

# Massive Blood Transfusion in a Patient with Immunoglobulin A Deficiency Undergoing Cesarean Delivery

Christopher Steel, MD, Sonia Vaida, MD, and Berend Mets, MB, ChB, PhD, FRCA, FFA(SA)

Patients with immunoglobulin (Ig)A deficiency develop autoantibodies against IgA, which render them vulnerable to severe anaphylactic reactions when transfused with conventional blood or blood products containing IgA. In this report, we describe a patient with IgA deficiency and placenta accreta undergoing emergency cesarean delivery who required massive blood transfusion. We discuss the workup and treatment options in patients with known IgA deficiency. (*Anesth Analg* 2010;110:1088–90)

**I**mmunoglobulin (Ig)A deficiency is defined as an inability to produce antibodies of the IgA<sub>1</sub> and IgA<sub>2</sub> subclasses. It is a frequently diagnosed immunodeficiency syndrome, with a reported incidence of 1:700.<sup>1</sup> Most patients who have this disease are asymptomatic; however, some patients develop recurrent respiratory tract infections, allergies, chronic diarrhea, and lymphoid malignancies. Up to 40% of IgA-deficient individuals may also develop autoantibodies to IgA, which render them vulnerable to severe anaphylactic reactions when transfused with standard blood or blood products containing IgA.<sup>1</sup> We describe a patient with known IgA deficiency who presented for emergency cesarean delivery that resulted in massive blood loss with consequent coagulopathy, requiring blood and coagulation factor replacement. The patient's permission was obtained to publish this case report.

## CASE DESCRIPTION

A 33-year-old, 70-kg, pregnant woman (gravida 7, para 6) was admitted to the labor and delivery unit at 33 weeks' and 3 days' gestation with vaginal bleeding and complete placenta previa documented on ultrasound 2 weeks previously, and high likelihood of placenta accreta, given her obstetric history. Her medical history was significant for IgA deficiency, with an IgA level <20 mg/dL (lowest value given in our hospital laboratory). Anti-IgA antibody titers were not measured. The IgA deficiency had been diagnosed in childhood upon workup for recurrent upper respiratory tract infections. Her surgical history consisted of 4 uneventful cesarean deliveries and a dilation and

curettage for a spontaneous abortion. Physical examination revealed a Mallampati class 1 airway and thyromental distance of 6 cm. The hemoglobin level was 10.9 g/dL.

Twelve days after admission, an emergency cesarean delivery was performed for persistent vaginal bleeding and a nonreassuring fetal heart rate tracing. The patient had 2 large-bore IV catheters in place, and 4 U washed packed red blood cells (PRBCs) was available. In view of the anticipated bleeding and possible hysterectomy, it was decided that the cesarean delivery should be performed under general anesthesia. Anesthesia was induced with propofol and succinylcholine and maintained with 70% N<sub>2</sub>O in O<sub>2</sub> and sevoflurane. Fentanyl, midazolam, and rocuronium were administered after delivery.

Approximately 5 minutes after induction, the fetus was delivered with 1- and 5-minute Apgar scores of 8 and 9, respectively. Placenta accreta was diagnosed, and the placenta was removed from the uterus. Despite the administration of IV oxytocin 20 IU and IM carboprost tromethamine 250 µg, an estimated 2500 mL of blood was lost over 15 minutes. Despite multiple figure-of-eight sutures, the lower uterine segment continued to bleed profusely. Therefore, a third large-bore peripheral IV catheter and a radial arterial line were placed. A hysterectomy was performed, followed by bilateral hypogastric artery ligation. Simultaneously, the available 4 U washed PRBCs was administered.

After administration of the PRBCs, the surgeons believed that the surgical field was "oozy." A blood sample was sent to the laboratory to assess coagulation variables, and the blood bank was contacted to obtain IgA-deficient fresh frozen plasma (FFP). Laboratory values obtained approximately 30 minutes after delivery and subsequent values are reported in Table 1. An additional 4 U washed PRBCs was administered to address the final estimated blood loss of 4 L. In addition, 7 L crystalloid solution and 1 L of 5% albumin were administered intraoperatively to maintain hemodynamic stability.

Three hours after delivery, the surgical team believed that surgical hemostasis had been achieved. Nevertheless,

From the Department of Anesthesiology, Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania.

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Address correspondence and reprint requests to Sonia Vaida, MD, Department of Anesthesiology, Penn State Milton S. Hershey Medical Center, 500 University Dr., H187, Hershey, PA 17033-0850. Address e-mail to svaida@hmc.psu.edu.

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**Table 1. Hematology and Coagulation Variables, Estimated Blood Loss, and Transfused Products**

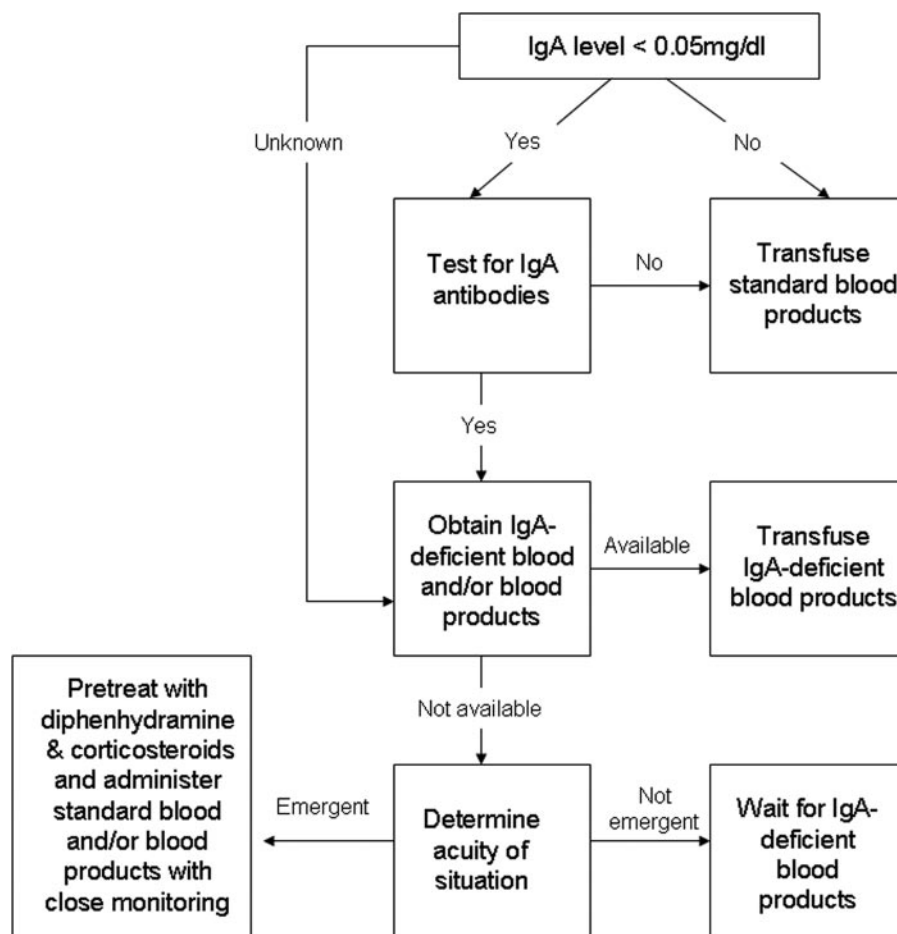
|                                    | Baseline values | Day 1 (1630) | Day 1 (1820) | Day 1 (2330)              | Day 2 (0359)              |
|------------------------------------|-----------------|--------------|--------------|---------------------------|---------------------------|
| Hemoglobin (g/dL)                  | 10.2            | 8.5          |              | 10.1                      | 10.3                      |
| Platelet count ( $\times 10^9/L$ ) | 233             | 146          | 124          | 116                       | 111                       |
| Prothrombin time (s)               | 10.0            | 12.0         | 11.6         | 10.8                      |                           |
| Partial thromboplastin time (s)    | 30              | 40           | 36           | 33                        | 29                        |
| Fibrinogen (mg/dL)                 | 398             | 115          | 129          | 170                       | 203                       |
| Estimated blood loss (mL)          | 0               | 2500         | 4000         | 4000                      | 4000                      |
| Cumulative transfused products     | 0               | 4 units PRBC | 8 units PRBC | 8 units PRBC, 2 units FFP | 8 units PRBC, 2 units FFP |

PRBC = packed red blood cells; FFP = fresh frozen plasma.

Normal values for prothrombin time (9.2–11.9 s) and partial thromboplastin time (24–34 s).

Operation from 1600 to 1830, delivery time: 1605.

**Figure 1.** Suggested workup and treatment of coagulopathy in a patient with a history of immunoglobulin (Ig)A deficiency.



the surgical field was still described as “oozy.” Postoperative ventilation was planned and the patient was transported to the intensive care unit (ICU). We elected not to administer FFP intraoperatively because IgA-deficient FFP was not immediately available. However, IgA-deficient FFP was administered when it became available approximately 2 hours after admission to the ICU, and 5 hours after delivery. After the administration of the FFP, coagulation test variables improved (Table 1). The patient was discharged from the ICU after 1 day and recovered fully.

## DISCUSSION

A significant number of individuals with IgA deficiency develop autoantibodies to IgA, thus there is controversy as to whether transfusion of standard blood products or

IgA-deficient blood products should be administered in emergency situations such as the one in this report. In our case, IgA-deficient FFP was not immediately available. Thus, we had to decide whether to pretreat with 200 mg hydrocortisone IV and 50 mg diphenhydramine IV<sup>2</sup> and administer standard FFP, or wait for IgA-deficient blood products. We judged that the patient was hemodynamically stable and we delayed administration of FFP until IgA-deficient FFP was available.

Vyas et al.<sup>3</sup> reported anaphylaxis after the administration of standard blood products, attributed to anti-IgA, in 1968. This and other case reports prompted the medical community to develop an IgA-deficient blood donor registry to facilitate obtaining compatible blood products for IgA-deficient individuals.<sup>4–6</sup> According to the American

rare donor program, a blood product is considered IgA-deficient for the purpose of transfusion if the serum IgA is  $<0.05$  mg/dL.<sup>6</sup>

Although patients may be defined as IgA deficient, they may still have high enough IgA levels to prevent IgA antibody production. Knowledge of the laboratory's lower limit of detection is essential. One of 1200 patients will present with a combination of IgA deficiency and anti-IgA antibodies, and it is estimated that the rate of anaphylactic transfusion reactions is 1:20,000 to 1:47,000. Therefore, only a low percentage of patients with IgA antibodies will actually have a reaction to blood transfusion.<sup>7</sup> In situations in which a patient has known IgA deficiency, washed PRBCs can be readied as was the case in this patient. By washing the red blood cells obtained from normal blood donors, the residual plasma is removed and thus the concentration of albumin and immunoglobulins is decreased by  $>95\%$ , with a resultant decrease in the potential for anaphylaxis.<sup>8</sup>

A potential problem with the administration of cryoprecipitate and platelets is that these products are suspended in plasma and may contain sufficient amounts of IgA to trigger allergic reactions.<sup>9,10</sup> Frozen blood products such as FFP and cryoprecipitate can be obtained from IgA-deficient blood donors. They can be stored in the frozen state for only 1 year and in the thawed state for 24 to 72 hours, thus limiting product availability in an emergency situation.<sup>4</sup> Platelets from normal blood donors can be washed; however, this is a demanding process and may result in *in vitro* platelet activation.<sup>9,11</sup> Hence, preparing platelets from IgA-deficient blood donors by apheresis remains the method of choice.<sup>4</sup>

Our patient was transfused in the past and there was no history of anaphylaxis; however, she did not know whether the previously transfused blood products were washed or obtained from an IgA-deficient donor. Unfortunately, she had not been tested for anti-IgA antibodies before the need for emergency delivery. Despite massive blood loss, we were able to maintain hemodynamic stability and we chose to wait 5 hours to administer IgA-deficient FFP. In Figure 1, we present our recommendations for managing a patient with known IgA deficiency with a coagulopathy. Although not yet reported, recombinant factor VIIa may be a potential option in a subset of these patients.<sup>12</sup>

In conclusion, anesthesiologists should be aware of the potential problems associated with IgA deficiency when transfusing blood products. A thorough discussion with the blood bank pathologist regarding measurement of IgA and anti-IgA antibodies, as well as detailing the specific blood products immediately available, is a necessity. The presence of any IgA before transfusion essentially excludes

the likelihood of an anti-IgA-mediated anaphylactic transfusion reaction.<sup>8</sup>

In hindsight, the presentation of our patient with placenta previa and a history of multiple cesarean deliveries and IgA deficiency should have prompted us to measure anti-IgA antibodies and discuss specific blood product availability with the blood bank pathologist. If the presence of IgA antibodies was documented and the risk of anaphylaxis was thought to be substantial, scheduling an elective procedure when these products were available may have been an option. The consequences of delay in transfusion of IgA-deficient blood and blood products should be balanced against the risk of an anaphylactic reaction. Nevertheless, in a life-threatening situation, blood or blood products should not be withheld based on an unknown risk of a transfusion reaction. This knowledge is essential to safely manage these patients in the perioperative period. ■■

#### AUTHOR CONTRIBUTIONS

All authors helped write the manuscript. CS and SV helped in clinical management of the case.

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