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Case Report

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Intrapartum Management of Sickle Cell Anemia With Rare Antibody and Minimal Blood Availability

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Abstract

Sickle cell disease (SCD) can pose serious maternal and fetal risk in pregnancy. Transfusion, both during and outside of pregnancy, can improve patient morbidity and mortality but carries risk of alloimmunization, complicating future management. This case describes a 29-year-old gravida 1, para 0 woman with sickle cell anemia and rare red blood cell alloantibody (anti-Rh46) who presented with severe vaso-occlusive crisis at 29 weeks with hemoglobin of 7.6 g/dL. Only one unit of compatible blood existed in the country. Planning for transfusion with least-incompatible blood was made. She ultimately underwent cesarean section at 31 weeks and 2 days for abnormal fetal testing. This case highlights that blood products should be utilized judiciously because their adverse effects, like alloimmunization, can increase patient morbidity and mortality.

Keywords: Intrapartum management; Rare antibody; Sickle cell disease; Pregnancy; Transfusion

Introduction

Sickle cell disease (SCD) is caused by homozygous mutation of hemoglobin S (HbSS), which deforms red blood cells and precipitates hemolysis and vaso-occlusion under hypoxic stress. Patients with SCD suffer from lifelong complications like end-organ damage and infection that shorten the mean life span to 39 years in the USA [1]. They are also known to have a more complicated pregnancy course. Approximately half of women with SCD require transfusion during pregnancy [2]. This is in stark contrast to the general obstetric population, of which 1.6% required transfusion in 2010 [3].

One of the greatest risks of transfusion is alloimmunization, the formation of antibodies to red cell antigens. Around 30% of adults with SCD have one or more clinically significant red blood cell alloantibodies [4]. Not only can alloimmunization harm the fetus by causing hemolytic disease, but it can limit available blood products for the mother during critical illness.

This case offers an example of alloimmunization from prior transfusions affecting a current pregnancy in a patient with SCD. Our patient had severe anemia and an alloantibody so rare that only one unit of compatible blood was available in the entire country.

Case Report

A 29-year-old gravida 1, para 0 woman with HbSS presented at 29 weeks with estimated date of delivery by 7-week ultrasound. Her past surgical history was notable for laparotomy for gunshot wound with an extensive abdominal scar. She smoked cigarettes and marijuana. Her SCD history included multiple episodes of acute chest syndrome, one exchange transfusion, and left hip avascular necrosis.

She presented in acute vaso-occlusive crisis with back and hip pain. She was anemic throughout her pregnancy, with hemoglobin of 7.1 g/dL at her first obstetric visit. She followed closely with hematology and was receiving weekly injections of 40,000 units of epoetin alfa. On admission, she received intravenous (IV) narcotics, IV fluids, and supplemental oxygen. Her hemoglobin was 7.6 g/dL. Blood transfusion was not an immediate option secondary to the following complications: 1) The presence of several alloantibodies, including anti-C, anti-E, and a very rare antibody to Rh46; 2) There was only one unit of donor-matched compatible blood available in the USA; and 3) The only known donor had recently died.

She remained inpatient due to persistent pain, oxygen requirement, and social stressors exacerbating her pain. Her epoetin alfa was increased to twice weekly when her hemoglobin dropped to 6.4 g/dL. A delivery plan was made with hematology to permit transfusion of least-incompatible blood if hemorrhage or blood loss anemia occurred with delivery. Transfu-

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sion with least-incompatible blood requires pre-treatment with IV steroids. The blood bank was notified, and they coordinated availability of least-incompatible blood. A plan was made for prophylactic administration of the one matched unit prior to delivery, as a single unit is unlikely to be sufficient in the setting of hemorrhage, but it could improve hemodynamics for delivery.

On hospital day 11, she had an increased oxygen requirement, and on hospital day 15 occasional late fetal heart rate decelerations were noted. With anticipation of possible delivery, antenatal corticosteroids (betamethasone) were administered. Her epoetin alfa was increased to three times per week. She was also given IV steroids (3 mg/kg methylprednisolone loading dose and 1 mg/kg Q8H) as premedication in the event the least-incompatible blood was required. The one unit of compatible blood was available at the Red Cross; timing was critical, as the unit would expire 24 h after de-glycerolization for transport. The pediatric team expressed concern that the neonate may also require this single unit of compatible blood.

On hospital day 17 at 31 weeks and 2 days, prolonged decelerations were noted. Her hemoglobin was 7.0 g/dL. Plan was made for cesarean delivery given her unfavorable cervix, non-reassuring fetal status, and inability to perform an emergent cesarean section given her extensive abdominal wall scar.

Her cesarean delivery was without complication. Estimated blood loss was 500 mL. There were numerous adhesions between the uterus and the anterior abdominal wall. The one unit of matched blood was split with her neonate; the patient received 200 mL, and her son received the remaining blood. Postoperative hemoglobin was 7.0 g/dL. Her IV steroids were weaned to 1 mg/kg Q12H on postoperative day 4 and were discontinued on postoperative day 7, when the risk of postpartum hemorrhage was thought to be low.

The patient reported increased bone pain postoperatively, which was attributed to bone marrow stimulation from her higher epoetin alfa dosing, as well as her IV steroids. By postoperative day 6 she was converted from IV to oral narcotics. She was discharged home on postoperative day 7.

Neonatal Apgars were 5 and 7 at 1 and 5 min, respectively. After delivery, the neonate was transferred to the neonatal intensive care unit on continuous positive airway pressure therapy. All three maternal antibodies were found in the baby as well, and he had hemolytic anemia. He required prolonged hospital stay and was discharged on hospital day 88.

Discussion

SCD during pregnancy can be dangerous to both mother and fetus. Pregnant women with SCD have risk of mortality six times that of a patient without this disease [5]. Patients with SCD also are 90 times more likely to have anemia during pregnancy [5], and almost half require a transfusion [2]. However, with transfusion also comes risk of alloimmunization. Not only are SCD patients more likely to have antibodies to foreign antigens from blood products received prior to pregnancy, but rates of novel alloimmunization developing during pregnancy were 5.3% and 16.6% in patients who underwent prophylactic partial exchange and exchange transfusions, respectively [6, 7]. It has also been demonstrated that patients with alloimmunization have worse pregnancy outcomes [2]. It is therefore important to know a patient's prior transfusion history during pregnancy, particularly in patients with hemoglobinopathies.

The antibody to Rh46 was first named in 1986. Anti-Rh46 is considered to be of clinical significance regarding transfusion during pregnancy; one specific complication caused by anti-Rh46 that has been previously described is hemolytic disease of the fetus and newborn (HDFN) [8]. HDFN occurs when maternal immunoglobulin G (IgG) antibodies sequester red blood cells that express certain antigens in the spleen, causing hemolysis and fetal anemia. In its severe form, this ultimately can cause hydrops fetalis and death. To our knowledge, anti-Rh46 has not previously been described in a pregnant patient with sickle cell anemia. We suspect the patient inherited this antibody either from massive transfusion after her shotgun wound, or during her previous exchange transfusion.

There has been controversy regarding prophylactic versus therapeutic transfusions for patients with SCD in pregnancy. Prophylactic transfusion aims to keep hemoglobin above 10 g/dL by transfusing every 3 - 4 weeks to maximize maternal and fetal oxygenation. A meta-analysis in 2015 demonstrated that prophylactic transfusion reduced maternal mortality, vaso-occlusive pain episodes, pulmonary complications, pulmonary embolism, pyelonephritis, perinatal mortality, neonatal death, and preterm birth [9]. However, opponents to this study say it was underpowered. Due to risks associated with transfusion, some authors support prophylactic transfusion only for those with complications or severe anemia. On-demand or therapeutic transfusion intends to avoid adverse effects of transfusion when possible, but is indicated in refractory pain or if the hemoglobin falls < 7 g/dL, as these levels are associated with poor fetal oxygenation and even fetal death [10]. Deciding when to transfuse above 7 g/dL should take into consideration the entire clinical scenario, including a patient's vital signs and symptoms, rather than solely treating a relatively low hemoglobin value.

This case presents an argument supporting on-demand transfusion, as it emphasizes the impact alloimmunization can have on blood availability for patients with SCD. These patients can have life-threatening anemia and it is important to maximize potential life-saving resources. However, as with all therapies, it is important to consider risks and benefits for each individual.

Use of least-incompatible blood requires advanced planning in order to coordinate with the blood bank and to pretreat with steroids to mitigate the severity of the inflammatory response to hemolysis. "Least-incompatible" blood is ABO compatible but free of all other antigens that could possibly be matched. In patients with SCD, this can be difficult as they can carry numerous antibodies, like our patient. Pretreatment with intravenous immunoglobulin and steroids has been shown to successfully attenuate hemolytic transfusion reactions in several patients [11]. However, due to sparse evidence, expert consensus is that intravenous immunoglobulin is not recommended for either prophylaxis or routine treatment of hemolytic transfusion reactions [4]. Therefore, our patient was treated with methylprednisolone only. Fortunately for our patient, she

never required the least-incompatible blood.

Our patient did, however, receive epoetin alfa throughout her pregnancy, with an increased frequency of dosing closer to delivery. Erythropoetin has been shown to be effective in pregnant women with anemia, concurrent dialysis, or antepartum or postpartum hemorrhage [12]. Recombinant human erythropoietin (containing epoetin alfa and beta) has been shown to provide symptomatic relief with less fatigue and shortness of breath and can raise hemoglobin up to 2.7 g/dL above baseline [12]. However, erythropoietin can increase risk of thrombotic vascular events as well as cause hypertension. In SCD, erythropoietin is also associated with increased pain as one's bone marrow is stimulated to release early stage erythrocytes and reticulocytes with increased adhesivity and tendency for vaso-occlusion. Therefore, it is important to consider risks and benefits of administering erythropoietin during pregnancy, when there is already an increased risk of venous thromboembolism. This case emphasizes the importance of a multidisciplinary approach involving the obstetrician, hematologist, and blood bank in order to create an optimal care plan individualized for each patient.

Finally, and perhaps most importantly, this case highlights the importance of using discretion when transfusing all reproductive-age women (not just those with SCD), as this treatment can be damaging to future pregnancies. Specifically, alloimmunization can cause HDFN. These potentially fatal consequences must be considered in order to protect patients and their future children.

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None to declare.

Conflict of Interest

None to declare.

Informed Consent

Not applicable.

Author Contributions

AMD, RP, NK and IO contributed to manuscript preparation, clinical care and decision making; PV contributed to clinical care and decision making.

Data Availability

The authors declare that data supporting the findings of this study are available within the article.

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