Splenectomy in post-transfusion purpura: Report of a case

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A severe case of post-transfusion purpura in a 26-year-old woman was successfully treated with corticosteroids, immune suppression, infusion of immune compatible platelets, and splenectomy. Specialized serologic testing suggested that immune reactions were responsible for the platelet destruction and detected the presence of the platelet specific antigen, Pl^{A1}, in this patient.

Post-transfusion purpura (PTP) is a rare clinical syndrome whereby thrombocytopenic purpura occurs approximately 1 week after blood transfusion. At least 28 cases of PTP have been reported,[1] but none have included splenectomy as treatment. However, splenectomy has an important role in the management of thrombocytopenia associated with a variety of disorders,[2] and in the present case of PTP, the patient was successfully managed by splenectomy. The case reported here suggests that PTP is a heterogenous syndrome of platelet destruction by antigen-antibody reaction.

Report of case

A 26-year-old white woman (gravida 4, para 1) was readmitted to Phoenix General Hospital on November 29, 1981, with complaints of bleeding from the gums, nose, and vagina, along with scattered bruising of 1 day's duration. She had been discharged the previous day following a normal recovery period from abdominal hysterectomy and left salpingo-oophorectomy. The patient was originally hospitalized on November 22, 1981; at that time she was found to have ruptured cornual pregnancy, with extensive uterine necrosis and hemoperitoneum. Two units of A-positive compatible packed red blood cells (PRBCs) were transfused during surgery. Complete coagulation profiles (including platelet counts) performed postoperatively and prior to discharge were normal. No history of any hematologic disorder was known and no blood transfusions were given prior to hysterectomy. The recent medication history included only an oxycodone-aspirin preparation.

Physical examination revealed signs of active hemorrhage. Blood-filled bullae were present on the lips, nose, and mouth, and diffuse petechiae were noted on the extremities and torso. There was no organomegaly or fever. Neurologic examination was unremarkable. Initial laboratory testing revealed gross hematuria and normal renal function studies. The hemoglobin value was 11.1 gm./dl. and the hematocrit value was 31.8 percent; the platelet count was 30,500/cu. mm. The peripheral smear showed no schistocytes. Coagulation protein levels were normal.

On the following day, the platelet count had fallen to 2,000/cu. mm. Direct and indirect Coombs' tests were positive and demonstrated anti-IgG and anti-c antibodies; anti-complement was not detected. Bone marrow biopsy and aspiration revealed myeloid hyperplasia and markedly increased numbers of megakaryocytes. Immunoglobulin electrophoresis demonstrated a polyclonal increase in IgG, IgA, and IgM components. An autoimmune disease screen was negative. Transfusion with random-donor platelets and washed PRBCs was performed, and administration of high-dose corticosteroids was started.

On the third day, the hemoglobin value continued to drop despite blood replacement (Table 1). There was no rise in the platelet count. Ultrasonography demonstrated splenomegaly, but no pelvic mass. In an attempt to increase the survival and effectiveness of transfused platelets, HLA antigen typing and platelet antibody studies were obtained. During the following 3 days, the patient was transfused with washed PRBCs and random-donor and single-donor platelets and was continued on the regimen of high-dose corticosteroids. Despite this therapy, there was no improvement in platelet counts and hemorrhage continued. Twelve days had elapsed since the initial transfusion of 2 units of blood.

The patient was prepared for splenectomy. Immune and reticuloendothelial suppression was further attempted with cyclophosphamide and vinblastine sulfate. Cefotaxime sodium and pneumococcal vaccine were administered prophylactically. The preoperative platelet count was 1,000/cu. mm. Random-donor platelets were transfused with induction of general anesthesia, and the patient was monitored by electroencephalography for signs of cerebral hemorrhage. A midline epigastric incision was utilized to enter the abdomen with minimal blood loss. The spleen was expediently deliv-

TABLE 1. HEMOGRAMS — BLOOD PRODUCT TRANSFUSION.

Hospital day	Postoperative day	Hemoglobin value (mg./dl.)*	Hematocrit value (percent)	Platelet count (x10³/mm.³)	Washed PRBCs	Transfusions (units) Random-donor platelets	Single-donor platelets	HLA-compatible platelets
1		11.1	31.8	30.5				
2		10.7	30.9	2.0	1	10		
3		10.3	29.7	2.0	4			
4		12.7	37.0	4.0	2	10	1	
5		11.6	33.8	2.0		10	1	
6	6 hours preoperatively	8.4	24.7	1.0	3	10		
	During surgery			1.0	3	30		
	6 hours postoperatively			2.0	3		2	1
7	1	11.8	34.3	45.0				
8	2	10.6	31.8	90.0				
9	3	11.1	31.4	176.0				
10	4	9.6	28.5	202.0				
11	5	11.2	34.2	245.0				
12	6	11.9	35.1	150.0				

*All blood results reported here were 6:00 a.m. values.

ered and the splenic vessels were clamped and ligated. A sump drain and irrigation catheter were placed in the left subphrenic space to monitor hemostasis postoperatively. A single-layer fascial closure utilizing polyglactin 910 was performed. Oozing from subcutaneous tissue was noted; therefore, soft rubber drains were utilized. The estimated blood loss of 1,000 ml. was replaced during surgery. The platelet count remained at 2,000/cu. mm. at the completion of surgery. Immune suppression with cyclophosphamide, vinblastine sulfate, and corticosteroids were continued during the immediate postoperative period. Also, during the 6 hours following surgery, additional blood, single-donor platelets, and HLA-compatible platelets were transfused.

On the first postoperative day, the platelet count was 45,000/cu. mm. There were no signs of active hemorrhage, and the abdominal drain and irrigation catheter were removed. The patient had an uneventful recovery. No further transfusions were required. Corticosteroids were continued on a decreasing dosage schedule. Prior to discharge 11 days after surgery, direct and indirect Coombs' tests remained positive and demonstrated anti-IgG, anti-complement, and anti-c antibodies. A short course of prednisone was completed after discharge. No further therapy was required, and the hemogram remained normal. Subsequently, the results of the specialized serologic testing demonstrated the presence of a high-titer antibody against platelets.

The presence of the platelet specific antigen, Pl[A1], was found in this patient by the American Red Cross Research Laboratory, St. Louis, Missouri. They also tested the serum for Pl[A1] antibody with a platelet panel by indirect immunofluorescence. The serum reacted strongly with all platelets—both Pl[A1] positive and negative. Lymphocyte cytotoxicity for HLA antibodies was performed, and the serum reacted with 40 of 42 cells on the panel. The 2 negative cells were retested by indirect im-

munofluorescence and were strongly positive. The results of the HLA lymphocyte test panel was also confirmed by the Department of Hematology at the University of Arizona Medical Center. Ninety-eight percent of HLA cell types evaluated were positive. HLA platelet typing was also performed. Based upon these studies, HLA-compatible platelets were given to this patient.

Discussion

PTP was first described by Zucker and associates[3] and by Van Loghem and coauthors[4] in 1959. Shulman and coworkers[5] provided a detailed study of PTP in 1961. They suggested that a potent complement-fixing antibody, which they named anti-Pl[A1], occurred in a Pl[A1]-negative patient and resulted in platelet destruction. They also postulated that a Pl[A1]-negative patient, who had been sensitized by either pregnancy or previous blood transfusions, had been given Pl[A1]-positive blood and had produced anti-Pl[A1] antibodies. The mechanism of platelet destruction was compared to an "innocent bystander" reaction, as occurs with the mechanism of drug-induced purpura. Problems exist with this hypothesis, which has not been supported by in vitro studies, as was noted later by Shulman[6] as well as by Cimo and Aster.[7]

The clinical picture of PTP has been consistent. Almost all patients (26 of 28 reported) have been women, whose ages ranged from the fourth to eighth decades.[1] The onset of purpura was preceded by blood transfusion, with a latent period of approximately 1 week. Abramson and associates[8] reported that in their patients, as well as in most

other cases, the transfusion was quickly followed by chills and fever, suggesting a platelet-antibody reaction. In virtually all cases the purpura was severe, with platelet counts in the range of 10,000/cu. mm. or lower, and marrow megakaryocytes were normal in number or marginally increased.[1] The duration of thrombocytopenia was from 5-60 days.[1]

Gockerman and Shulman[9] have reported the only death due to PTP. The remainder of cases have recovered without sequelae. The only recurrence or second episode of PTP has been reported by Soulier and coworkers.[10]

Zeigler and associates[11] noted that almost every patient described was previously sensitized to Pl^{A1}-positive blood by prior transfusion or pregnancy; however, 2 cases without prior sensitizing events were reported by Seindenfeld and coauthors.[12]

Shulman[6] points out that 95 percent of the general population possess the Pl^{A1} platelet antigen, yet most cases of PTP have occurred in patients with Pl^{A1}-negative platelets and have demonstrated anti-Pl^{A1} antibodies. One Pl^{A1}-positive patient with PTP was described by Zeigler and associates.[11]

The pathogenesis of PTP remains to be fully defined. The role of platelet-associated alloantigenic determinants with platelet destruction has been thoroughly reviewed by Klein and Blajchman.[13] They described these determinants, including platelet-specific alloantigens such as Pl^{A1} and the HLA antigens. As discussed recently by Schechter and McFarland,[14] the number of IgG-secreting lymphocytes increases shortly after blood transfusion. The HLA antigens of transfused blood cells may be responsible for this post-transfusion immune reaction. Current concepts suggest that antibodies to the Pl^{A1} antigens cause the platelet destruction of PTP. But in light of this case and of those presented by Vaughan-Neil and coworkers[15] and Zeigler and associates,[11] other alloantibodies or immune antibody complexes involving the HLA system may be responsible for the thrombocytopenia.

Various treatments for PTP have been tried. Exchange transfusions[5,7] and plasmapheresis[8,16] have been reported to be effective. Corticosteroids have not been demonstrated to be beneficial, except in 1 case described by Seidenfeld and coauthors.[12] Platelet transfusions have generally failed to improve the thrombocytopenic state or to relieve bleeding symptoms.

Comment

This case illustrates the syndrome of post-transfusion purpura occurring in a Pl^{A1}-positive patient who was treated with splenectomy. A high-titer antibody against a very-high-frequency antigen that appears to be common to both platelets and lymphocytes was demonstrated. The antibody may be HLA related, and most likely it originated with the transfusion of blood 7 days prior to the onset of purpura. The antibody may also have caused the delayed hemolytic anemia manifested by the positive Coombs' study.

Splenectomy was performed when treatment with corticosteroids and platelet and blood transfusions did not improve the patient's condition. Immune suppression with cyclophosphamide and monocyte macrophage inhibition with vinblastine sulfate (as described by Ahn and associates[17]) was utilized perioperatively to enhance platelet survival. The surgical technique for splenectomy was tailored for a relatively avascular abdominal incision and expedient clamping of the splenic vascular pedicle. HLA-compatible platelet infusion completed this patient's treatment. The combined effect resulted in resolution of the patient's thrombocytopenia by the fourth postoperative day.

Plasmapheresis was not attempted in this case. Plasmapheresis to remove immune reactive substances has not been definitive, but could be a "time buying" procedure. An immediate risk to the patient, in terms of adverse effect on blood pressure and cardiovascular status, would exist while plasmapheresis was being performed. Two physician-directors of blood banking services who were consulted on this case felt that this procedure was ill advised because of the preceding considerations. Also, the only reported case of death from PTP had been treated by plasmapheresis.

Conclusion

This case supports the proposition of Zeigler and associates[11] that PTP is a heterogenous disorder. This Pl^{A1}-positive patient developed a high-titer antibody, which appeared to be HLA related and was reactive to more than one circulating blood cell class. The patient's clinical course and presentation was consistent with other reported cases of PTP. This case was the first in which the severe thrombocytopenia was treated by and responded to splenectomy.

Post-transfusion purpura, although rare, must be considered a severe clinical complication following blood transfusion. Specialized serologic testing will aid in classification and therapy. Splenectomy, immune suppressive therapy, and infusion of immune compatible platelets can help achieve complete recovery when a rapidly deteriorating, life-threatening situation occurs in a case of PTP

that has not responded to conservative therapy.

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