Sickle Cell Disease

A 22-year-old male with a history of sickle cell anemia presented to the hematology clinic for a new patient appointment. He had recently moved to the area from another state. He complained of mild joint pain but was otherwise in good health. His condition had been managed with hydroxyurea and he had previously received blood transfusions but had not been transfused in the last 6 months. No blood bank test records were available.

Participants were asked to perform routine testing including ABO, Rh(D), Antibody Screen, and, if indicated, Antibody Identification.

Actual results on these samples were as follows:

<table>
<thead>
<tr>
<th>Sample</th>
<th>ABO</th>
<th>Rh (D)</th>
<th>Antibody Screen</th>
<th>RBC Phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td>EDU-01</td>
<td>B</td>
<td>Positive</td>
<td></td>
<td>R_o, K-, Fy(a-b-), Jk(a+b+), S-s+</td>
</tr>
<tr>
<td>EDU-02</td>
<td>B</td>
<td></td>
<td>Positive (Anti-C, -Fya)</td>
<td></td>
</tr>
</tbody>
</table>

Discussion

Sickle Cell Disease (SCD) is a group of inherited disorders of hemoglobin synthesis that result in the presence of at least one hemoglobin S chain (HbS). Sickle cell anemia (SCA) or HbSS disease is the most common and severe form, and occurs when a person is homozygous for the HbS gene. Other forms of sickle cell disease include but are not limited to Hemo
globin S C disease (HbSC) and HbS beta thalassemia. SCD affects approximately 100,000 Americans and occurs in 1 out of every 365 African-American births. Sickle cell disease also affects about 1 out of every 16,300 Hispanic-American children.

Red blood cells from patients with HbSS become rigid and transform into "sickled" shapes in the presence of low oxygen levels or high hemoglobin concentrations. The abnormal red cells become trapped in blood vessels leading to multiple issues. Pain crises and organ ischemia as a result of blood vessel occlusion frequently occur, with pain crises being the most distinguishing feature of SCD and the leading cause of emergency visits for SCA patients. Chronic mild pain in bones and joints is common and hemolytic anemia is a universal symptom. In addition, the risk of stroke and cerebral ischemia in SCA patients is very high, with approximately 11% of patients having strokes before age 20. Many other complications of sickle cell anemia exist including the potential for aplastic crisis, acute chest syndrome, infection, splenic sequestration, and pulmonary hypertension.
Sickle Cell Disease (cont.)

Treatment for sickle cell disease usually consists of a combination of transfusion and drug therapies. Transfusion therapy may occur as an exchange transfusion or as a simple transfusion. Exchange transfusion is the removal of the patient’s circulating red blood cells and replacement with donor red blood cells by either a manual procedure or by an automated apheresis procedure. The procedure may be performed in an inpatient or outpatient setting, and can take several hours depending on blood volume to be exchanged. Goals of red cell exchange are reduction of HbS levels while maintaining total hemoglobin levels at <10 g/dL and preventing hyperviscosity, as well as decreasing erythropoiesis of sickle cells.\(^5\)\(^6\) Red cell exchange may be indicated for SCA patients with severe acute chest syndrome, as a monthly preventative treatment in patients with a history of stroke, or for multisystem organ failure.\(^7\) Simple transfusion (i.e., the transfusion of one or more units of blood without removal of the patient’s circulating red cells) may be indicated for patients in aplastic crisis, patients experiencing acute splenic sequestration with severe anemia, or those with symptomatic anemia.\(^7\)

While simple or exchange transfusion may often be warranted, it is important to consider the type of blood transfused to sickle cell patients. At a minimum, red cells should be leukoreduced and negative for hemoglobin S.\(^8\) Prophylactic antigen matching to prevent alloimmunization in sickle cell patients has been a topic of discussion for many years; there has been no definitive consensus on how closely red cells should be antigen matched to the recipients.\(^9\) Alloimmunization occurs in approximately 8-35% of multiply transfused sickle cell patients, with Anti-C, Anti-E, and Anti-K being the most commonly encountered antibodies.\(^10\) Antibody formation in these patients can lead to severe consequences, including long delays for needed transfusions and hemolytic transfusion reactions.\(^11\)

While some institutions perform serologic phenotypes prior to transfusion and at least partially match the patient’s red cell phenotype, not all centers have this policy.\(^8\)\(^11\) Some centers use red cells matched to the patient’s Rh and K phenotype, while others match red cells to the patients’ full red cell phenotype to include Rh, K, Fy, Ss, and Jk. Additional institutions may wait for a patient to form an antibody prior to antigen matching.\(^9\)\(^12\) Extended antigen matching for Rh and K antigens (and fully antigen matched units) has been shown to reduce the rate of alloimmunization in sickle cell patients from 30% down to 10%, but full extended phenotype matching can be time consuming and costly.\(^12\) It is up to individual institutions to determine their own guidelines for antigen matching for sickle cell patients based on their patient population.

Allogeneic stem cell transplant has shown to be a curative treatment for sickle cell disease. It is typically only performed in children younger than 16 years of age, but efforts are being made to be able to extend transplant to adults. In addition, there is debate about which patients qualify for transplant and what clinical situations warrant the risk of transplant in hope of the potential benefits. While allogeneic stem
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cell transplant gives hope for a cure, there is no guarantee and the process carries a high degree of morbidity and mortality.\(^{13}\)

Finally, the drug hydroxyurea has been shown to provide substantial benefits to SCA patients. Hydroxyurea is a myelosuppressive drug approved by the FDA for use in adults and children over 2 years of age.\(^{14,15}\) It works by increasing the level of hemoglobin F (fetal hemoglobin) in the blood, providing the body with a normally functioning hemoglobin chain. Hydroxyurea has been shown to reduce episodes of vaso-occlusive crisis and acute chest syndrome, but is significantly underutilized.\(^{15}\)

**Conclusion**

The above patient presented to a clinic with sickle cell anemia that had been controlled using hydroxyurea therapy. A red cell phenotype was ordered in addition to his type and screen. The patient had already made two clinically significant allo-antibodies (Anti-C and Anti-Fya). In addition to providing red cells negative for C and Fya antigens, prophylactic red cell antigen matching for the other antigens the patient lacked should be strongly considered if future transfusion was indicated.

**References**


Sickle Cell Disease (cont.)


This case study and discussion was provided by Hemo bioscience (www.hemobioscience.com), the manufacturer of these Blood Bank proficiency samples.