Transfusing Patients with Sickle Cell Disease

Sickle cells are prematurely removed from the circulation by the spleen, resulting in hemolytic anemia. The circulating half life of sickle cells is 16 to 20 days, compared to 120 days for normal RBCs.

RBC transfusion provides many benefits including increasing the patient’s hemoglobin, diluting the concentration of Hgb S with Hgb A and providing RBCs with longer circulating half times that do not sickle nor polymerize. In addition, transfusion suppresses the patient’s own erythropoiesis, reducing production of sickle RBCs.

RBCs can be transfused as a simple or exchange transfusion. A simple transfusion involves transfusing one or two units of RBCs through a peripheral IV. Exchange transfusion uses an apheresis machine to more rapidly replace one to two red blood cell volumes with donor RBCs.

Indications for transfusion in sickle cell disease include:
- Aplastic Crisis
- Stroke
- Splenic Sequestration
- Pregnancy with complications of sickle cell disease
- Priapism if not responsive to hydration and analgesia
- Presurgical
- Acute Chest Syndrome

Simple transfusions are preferred for pediatric patients who suffer a stroke. Exchange transfusion can be used to rapidly reduce the amount of Hgb S. Once a patient has a stroke, they are at risk for additional strokes. Monthly transfusions, either simple or exchange, to maintain HbS concentration below 30% reduces the risk of recurrent stroke. Transfusion of about 10 mL/kg of red blood cells every 3 to 4 weeks is usually sufficient to maintain HbS near 30% and the pretransfusion hematocrit between 25 and 30%.

During transfusion of patients with splenic sequestration, hemoglobin often increases beyond the expected level, so it is important to transfuse slowly to avoid over-transfusion.

Simple transfusion or exchange transfusion should be considered for patients with refractory priapism. Exchange transfusion has been associated with adverse neurologic sequelae, such as seizures and increased intracranial pressure, so this alternative should be reserved for the most refractory cases.

Patients with sickle cell disease are at high risk for complications during major surgery. Some practitioners recommend that patients be transfused to a hemoglobin of 10 g/dL prior to surgery. Exchange transfusion is not necessary.

Patients with the acute chest syndrome benefit from transfusion early in the course of their disease. Simple transfusion is preferred for patients who are stable. Simple transfusion should only be performed until the hemoglobin reaches about 10 g/dL since higher levels have been associated with vaso-occlusion. Exchange transfusion is recommended for patients who have a rapidly evolving course or do not respond to simple transfusion. There does not appear to be any role for transfusion in the management of routine, uncomplicated painful crises.

Adverse consequences of transfusion of patients with sickle cell disease include alloimmunization, hyperhemolysis and iron overload. Patients with sickle cell disease are chronically transfused and have a high rate of alloimmunization (18-36%). Most patients with sickle cell disease in the United States are African American, and most donors are Caucasian from Western European descent. As a result of this ethnic difference, patients with sickle cell disease are exposed to RBC antigens that they lack, increasing the likelihood of alloantibody formation. The most common antibodies formed in
this population are C, E, K1 and Fya. In order to prevent alloimmunization, Saint Luke’s Hospital transfusion service routinely determines patients’ RBC phenotypes and only transfuses RBCs that lack C, E, K1 and Fya, if the patient is negative for these antigens. A complimentary strategy, which has been undertaken by the Charles Drew Program of the American Red Cross, is to recruit donors who are ethnically similar to sickle cell patients.

The hyperhemolytic syndrome is a serious complication of transfusion that occurs in patients with sickle cell disease. In this syndrome, a patient’s hemoglobin falls, instead of rises, after transfusion. Both the patient’s own RBCs and the transfused RBCs are destroyed even though the transfused RBCs are crossmatch compatible and no new alloantibodies are detectable at the time of transfusion. Further transfusion compounds the problem. Therefore, it is important to recognize this syndrome early and, if possible, discontinue transfusion. If additional transfusions are required because of life-threatening anemia, they should be done cautiously, using concurrent IVIG and steroids.

Each unit of transfused RBCs contains about 200 to 250 mg of iron. With chronic transfusion, iron accumulates in the heart, liver, and endocrine glands. In order to prevent this complication, iron chelating medication is administered. Serum ferritin is serially measured to assess iron stores.

Patients with sickle cell disease should not be transfused with RBCs containing Hgb S. Therefore, SLH transfusion service selects units that lack Hgb S. Patients with sickle cell disease should also be transfused with leukocyte reduced blood products to decrease the risk of cytomegalovirus (CMV) transmission, febrile non-hemolytic transfusion reactions, immune suppression, HLA alloimmunization and RBC alloimmunization.

In summary, RBCs selected for transfusion of patients with sickle cell disease should be:

- Hgb S negative
- Leukocyte reduced
- Negative for C, E, K1 and Fya antigens if the patient lacks these antigens
- Negative for any other antigens to which the patient has already been sensitized
- Collected from African American donors if a program exists

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**CD23-Positive Mantle Cell Lymphoma By Flow Cytometry**

Typically, CD20/CD5-negative, CD23-positive flow cytometry cases with monotypic expression of surface immunoglobulin light chain are consistent with mantle cell lymphoma (MCL).

CD20/CD5/CD23-positive cases are compatible with a diagnosis of chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), however the differential diagnosis includes MCL, in which a small but significant subset of MCL cases is CD23 positive.

Several investigators have analyzed the intensity of CD23 in CD23-positive MCL cases and compared the intensity to CLL/SLL (Hematol Oncol. 2008 Apr 1;26(3):167-170, Am J Clin Pathol. 2001 Dec;116(6):893-7, Am J Clin Pathol. 2003 Nov;120(5):760-6). These studies showed that CD23 demonstrates weak or dim expression in CD23-positive MCL cases, whereas CD23 is moderate to strong or brightly expressed in CLL/SLL. The intensity of CD20 and surface immunoglobulin light chain further helps to distinguish CD23-positive MCL cases from CLL/SLL. In MCL, CD20 and surface light chain expression is usually moderate or strong compared to CLL/SLL where the expression of these markers is typically weak or dim.

An association between the expression of CD23 in MCL flow cytometry cases and improved patient survival rates has also been reported. In a recent paper published in the American Journal of Clinical Pathology (Am J Clin Pathol. 2008 Aug;130(2):159-61), investigators reported that patients with CD23-positive disease had 4-year event-free and overall survival rates of 45% and 75%, respectively, compared to 19% and 51% for patients with CD23 negative MCL. Furthermore, extranodal disease was found more frequently in CD23-negative MCL compared to those cases in which CD23 was positive.

Cyclin D1 immunohistochemistry and/or FISH analysis for the t(11;14)(q13;q32) translocation should be performed on monoclonal CD20/CD5/CD23-positive flow cytometry cases when the findings are suspicious (CD23 weak or dim, CD20 and surface light chain strong or bright), but not characteristic for MCL.