

# Acute Hemolytic Transfusion Reaction Due to Anti-c Rhesus Antibody in a Patient With Subdural Hematoma: A Case Report Emphasizing the Shortcoming of Spin Cross-Match

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**Abstract-** The Rh blood group system is a complex blood group which includes different antigen specificities such as c antigen. Anti-c antibody is associated with both acute and delayed hemolytic transfusion reactions as well as hemolytic disease of the newborn (HDN). Rh mediated hemolytic transfusion reactions (HTR) are mostly immunoglobulin G (IgG) mediated and results in extravascular hemolysis and delayed HTR (DHTR). However, we are presenting a case of acute intravascular hemolytic transfusion reaction due to anti-c in a patient with acute subdural hematoma. A 77-year-old woman was referred to our hospital with a loss of conscious and left-sided hemiparesis. After an emergency MRI, she was diagnosed with Acute Subdural hematoma, and an emergency craniotomy was performed. Since Acute Subdural hematoma is a neurosurgery emergency, laboratory technician performed an Immediate-spin crossmatch for blood bag to preserve time. During the transfusion of the first packed cell, the patient developed severe hypotension and tachycardia. Thus, the transfusion was stopped. Laboratory results raised the suspicion of an Acute Intravascular Hemolysis. Antibody identification revealed that the patient had an irregular blood phenotype (C2+/c-/E-/e3+/K-), and the presence of alloantigen-c Rh antibody confirmed the suspicion of HTR. In patients with multi transfusion history and pregnant women, pre-transfusion screening of irregular antibodies must be performed. The immediate spin crossmatch must be prevented in patients with a history of multi transfusions, even in emergency situations.

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## Introduction

Hemolytic complication of blood transfusion generally may be divided into two categories depending on the time of the appearance of the first symptoms: (1) Acute hemolytic transfusion reactions (AHTRs) and (2) delayed hemolytic transfusion reactions (DHTRs). AHTRs may occur within 24 hours after the transfusion of incompatible blood, while DHTRs occur due to the delayed antibody response from 24 hours up to months or years after transfusion of apparently compatible blood

(1). Common reported non-ABO AHTRs are due to Kidd, Diego, and P antigens, etc. Most DHTRs are mild and may not be diagnosed clinically, while a few ones can cause massive hemolytic reactions followed by renal failure (2,3). Hemolysis is usually due to the presence of preformed alloantibodies produced as a result of a previous transfusion or pregnancy. Common laboratory features of AHTR, which are signs of increased red cell destruction due to hemolysis, include hemoglobinemia, hemosiderinuria, hemoglobinuria, decreased serum haptoglobin, unconjugated hyperbilirubinemia, increased

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## Acute hemolytic transfusion reaction due to anti c

Lactate dehydrogenase and decreased hemoglobin (1).

Rh blood group system is a clinically important and polymorphic blood group comprising more than forty antigens. Rh antibodies are produced in Rh-negative individuals following exposure to exotic RBCs after transfusion or pregnancy (4). Rh system has five significant antigens including D, C, c, E, e while D and c have the most immunogenicity, among others (5). Rh antibodies are mostly immunoglobulin G (IgG) mediated and lead to DHTR and Extravascular hemolysis (1). However, a case of acute intravascular hemolytic transfusion reaction due to anti-c in a patient with acute subdural hematoma is presented in this case report.

### Case Report

A 77-year-old woman was referred to our hospital with loss of conscious and left-sided hemiparesis. She had been taking Warfarin for 5 years because of her Mitral valve replacement. She was also a known case of hemolytic anemia with a history of multiple blood

transfusions. After an emergency MRI, she was diagnosed with Acute Subdural hematoma, and an emergency craniotomy was performed. The patient's blood group (ABO/Rh) was A+, and due to her anemia (HB=9.5), she received two packs of crossmatched red blood cells with A+ phenotype during the surgery. Since Acute Subdural hematoma is a neurosurgery emergency, laboratory technician performed an Immediate-spin crossmatch for blood bag to preserve time. During the transfusion of the first packed cell, the patient developed severe hypotension and tachycardia. Thus, the transfusion was stopped. After the surgery, she was transferred to the Intensive Care Unit (ICU). Within a few hours, we observed an increase in Blood Urea Nitrogen (BUN), Creatinin (Cr), Bilirubin (Direct and Indirect), Prothrombin Time (PT), Partial Thrombin Time (PTT), Lactate dehydrogenase and Neutrophilia while Hemoglobin and Hematocrit were decreased (Figure 1). In Urine analysis, Blood 3+, Protein 3+, and RBC 6-8 in each HPF were seen, and hemoglobinuria was detected. The laboratory results of the patient are shown in Table 1.

**Table 1. Patient's laboratory results during the hospitalization**

	First Day	Second Day	Third-Day	Fourth Day	Fifth Day	Sixth Day	Seventh Day	Eight Day	Ninth Day	Tenth Day	Eleventh Day	Twelfth Day	Thirtieth Day
<b>WBC</b>	7400	64800	44400	37200	11600	7400	5700	8900	8200	8700	8400	6800	8300
<b>RBC</b>	3.73	3.3	2.73	2.67	2.45	2.45	2.77	3.2	3	3.05	2.74	2.77	2.5
<b>HB</b>	9.5	9	7.1	7	6.5	6.7	6.9	8.5	8.3	7.8	7.3	7.2	6.8
<b>HCT</b>	31.2	28.5	23.1	22.2	20	19.5	23.3	26.5	33.7	24.4	23.1	23	19.7
<b>MCV</b>	84	86	85	83	82	80	81	83	112	80	84	83	79
<b>MCH</b>	25	27	26	26	27	27	25	27	28	26	27	26	27
<b>PT</b>	1.1	8	3.4	1.7	2.6	2.2	2.8	1.7	1.6	1.6	1	1.8	1.5
<b>PTT</b>	31	48	44	41	92	35	42	35	53	30	39	84	130
<b>BUN</b>	17	42	64	53	51	59	73	61	83	90	97.4	47	85
<b>Cr</b>	0.8	2.3	4.1	4.1	4.46	5	6.2	4.6	6.7	7.1	8	2.2	3.7
<b>Bilirubin Total</b>	N/A	10.5	10	15	11.4	9.6	8.5	5.9	5.4	4.5	3.6	2.9	N/A
<b>Bilirubin Direct</b>	N/A	5.84	4.49	8	7.51	4.89	4.32	3.2	2.78	2.34	1.9	1.6	N/A
<b>AST</b>	N/A	241	99	39	23	24	N/A	N/A	N/A	N/A	N/A	N/A	N/A
<b>ALT</b>	N/A	20	22	21	19	20	N/A	N/A	N/A	N/A	N/A	N/A	N/A
<b>ALP</b>	N/A	152	138	174	208	164	N/A	N/A	N/A	N/A	N/A	N/A	N/A
<b>Plt</b>	360000	220000	150000	127000	100000	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A

These results raised the suspicion of an Acute Intravascular Hemolysis, and since PT and PTT had risen afterward, DIC was diagnosed, and FFP therapy was started. During the hospitalization, twenty pack cells were tested for compatibility, and only two of them were compatible, and she was received two of them. In order to examine the irregular antigens, the Anti Globulin test (Direct Coombs) and Indirect Globulin test (Indirect Coombs) were performed. Direct Coombs was negative, whereas Indirect Coombs was positive. According to the

results of antibody screening, antibody identification was performed. It revealed that the patient had an irregular blood phenotype (C2+/c-/E-/e3+/K-), and the presence of alloantigen-c Rh antibody confirmed the suspicion of HTR. Later, the patient was a candidate for blood dialysis, and a Shaldon catheter was placed into her superior vena cava. Unfortunately, in spite of continued care, our patient passed away during the blood dialysis after 13 days of hospitalization.

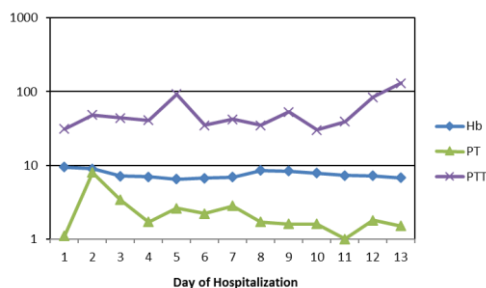


Figure 1. PT, PTT and Hb changes during the hospitalization

## Discussion

ABO is the most important blood group system with highly immunogenic antigens. Other irregular antigens such as K and the Rh antigens C, c, E, and e are less immunogenic. They can only be considered in special patient groups such as pregnant women, multi-transfusion patients with irregular alloantibodies, or with RBC autoantibodies. Since these uncommon antibodies may complicate finding suitable packed red blood cells in the future, packed cells without those antigens that are not present in the recipient should be selected for transfusion to prevent patients from producing new irregular antibodies (1,6). Due to logistic reasons, this principle cannot be followed for other groups of patients. Thus, the aforementioned antigens can only be considered in a population-based on the immunogenicity and frequency of the antigen. Unfortunately, pre-transfusion screening of irregular antibodies is not a routine practice in most blood banks in developing countries.

AHTR associated with Anti-c Rh antibody secondary to the blood transfusion has not been much reported, and the possibility of Rh antibodies being the cause of intravascular hemolysis is still under debate (1). Anti-c may be associated with both acute and delayed hemolytic transfusion reactions as well as hemolytic disease of the newborn (HDN) (7). Anti-c antibody is mostly IgG type and can induce severe intravascular hemolysis secondary to the blood transfusion (8).

Cross-match is an essential routine test before any transfusion, and it is performed in three-phase RT, 37° c, and antiglobulin phase. RT phase is for the detection of cold antibodies, specially ABO antibodies. The two other phases are for the detection of warm and incomplete antibodies and complement (9).

Historically, the crossmatch of choice for all blood recipients was the antiglobulin crossmatch because of its ability to detect immunoglobulin (Ig) G and complement. Currently, It is acceptable to perform only the RT phase in urgent situations if only no history of clinically

significant antibodies exists (10). This technique is called immediate spin crossmatch, and it is performed in emergency situations for identifying the ABO incompatibilities. However, this technique cannot detect the warm, incomplete antibodies and complement. The risk of acute hemolytic transfusion reaction due to the missed antibody of low-frequency antigen has been estimated at 1 per 650,000 crossmatchess using immediate spin or electronic crossmatch technology (11).

In urgent situations, the spin crossmatch is performed in patients without any evidence of clinically significant antibodies. Spincrossmatchh takes lesser time, and it does not have the antiglobulin phase and RT. Therefore, IgG-mediated antibodies are not detected in the spin crossmatch.

Blood safety is the most concern of blood transfusion worldwide (12). Therefore to ensure blood safety, the history of previous transfusions and hematological disorders must be taken into account before performing any blood transfusion. Also, in patients with multi transfusion history and pregnant women, pre-transfusion screening of irregular antibodies must be performed.

The immediate spin crossmatch must be prevented in patients with a history of multi transfusions, even in emergency situations. Every patient with multi transfusion history must have a transfusion file, including details on RBC phenotype and antibody identification. These files can ease the transfusion in case of emergencies.

Since Alloanti-c can cause both acute and delayed hemolytic transfusion reactions as well as hemolytic disease of the newborn (HDN), the authors suggest conducting a survey to determine the prevalence of this antibody in populations with reported cases of AHTR, DHTR and HDN associated with anti-c.

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