The Ineffectiveness of Random Donor Platelet Transfusion in Splenectomized, Alloimmunized Recipients

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The effect of splenectomy on the response to random donor platelet transfusion in 15 multitransfused thrombocytopenic patients is presented. Eight patients responded poorly, with low corrected platelet count increments at 1 and 24 hours posttransfusion. These eight patients were clinically alloimmunized and had lymphocytotoxic antibody (LCTAb) in their sera. They responded well to closely HLA-matched transfusions. In contrast, seven splenectomized patients responded well to random donor platelets. Five of these patients had no LCTAb and no other evidence of immunization. Two patients who responded well to random donor platelets had "weak" LCTAb, and one responded to platelets pre-splenectomy in the presence of this antibody. Splenectomy does not improve the response to random donor platelets in alloimmunized recipients.

The major challenge of platelet transfusion therapy today continues to be the management of the alloimmunized thrombocytopenic patient. To date, the only effective method of providing platelets for these individuals is by apheresis of HLA-compatible donors.1 As this requires the maintenance of hundreds of HLA-typed potential donors on computer file and the availability of staff to recruit, locate, and apherese these donors, it greatly increases the expense and inconvenience of platelet transfusion for alloimmunized patients.

The spleen has been shown to be a major site of removal of immunologically damaged platelets from the body in both autoimmune thrombocytopenia (ATP) and patients with alloantibodies formed against transfused platelets.2 Although splenectomy is a common and usually successful treatment for ATP,3 there is very little information on its usefulness in the management of alloimmunization against platelets. We have had the opportunity to study the response to platelet transfusion in a series of 15 splenectomized thrombocytopenic patients, a number of whom were alloimmunized.

Materials and Methods

Patients were selected for study from the case records of the University of Maryland Cancer Center. Patients were included if they had been splenectomized for any reason and had subsequently received platelet transfusions as part of their routine care. All patients were clinically stable at the time of the evaluated platelet transfusion. None had fever greater than 101°F, hemorrhage, autoimmune or drug-induced platelet destruction, or disseminated intravascular coagulation. Lymphocytotoxic antibody (LCTAb) testing was done on patient serum at diagnosis and was repeated at monthly intervals or more frequently if clinically warranted by changing response to random donor platelets. LCTAb was determined as percent cytotoxicity of patient serum against a large 80–100-cell panel of lymphocytes of different antigenicity using standard methods.4

All platelet transfusions were evaluated by posttransfusion counts on the recipient and by determination of the total number of platelets (count x volume) in the donation bag of platelets. All platelet counts were done electronically, in duplicate, on both the recipient and platelet bag. All transfusions were assessed by corrected count increments (CCI).

\[ CCI = \frac{\text{Platelet count increment/}uL \times \text{Body surface area (m}^2)}{\text{Number of platelets transfused} \times 10^{11}} \]

For example, a recipient with a posttransfusion peripheral blood platelet count increment of 40,000/μL (increment = platelet count posttransfusion – platelet count pretransfusion) and a body surface area of 2 m² would have a CCI, after receiving a transfusion of 4 x 10¹¹ platelets, determined as follows: \[ CCI = \frac{(40,000 \times 2)}{4} = 20,000 \]

The CCIs were calculated after all transfusions at 24 hours; the majority of transfusions were also evaluated by a CCI 1 hour after transfusion. All transfusions consisted of pooled random donor platelet concentrates or single donor platelets that were at best partially HLA-matched, administered within 24 hours of collection, and stored with agitation at 22–24°C. Patients received between one and seven transfusions, each given at a time when their LCTAb level was stable. Data are presented as the mean CCI at 1 and 24 hours for each patient transfusion sequence to establish an overall transfusion response for each patient.

Results

Patients who met the criteria for inclusion in this study had a variety of hematologic neoplasms (Table 1): ten had acute nonlymphocytic leukemia, four chronic myelogenous leukemia in blast crisis, and one Hodgkin's disease with aplastic anemia following therapy. Nine of these patients had been splenectomized as...
part of an experimental protocol for the treatment of acute nonlymphocytic leukemia, one as part of staging evaluation for Hodgkin’s disease, and five for intercurrent complications of their disease, including hypersplenism with thrombocytopenia (three patients), splenic infarction and hemorrhage (one patient), and traumatic rupture (one patient).

The 15 patients fall into two groups: seven who responded well to random donor or partly matched platelet transfusions, and eight who responded poorly. We accept a 1-hour corrected count increment of 10,000 or greater and a 24-hour corrected count increment of more than 7,500 as an adequate response to platelet transfusion. Using these criteria none of the seven patients who had counts performed had CCIs greater than 20,000, and at 24 hours posttransfusion, 6 of the 7 patients who had counts performed had CCIs greater than 9,000.

Seven splenectomized patients had good responses to random donor platelets at 1 and 24 hours following transfusion. Five of these patients (patients 11–15, Table 1) had no evidence of LCTAb in their serum. Patients 9 and 10, with good CCIs, had LCTAb demonstrated. Both of these patients had LCTAb reactions that were described as “weak,” meaning a low percentage of cells in each of the wells on the lymphocyte panel were killed by patient serum. Patient 10 also had LCTAb that had specificity against HLA-A23 and -A24, so that some of the random donor platelets given to her may have been compatible by chance. This patient had LCTAb present in her serum and a good response to random donor platelets before her spleen was removed. Patient 9 did not develop LCTAb until after splenectomy, so that her presplenectomy response to platelets in the presence of antibody cannot be assessed.

**DISCUSSION**

The rationale for splenectomy in autoimmune thrombocytopenia is based on the demonstration that the spleen is a major site of platelet destruction and antiplatelet antibody production in that disease. The platelet antigen against which this antibody is directed is uncertain. Seventy-five percent of patients

### Table 1. Response to Platelet Transfusion in Splenectomized Thrombocytopenic Patients

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Diagnosis</th>
<th>LCTAb</th>
<th>Mean 1-h CCI (x 10⁹)</th>
<th>Mean 24-h CCI (x 10⁹)</th>
<th>Mean 1-h CCI (x 10⁹)</th>
<th>Mean 24-h CCI (x 10⁹)</th>
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<td>1</td>
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<td>3</td>
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<td>6.3</td>
<td>2</td>
<td>30.2</td>
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<td>4</td>
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<td>1.8</td>
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<td>5</td>
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<td>19.0</td>
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<td>1.2</td>
<td>46.8</td>
<td>1</td>
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</table>


†N, number of evaluated transfusions.

‡The number of evaluated transfusions indicated in parentheses was single donor, poorly HLA-matched.
with ATP will respond to splenectomy with a significant rise in platelet count. In alloimmunized patients, the situation is quite different. The antibodies responsible for the destruction of transfused platelets are directed primarily against foreign HLA antigens. They are often present in very high titer in multitransfused patients and reduce the half-life of transfused platelets to less than 1 hour, as indicated by the low 1-hour posttransfusion increments typically seen in our patients and data from isotopic labeling of platelets and survival studies performed by other investigators. Although the spleen undoubtedly plays a role in the destruction of transfused platelets coated with antibody in alloimmunized patients, it is not the only site at which these damaged cells are removed from the circulation. The liver has been shown to play a role in platelet destruction in the most severe cases of ATP, which are often refractory to splenectomy. There is evidence that the liver similarly can be a major site of removal of incompatible transfused platelets in alloimmunized patients. Intravascular platelet destruction has not been shown to be an important component of platelet loss in ATP, and there are no data to demonstrate the frequency or importance of intravascular platelet loss in alloimmunized patients. The eight alloimmunized, splenectomized patients in the present series had posttransfusion platelet recoveries indistinguishable from those seen in alloimmunized patients with their spleens intact. In a series of 60 such immunized patients, we have previously found mean 1-hour and 24-hour CCIs of 5,600 (±5,400 SD) and 2,600 (±3,400), respectively.

In contrast, splenectomized patients who are not immunized will typically show an improved response to random donor platelet transfusion, with higher count increments than obtained presplenectomy. This was true in our five nonimmunized, splenectomized patients. We have found mean 1-hour and 24-hour CCIs of 16,100 (±6,100 SD) and 12,000 (±5,300), respectively, in a series of 137 nonimmunized, non-splenectomized patients. Each of our nonimmunized, splenectomized patients have CCIs higher than the mean reported in that series, particularly at 1 hour posttransfusion. This phenomenon is to be expected in view of the known sequestration of approximately one third of the extramedullary platelet stores in the normal spleen.

Two previous studies have examined the effectiveness of splenectomy on the response to platelet transfusion in patients with aplastic anemia. In the study by Flatow et al., three patients were splenectomized who had a poor response to both random donor and single donor platelets. All responded with improved posttransfusion count increments. However, it is not clear from the data presented that these three patients were alloimmunized. Preoperative platelet transfusions were able to raise the platelet count to greater than 100,000/µL in all three patients, which would be unusual in alloimmunized patients. Patients 2 and 3 in that series had a number of significant posttransfusion platelet count increments before splenectomy, which is also unusual in severe alloimmunization. No serologic confirmation of the presence of HLA antibodies is reported in this study, and antiplatelet antibodies could not be detected by complement fixation techniques. An improvement in post platelet transfusion count increments in a nonimmunized patient is to be expected after splenectomy, as illustrated by patients 11–15 in our study. This is especially true in patients with documented hypersplenism, such as patient 3 in Flatow’s study. In contrast to Flatow’s results, Grumet et al. reported on the results of splenectomy in six aplastic patients who were clearly refractory to random donor platelets. In agreement with our results, they found no improvement in response to random donor platelets after splenectomy. The response to HLA-compatible platelets was improved after splenectomy, as would be expected with the loss of normal splenic sequestration.

In conclusion, splenectomy has very limited application to the management of suboptimal response to platelet transfusion. In the absence of documented hypersplenism, alloimmunized thrombocytopenic patients should not be subjected to splenectomy, but should be managed with HLA-matched transfusions alone.

REFERENCES


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DE Hogge, JP Dutcher, J Aisner and CA Schiffer