

Anaphylactic transfusion reactions associated with anti-haptoglobin in a patient with ahaptoglobinemia

Anaphylactic transfusion reactions caused by antibodies to normally occurring plasma proteins are uncommon, but they have been reported in persons with selective deficiencies of specific plasma proteins who have also developed the corresponding antibody. For example, anaphylactic transfusion reactions have occurred in persons with selective deficiency of IgA and who have developed anti-IgA,^{1,2} as well as in persons with a deficiency of C4 who have developed anti-C4.³ We describe here an anaphylactic transfusion reaction in a patient who was subsequently recognized to have ahaptoglobinemia associated with a haptoglobin gene deletion and a precipitating antibody to haptoglobin.

A 33-year-old Japanese woman in the 31st week of her first pregnancy was hospitalized for threatened premature delivery due to chronic polyhydramnios. The volume of amniotic fluid increased to approximately 4 L during the next month. Because the serum albumin level had decreased (2.8 g/dL) and her extremities were edematous, 25-percent albumin was infused. After several drops (<1 mL), she experienced generalized flushing, diaphoresis, a seizure, severe laryngeal edema, dyspnea, hypotension, and cyanosis. Her pulse was not palpable. The infusion was interrupted immediately, and her symptoms improved after treatment with intravenous corticosteroids. A dead fetus was removed by Caesarean section. Autopsy revealed hermaphroditism, anal atresia, and membranous occlusion of the duodenum. Blood transfusions were required to manage massive hemorrhage from the surgical site, probably due to disseminated intravascular coagulation. Transfusions of red cells (RBCs) stored in manitol-adenine-phosphate medium were followed by anaphylactic attacks, which were treated with repeated injections of corticosteroids. The patient recovered progressively but slowly and left the hospital 6 months later. Subsequently, after we had identified anti-haptoglobin as the cause for the anaphylactic transfusion reactions, the patient tolerated the transfusion of RBCs washed three times with 0.9-percent sodium chloride.

The patient's serum did not contain RBC alloantibodies when tested by the indirect antiglobulin test. However, a precipitin line was formed between the patient's serum and fresh normal serum by double immunodiffusion. We attempted to identify the specific antibody by using several purified serum proteins—namely, IgA, C4, C9, α 1-antitrypsin, α 1-acid glycoprotein, HS-glycoprotein, transferrin, and haptoglobin—by enzyme-linked immunosorbent assay; the only antibody detected was IgG anti-haptoglobin, which remained in her serum for at least 6 months after the anaphylactic reactions. Haptoglobin was undetectable by enzyme-linked immunosorbent assay in the patient's sera at 1, 3, and 6 months after anaphylaxis. After extraction of

DNA from a white cell-rich fraction of the patient's blood, we examined the haptoglobin gene by the polymerase chain reaction method described previously and found no amplified band by agarose gel electrophoresis.⁴ These findings suggest that the patient is homozygous for the haptoglobin gene deletion (Hp^{del}) that is responsible for ahaptoglobinemia.⁴

Because the patient was not aware that she had ever received human blood or blood components, the antibody to haptoglobin is of unknown origin. This situation is similar to that of many IgA-deficient patients with anti-IgA and anaphylactic transfusion reactions, who also have no history of transfusion.^{2,5} Thus, the absence of such a history does not reliably predict risk for an anaphylactic transfusion reaction.⁵ Theoretically, pregnancy could stimulate the development of anti-haptoglobin, but this is improbable, as it is well known that neonates have ahaptoglobinemia or hypohaptoglobinemia, which suggests extremely low expression of haptoglobin (or none) in the fetal stage. Accordingly, we do not believe that pregnancy is the likely source of anti-haptoglobin in this patient.

Whereas anaphylactic transfusion reactions to plasma proteins are rare events, transfusions of autologous blood or washed RBCs should be useful in managing patients with known antibodies or histories of reactions.²

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