

## **Practical Problems in Transfusion Medicine**

### **Transfusion Therapy Case Study 2**

#### **Part 3: Diagnosis and Treatment**

This patient was clearly refractory to platelet transfusion confirmed by a CCI of only 4000/ $\mu$ L. The patient has no evidence of DIC or splenomegaly, and has only a low grade fever. It can therefore be concluded that the cause is immunologic. This is reinforced by the knowledge that she is multiparous. Her physician should be informed that until compatible platelets can be found, she should not receive further platelet transfusions. Further immediate transfusion would only be appropriate if she is experiencing life threatening bleeding (e.g. intracerebral, intrapulmonary, or massive gastrointestinal). If not yet known, it is necessary to determine if the patient was HLA typed prior to induction therapy. The approach to further evaluation and the management of providing matched platelet products varies among institutions depending on the availability of laboratory and platelet resources.

#### **Diagnosis of Platelet Refractoriness**

Casual review of this patient's history of a daily platelet transfusion requirement and persistent marked thrombocytopenia allows conclusion that she is refractory to platelet transfusion. To document a refractory state in cases not quite as obvious, it is necessary to calculate the count increment one hour after transfusion corrected to a uniform body surface area of one  $m^2$ . The Corrected Count Increment (CCI) is calculated as follows:

$$\frac{(\text{post transfusion} - \text{pre transfusion platelet count}) \times (\text{body surface area})}{(\text{no. of platelets transfused})}$$

"Body surface area" is the square root of BSA in square meters.

"No. of platelets transfused" is expressed as multiples of  $1 \times 10^{11}$ . The average content of one SDP unit is  $4-5 \times 10^{11}$  platelets.

$$\text{In this case the calculation would be: } (14,000 - 2000) \times 1.5 / 4.5 = 4000$$

Repeated CCIs below 7500/ $\mu$ L per unit of SDP transfused is considered suboptimal and below 4500/ $\mu$ L is clearly indicative of a refractory state.

#### **Providing Matched Platelets for Refractory Patients**

In some institutions, the immunologic basis of the refractory state is documented immediately by testing for the presence of lymphocytotoxic HLA antibodies, while in others the antibody screen is performed only in patients who fail to respond to HLA matched platelet transfusions. In general, refractory patients who have been HLA typed are transfused with A or B matched SDP platelets, if available. For those who have not been typed, (unfortunately still not an uncommon occurrence), regional centers may be asked to perform an antibody screen for HLA and platelet specific antibodies and then crossmatch random ABO compatible SDP units for the patient.

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## ***Strategies for managing complex cases of platelet refractoriness***

Failure to respond adequately to matched platelets should lead to a renewed effort to identify non-immunologic reasons for the refractory state. The management of patients for whom no compatible platelets can be identified presents a special challenge. Prophylactic platelet transfusions are avoided with the hope that the antibody titer will fall. While the infusion of IVIgG and/or the performance of plasma exchange to reverse the refractory state has been suggested, little evidence supports their use. Administration of full oral doses of e-aminocaproic acid (Amicar) has been shown to prevent bleeding in patients with amegakaryocytic thrombocytopenia, and its administration until recovery of counts should be considered if the presence of low grade DIC can be eliminated by finding a negative D-dimer test or a negative test for soluble fibrin monomer complexes. Greater caution should accompany its use in patients with M3 AML or in patients with ALL receiving asparaginase. Alternatively, the administration of desmopressin to prevent or treat mucosal bleeding has been reported to be effective. The onset of intracranial or other severe bleeding in these patients constitutes a life-threatening situation. While the outlook is grim, hemostasis has been occasionally achieved by slowly infusing 6 to 8 units of platelet concentrates (prepared from whole blood donations) followed by the rapid infusion of a large bolus of 10 to 12 units. More recently, the use of recombinant activated factor VII (NovoSeven) has been suggested for such extreme situations, but data on its efficacy is lacking.