Posttransfusion Purpura

Posttransfusion purpura (PTP) is exceedingly rare with an approximate incidence of 1 in 50,000 to 100,000 blood transfusions. PTP typically presents with precipitous and severe thrombocytopenia 5 to 10 days after transfusion of RBC or platelet components. Signs and symptoms associated with PTP include purpuric rash, bruising, and bleeding from mucous membranes. It is possible for life-threatening intracranial bleeding to occur, which may result in a fatality.

The occurrence of PTP in females compared to males is 5:1. Furthermore, multiparous women are more likely to be affected, because pregnancy and blood transfusion are sensitizing events associated with increased risk for alloimmunization. Although the mechanism is not fully understood, PTP is believed to be mediated by immune-mediated platelet destruction. Antibody against platelet antigen HPA-1a is most frequently associated with PTP. Other associated antibody specificities include anti-HPA-1b; -HPA-2a, -2b; -HPA-3a, -3b; -HPA-4a; -HPA-5a, -5b; -GPIIb/IIIa, and -GPIV (CD36). Although reactivity against HLA Class I antigens (A and B) has also been detected, its clinical significance is unknown at this time. In addition, along with alloantibodies, mounting evidence suggests that pan-reactive autoantibodies can develop and mediate the destruction of both donor and recipient platelets. The result is a profound thrombocytopenia that can reach a platelet count as low as <10,000/µL.

Diagnostic work-up is based on the detection of platelet-specific alloantibodies. Once reactivity to platelet-specific antigens is detected, genotyping is performed to verify that the patient is negative for the particular antigen. Although these laboratory results may not be available in time to guide therapy, they may be used for future management of the patient. After the acute event, if it is feasible, future platelet transfusion should be from antigen-negative donors. Autologous transfusion may also be considered.
Iron Overload

Multitransfused patients [ie, those with thalassemia, sickle cell disease (SCD), myelodysplastic syndromes (MDS), or history of hematopoietic stem cell transplant] are at risk of transfusion-related iron overload (hemosiderosis). Over time, simple RBC transfusion in the absence of red cell loss leads to iron deposition in tissues (hemosiderin) and insidious damage of the heart, liver, pancreas, pituitary gland, and other organs. With the advent of more effective chelation therapy, malignant transformation has become an emerging complication. With chronic RBC transfusion, iron is not only toxic but potentially lethal.

Clinical presentation depends on the organ system affected. Possible clinical signs and symptoms include bronze skin, joint pain, fatigue, hypogonadism, abnormal liver function, diabetes mellitus, cardiac failure, and arrhythmias. Cardiac dysfunction may be detected by abnormal echocardiogram or elevated BNP. Iron overload can be detected on magnetic resonance imaging (MRI), which does not detect iron or ferritin but primarily hemosiderin, which is made up of aggregates of ferritin.

Screening should begin after a patient has received more than 20 units of RBCs. In pediatric patients who require chronic transfusion, evaluation is recommended after receiving more than 100 mL/kg of RBCs. Tests used to evaluate iron overload include serum iron, total iron binding capacity (TIBC), transferrin saturation, and ferritin. Measuring serum iron alone is not advisable as it is affected by fasting, pre- and post-prandial states, and has diurnal variation. Patients taking iron chelators may have misleadingly normal serum iron levels. Serum ferritin is, therefore, preferable to serum iron but for a complete evaluation, transferrin saturation and ferritin should both be measured.

In normal iron hemostasis, iron is stored in the reticuloendothelial system. Once the iron storage capacity of the liver and spleen is exceeded, the amount of free transferrin and TIBC decreases and circulating iron not bound to transferrin increases. Hemosiderosis can be diagnosed when ferritin is greater than 1000 µg/L and transferrin saturation is 60-100%. High levels of ferritin may be seen in other conditions including
hemophagocytic lymphohistiocytosis, hepatitis, rheumatoid arthritis, and in the setting of inflammation. Therefore, clinical and transfusion history are critical during the workup of transfusion-related iron overload. For example, for patients with SCD, the American Society of Hematology suggests iron overload screening by MRI for liver iron content (but not cardiac iron content) every 1 to 2 years in patients receiving chronic transfusion (not by red cell exchange with neutral or negative iron balance) when ferritin is greater than 1000 ng/mL.

To prevent transfusion-related iron overload, RBC transfusion should be limited to when truly indicated. For patients with thalassemia and SCD, when chelation therapy is not successful, red cell exchange should be considered.

Transfusion-Associated Graft-vs-Host Disease

Overview

Transfusion-associated graft-vs-host disease (TA-GVHD) is a rare and often fatal complication of blood transfusion in which viable donor lymphocytes from the transfused blood component engraft, proliferate, and attack the recipient’s tissues. The recipient’s immune system either is unable to mount an effective immune response due to severely immunocompromised state or fails to recognize the transfused donor lymphocytes as foreign due to HLA similarity.

Three primary factors influence the risk for development of TA-GVHD. They include: 1) extent of immunosuppression of the recipient that limits the ability to reject the transfused donor lymphocytes; 2) degree of HLA antigen sharing between the donor and the immunocompetent recipient where donor lymphocytes are HLA homozygous for one of the recipient’s haplotypes (see Fig 9); and 3) number and viability of lymphocytes in the cellular component.