performed with reagents from General Diagnostics (Morris Plains, N.J.) and platelet aggregation studies were done with increasing molar concentrations of calcium chloride or calcium gluconate as described. Coagulation factors were determined by the one-stage method, mixing PPP with appropriate deficient substrate plasma. Platelet counts were determined in whole blood or in PRP by the method of Brecher and Cronkite. Platelet aggregation was carried out within 2 hr of blood collection using the method of Born. Platelet aggregation was carried out within 2 hr of blood collection using the method of Born. A baseline value of 100% light transmission was obtained with the platelet’s own PPP; 0.4 ml of PRP containing 350–400 × 10^3 platelets/μl was stirred in the aggregometer cuvette for 2–3 min at 37°C. One-tenth milliliter of aggregating agent was added to the PRP and the change in light transmission recorded. Maximum light transmission was read at 3 min. This value was expressed as percentage after comparing the light transmission of the patient’s own PPP. Euglobulin lysis time was determined using PPP as described. Fibrinogen determination in plasma was measured by the ammonium sulfate precipitation method. Other studies included a bleeding time carried out by the method of Ivy et al. and platelet factor 3 availability (PF-3) measured by the Rabiner and Hrodex measurement of the Hardisty and Hutton method.

Factor V inhibitor plasma, congenital factor V deficient plasma, and normal plasma were treated with staphylococcal protein A (SPA) in order to absorb the immunoglobulin G. Five-hundred milligrams of SPA (Behringwerke, Sommerville, N.J.) was washed 3 times with Tris buffer (pH 7.4); after the third wash, the supernatant was discarded. One milliliter of factor V inhibitor plasma, congenital factor V deficient plasma, and normal plasma were then added to the precipitated SPA material. They were mixed by gentle agitation and then incubated at room temperature for 10–15 min; the mixtures were then centrifuged at 4000 rpm for 10 min. The supernatant was used to perform PT, PTT, factor V inhibitor test, factor V levels (only on the normal plasma), and immunoglobulin determinations.

**Reagents**

Adenosine-5-diphosphate (ADP) from Sigma Chemical Corporation (St. Louis, Mo.) was dissolved in Tris-saline buffer, pH 7.4 (1 part of 0.25 M Tris mixed with 2 parts of 0.9% sodium chloride). Epinephrine (1:1000) was obtained from Parke Davis (Detroit, Mich.) and dissolved in 0.9 g/liter sodium chloride to give final concentrations of 1.16 × 10⁻³ M; it was kept in the dark by covering the tube with aluminum foil. Arachidonic acid purchases in 10-mg vials from Sigma Chemical was dissolved in sodium carbonate, pH 10.4, and used at 300 μg/ml PRP. Bovine tendon collagen (500 mg) from Sigma Chemical was dissolved in 10 ml of 0.9% sodium chloride. This material was homogenized in a blender for 10 min and then centrifuged at 300 rpm. The supernatant was divided into aliquots and kept frozen at −25°C until use. This material was called undiluted collagen; further dilution was done if necessary (when compared to results in normal controls). Ristocetin sulfate, lot no. O.20, was purchased from Lenau Kengevi (DK 1850 Copenhagen, Denmark); the manufacturer stated that it contained more than 90% ristocetin A. This material was dissolved in 0.9 g/liter sodium chloride to give a final concentration of 1–2 mg/ml when added to citrated PRP.

**RESULTS**

The results of routine coagulation tests, factor analyses, and platelet function tests are presented in Table 1; they show a markedly prolonged PT, PTT, and RVVT with a normal thrombin time. The addition of increasing molar concentrations of calcium chloride or calcium gluconate did not decrease the prolonged PT and PTT as in the case described by Coots et al. Factor analysis performed on several occasions disclosed diminished amounts of factor V, ranging from 3% to 5%. The rest of coagulation tests and platelet function studies were normal. Initial attempts to demonstrate the presence of a factor V inhibitor were not successful since the patient had received fresh frozen plasma before being transferred to our institution. A few days later, however, while not receiving plasma, a screening procedure to detect the presence of an inhibitor was positive: the addition of an equal volume of normal plasma did not completely correct the patient’s prolonged PT, PTT, or RVVT. The factor V inhibitor was investigated by incubating equal amounts of several dilutions of the patient’s plasma with normal pooled plasma. Residual factor V was measured after 1 and 2 hr incubation at 37°C. A control curve of normal pooled plasma mixed with plasma from a patient with congenital deficiency of factor V (factor V level was 3%) was prepared. A residual factor V of 17% was obtained at 1 hr incubation when patient’s plasma was used, whereas the control pooled plasma mixed with a congenital factor V deficient plasma gave a value of 75%. Longer incubation time did not significantly decrease factor V levels (Fig. 2). The factor V inhibitor was identified in up to 1:10 dilution of patient’s plasma mixed with buffer.

Because of massive nontraumatic retroperitoneal bleeding, fresh frozen plasma was infused in amounts of 15 ml/kg body weight. Plasma infusion had no corrective effects on PT, PTT, and factor V levels. A further drop in his hemoglobin concentration asso-
associated with persistence of severe back pain was indicative of active bleeding. Before performing plasmapheresis in order to decrease the inhibitor titer, it was decided to examine the effectiveness of platelets. The clinical and laboratory response to the infusion of 15 U of platelets was remarkable, since the PT and PTT almost corrected and there was improvement in factor V levels (Fig. 2). A similar type of clinical and laboratory response was observed a month later (5/17/79) when an intramuscular bleed was also treated with platelet transfusions. Thus, on two separate occasions, the transfusion of platelets not only corrected the PT and PTT, but also neutralized the anticoagulant activity of the inhibitor. At the same time, factor V activity increased from 4% to 8%–9%. The corrective effect of the transfused platelets lasted approximately 6 days (Fig. 3). Two subsequent bleeding episodes were also treated with platelet transfusions obtaining similar clinical and laboratory results. One was gum bleeding resulting from dental floss. There was a rapid cessation of bleeding and partial correction of his PT, PTT, and RVVT. His hospitalization lasted less than 24 hr.

The in vitro effect of platelet pellets obtained from different subjects on the patient’s inhibitor plasma was then assessed. Normal nonwashed platelet pellets at concentrations of 100,000/μl were capable of correcting the abnormally prolonged PTT from 280 sec to 90 sec (average of five separate determinations). When higher platelet concentrations were used, there was very little additional improvement on the PTT (Fig. 4A). Nonwashed platelet pellets obtained from our patient during remission (factor V level was 69%) behaved like normal platelets when they were mixed with the inhibitor plasma. Finally, nonwashed platelet pellets obtained from a patient with congenital factor V deficiency had no corrective effects. Factor V inhibitor activity was tested in the supernatant of control platelet pellets mixed with the patient’s inhibitor plasma and found to be negative. Thus, control platelet pellets (300 and 600 × 10⁸/μl) were capable of neutralizing the patient’s inhibitor.

Factor V levels increased when nonwashed control platelet pellets were mixed with the patient’s inhibitor plasma, but failed to increase when similarly treated platelet pellets from a congenitally factor V deficient
patient were mixed with patient’s inhibitor plasma. Platelet pellets prepared from our patient’s blood while on remission behaved like normal platelets. The increments of factor V levels were proportional to the amount of platelets contained in the pellets (Fig. 4B).

Twice washed normal platelet pellets or ADGS-treated samples showed no corrective effect on the PT, PTT, or factor V levels when mixed with inhibitor plasma. The results on the PT and PTT comparing nonwashed platelet pellets with either washed or ADGS platelets is presented in Table 2.

The supernatant of the patient’s inhibitor plasma treated with SPA had no anticoagulant effect and it behaved as nonabsorbed congenital factor V deficient plasma when mixed with normal plasma. A 1:1 mixture of SPA-treated supernatant inhibitor plasma mixed with normal plasma gave a PTT of 43 sec, whereas a 1:1 mixture of factor V deficient plasma mixed with the same normal plasma gave a PTT of 41 sec. Staphylococcal protein A treated samples (inhibitor plasma, congenital V deficient plasma, or normal plasma) showed a reduction of about 70% of the starting immunoglobulin G levels.

Table 2. Corrective Effect of Three Different Type of Platelet Pellets on the PT and PTT of a Patient With Factor V Inhibitor

<table>
<thead>
<tr>
<th>Mixtures</th>
<th>Platelet Count (10^9/μl)</th>
<th>PT (sec)</th>
<th>PTT (sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PPP (inhibitor plasma)</td>
<td>0</td>
<td>30 (11.0)</td>
<td>207 (39)</td>
</tr>
<tr>
<td>PPP + nonwashed platelet pellets</td>
<td>204</td>
<td>19 (11.0)</td>
<td>80 (42)</td>
</tr>
<tr>
<td>PPP + washed platelet pellets</td>
<td>200</td>
<td>29 (11.2)</td>
<td>199 (40)</td>
</tr>
<tr>
<td>PPP + ADGS platelet pellets</td>
<td>205</td>
<td>29 (11.0)</td>
<td>155 (43)</td>
</tr>
</tbody>
</table>

*Mixtures were incubated at 37°C for 30 min, centrifuged at 4500 rpm for 10 min, and the supernatant was used for the determination of PT and PTT. ADGS refers to albumin density gradient separation and PPP to platelet poor plasma. In parentheses are the values of the control system.

DISCUSSION

The successful treatment of this patient during four separate bleeding episodes clearly indicates the usefulness of platelet transfusions in this patient with factor V inhibitor. Three of the bleeding episodes were clinically assessed and laboratory data obtained. All of them showed a prompt clinical improvement associated with partial correction of the abnormal laboratory tests and neutralization of the inhibitor. The corrective effect of platelet transfusions lasted 5–6 days, which is approximately the lifespan of transfused platelets.24 Of interest is the observation of Borchgrevink and Owren25 that platelet transfusions were effective in correcting the secondary bleeding time in a patient with congenital factor V deficiency without inhibitor for as long as 6 days. Onuora et al.26 reported partial correction of the PTT when platelet transfusions were given to a patient with a factor V inhibitor. In neither of these two reports was an increase in factor V activity noted. The corrective effect of the transfused platelets was interpreted as a local effect at the bleeding site.

A likely mechanism for the corrective effect of platelet transfusions in our patient is the possibility that homologous platelets provided factor V coagulant that not only neutralized the inhibitor but also provided measurable circulating factor V activity. Several groups of investigators have shown that factor V is present within the human platelet and that different stimuli will activate, expose, or release factor V.8,9,27 The amount of factor V available after platelet activation either at their surface or release into the platelet milieu is variable and depends on the type of stimulus.27

An alternative explanation is that homologous platelets provided receptor sites for the inhibitor. Giddings et al,10 using immunofluorescence tech-
niques, have demonstrated the presence of factor V antigen on the surface of platelets from normal subjects and in a subject with factor V deficiency. It is possible, therefore, that all antigen sites on our patient’s own platelets were combined with the inhibitor, and that the transfusion of platelets provided new receptor sites; the platelet-bound inhibitor was then removed from the circulation. The increment in factor V levels detected after platelet administration could have originated either from the transfused platelets or the increment could have represented de novo production by the patient.

A third possible mechanism is related to the local hemostatic effects of platelets. It has been recently shown that the binding of activated factor X (Xa) and thus, thrombin formation, depends on the presence of activated factor Va. It has also been shown that an IgG antibody directed against factor V blocks the binding of Xa by platelets. It is possible that the exposure of factor V on the platelet surface in patients with factor V inhibitors is impaired or its activity is immediately neutralized by the circulating anticoagulant; therefore, the transfusion of homologous platelets provided an intact surface for Xa and Va interactions leading to thrombin formation. In a recently described case of a patient with abnormal procoagulant activity, it was shown that there was decreased factor Xa binding on the platelet surface. It remains to be determined how factor Va interacts with the platelet procoagulant activity.

The neutralization of the inhibitor and the increased levels of factor V in the circulation following platelet transfusion correlated with the in vitro experiments performed with the patient’s inhibitor plasma. Of interest is that nonwashed platelets partially corrected the prolonged PT and PTT, whereas washed platelets or ADGS platelets (which are also washed) did not. This indicates that nonwashed platelets have exposed factor V or Va on the surface and that the washing procedure removes it. Platelets from a patient with congenital factor V deficiency were unable to correct the prolonged PTT, indicating either that the inhibitor was not neutralized or, more likely, that these platelets did not provide sufficient factor V. The disappearance of the anticoagulant activity of the patient’s inhibitor plasma by absorbing the plasma with SPA is an indirect evidence that the inhibitor was an IgG.

We have been unable to elucidate the underlying disease(s) responsible for the appearance of this factor V inhibitor. As far as we know, rauwolfia preparations have not been reported to be associated with the appearance of factor V inhibitors. It was observed that therapy with cyclophosphamide and prednisone was associated with the disappearance of the inhibitor, whereas azathioprine administered for approximately 10 wk was not. In favor of a drug-induced response is the fact that in the majority of cases of spontaneous remissions, the improvement has been noted in less than 4 wk, whereas our patient had bleeding manifestation related to the inhibitor for at least 6 mo. The laboratory detection of a low factor V due to the presence of the inhibitor lasted about 5 mo. Patients with mild factor VIII inhibitors have also shown improvement when treated with immunosuppressive drugs.

While the exact mechanism of the corrective effect of platelet transfusion was not completely elucidated, the treatment was simple and effective in controlling acute hemorrhage. This approach may be useful in other patients with bleeding due to inhibitors to factor V.

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