The Turkish Journa .of Pediatrics
Volume 19 / Nos. 1-2 / Jan.-April 1977 / pp. 31 - 38

Isoimmunization and Hemolytic Transfusion Reaction Due to Anti-c and Anti-Jk^a Combination*

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In this paper we would like to report a case of isoimmunization showing symptoms of hemolytic transfusion reactions. An antibody combination with the specificity of anti-c and anti-Jk^a was identified, and the patient underwent surgery and was transfused with five units of compatible blood, without any ill effect.

Case Report

A. D., a fourteen year old male patient, was admitted to Hacettepe University Children's Hospital on 17.11.1975, with the complaints of malaise, epistaxis, abdominal pain, and distension. From the history it was learned that, before the present admission he had entered a city hospital because of epistaxis and anemia, which had been treated conservatively with blood transfusion.

On physical examination the patient was pale and exhausted. Abdominal distension, 3 cm palpable liver and 6 cm palpable spleen were noticed.

Laboratory Findings: Bilirubin was 0.8 mg total, Hb was 4.6 g/dl. Blood group was A, Rh positive. The patient was diagnosed as having hepatosplenomegaly due to portal cirrhosis and peptic ulcer. A splenoportography was performed and shunt operation was indicated. On 19.11.1975, after a routine crossmatching test which did not show any incompatibility, the patient was transfused with A Rh positive blood.

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During the transfusion the patient developed chills, fever, nausea, and vomiting. Hb level was 6.45 g/dl after transfusion. Four days later, during a second transfusion, the patient again developed mild chills and fever, nausea and vomiting. The Hb was 6.60 g/dl after the transfusion.

On 27.11.1975, the patient was transfused for the third time. During transfusion he again developed chills, fever, nausea, and vomiting. In addition, epistaxis, lumber pain, and hemoglobinuria were noticed. Transfusion was stopped immediately. After the transfusion, jaundice with a bilirubin level of 4.3 mg % (2.6 mg I. D.) developed. Hb was 5.5 g/dl and haptoglobin level was 0.

A blood sample from the patient was sent to the blood bank after transfusion. The blood group of the patient was A Rh positive, (CDe/CDe R_1/R_1), M + N − S + s + K − k + Fy^a + Fy^b + Jk^a − Jk^b + Le^a − Le^b + P +.

Direct antiglobulin test was slightly positive. The patient's serum was reacting with the transfused red cells, and with ten different A Rh positive and negative red cells. Reations with the indirect antiglobulin tests were stronger than with saline.

Positive reactions with ten different red cell specimens suggested either an antibody to a high frequency antigen or an antibody combination.

For the antibody identification a panel was performed in saline, enzyme, and indirect antiglobulin tests, using different 0 group panel cells. These cells had been frozen in glycerol and stored at −70° C.

As can be seen in the following panel, the antibody was reacting in saline, in enzyme, and indirect Coombs test. (Table I).

According to the results of the panel, the antibody was identified as anti-c and anti-Jk^a combination.

In order to demonstrate each antibody the patient's serum was absorbed with equal volumes of washed, packed O group red cells of type cde/cde and Jk^a negative.

The absorption test was performed at 37° C for two hours. After absorption, red cells were washed five times and an ether-heat elution was performed.[7] Eluted antibody from the red cells was tested with the same panel cells. (Table II).

After demonstration of anti-c, absorption was continued. All activity of the anti-c could be removed after four consecutive absorptions. The patient's serum was then tested against the panel cells. (Table III).

TABLE I

REACTION OF THE ANTIBODY IN THE PATIENT'S SERUM

Panel cells	C	D	E	c	e	M	N	S	s	K	k	Fy^a	Fy^b	Jk^a	Jk^b	Le^a	Le^b	P	Saline			Enzyme	
																			RT.	37°C.	IDCT.	RT.	37°C
1	+	+	0	+	+	+	0	+	0	0	+	+	0	+		+		+	+	++	+++	+	+
2	+	+	0	0	+	0	+	+	+	0	+	+	0	0		+	0	+	0	0	0	0	0
3	+	+	0	+	+	+	+	+	+	+	+	0	+	+		+	+	+	++	+++	+++	+++	+++
4	+	+	0	0	+	+	+	0	+	0	+	+	0	0		0	+	0	0	0	0	0	0
5	0	+	+	+	0	+	+	+	+	0	+	+	+	0		0		+	++	+++	+++	+++	+++
6	+	+	0	0	+	+	0	+	0	0	+	0	+	0		+	0	+	0	0	0	0	0
7	0	0	0	+	+	+	0	0	+	0	+	+	0	+		+		0	++	+++	+++	+++	+++
8	+	+	0	0	+	+	0	+	+	0	+	0	+	+		0		+	0	0	+++	0	0
9	0	+	+	+	+	0	+	0	+	0	+	+	0	0		0		0	++	+++	+++	+++	+++
Patient	+	+	0	0	+	+	0	+	+	0	+	+	+	0		0	+	+					

Anti –c + Anti – Jk^a

TABLE II

ELUTION WITH O cde/cde AND Jk^b Jk^b RED CELLS

Panel Cells	C	D	E	c	e	M	N	S	s	K	k	Fy^a	Fy^b	Jk^a	Jk^b	Le^a	Le^b	P	Saline RT	Saline 37°C	Saline IDCT
1	+	+	0	+	+	+	0	+	0	0	+	+	0	+		+		+	+	+	++
2	+	+	0	0	+	0	+	+	+	0	+	+	0	0		+	0	+	0	0	0
3	+	+	0	+	+	+	+	+	+	+	+	0	+	+		+		+	0	∓	++
4	+	+	0	0	+	+	+	0	+	0	+	+	0	0		0	+	0	0	0	0
5	0	+	+	+	0	+	+	+	+	0	+	+	+	0		0		+	+	+	+++
6	+	+	0	0	+	+	0	+	0	0	+	0	+	0		+	0	+	0	0	0
7	0	0	0	+	+	+	0	0	+	0	+	+	0	+		+		0	+	++	+++
8	+	+	0	0	+	+	0	+	+	0	+	0	+	+		0		+	0	0	0
9	0	+	+	+	+	0	+	0	+	0	+	+	0	0		0		0	+	+	++

Anti-c–

TABLE III

PATIENT'S SERUM AFTER ABSORPTION WITH O cde/cde AND Jk^b Jk^b CELLS

Panel Cells	C	D	E	c	e	M	N	S	s	K	k	Fy^a	Fy^b	Jk^a	Jk^b	Le^a	Le^b	P	Saline RT	Saline 37°C	Saline IDCT
1	+	+	0	+	+	+	0	+	0	0	+	+	0	+		+		+	0	0	++
2	+	+	0	0	+	0	+	+	+	0	+	+	0	0		+	0	+	0	0	0
3	+	+	0	+	+	+	+	+	+	+	+	0	+	+		+		+	0	0	++
4	+	+	0	0	+	+	+	0	+	0	+	+	0	0		0	+	0	0	0	0
5	0	+	+	+	0	+	+	+	+	0	+	+	+	0		0		+	0	0	0
6	+	+	0	0	+	+	0	+	0	0	+	0	+	0		+	0	+	0	0	0
7	0	0	0	+	+	+	0	0	+	0	+	+	0	+		+		0	0	0	+
8	+	+	0	0	+	+	0	+	+	0	+	0	+	+		0		+	0	0	++
9	0	+	+	+	+	0	+	0	+	0	+	+	0	0		0		0	0	0	0

Anti-Jk^a

After identification of the antibody combination five units of A Rh positive blood c negative (CDe/CDe) and Jk^a negative were crossmatched for the patient. A spleno-renal shunt had been decided before the operation but because of the insufficiency of the vessels, only a splenectomy could be performed. During the operation 5 units of compatible blood was transfused without any reaction.

Discussion

Isoimmunization and hemolytic transfusion reaction are two of the potential and most severe complications of blood transfusions.

It must be remembered that every blood transfusion can cause isoimmunization and potential dangers due to isoantibodies. A hemolytic transfusion reaction may be defined as the occurrence of signs of red cell destruction following an incompatible blood transfusion, the most obvious of these signs being hemoglobinuria and jaundice. One must remember that every hemolytic transfusion reaction can cause a severe renal failure and death.

Two main kinds of imcompatibility have to be considered; that in which the donor's cells undergo immediate destruction and that in which the donor's cells survive well intially but provoke an immune response which curtails their survival. In both types of incompatibility antibodies are normally, but not invariably, demonstrable in vitro at the time of the rapid destruction.

In our case, incompatibility in the crossmatch was not noticed by the laboratory technician during the routine tests. It might have been a result of technical errors probably due to the low level of antibodies in the patient's serum. On the other hand, the most careful crossmatch may occasionally fail to demonstrate what one may call "sleeping incompatibility", between a patient's serum and donor cells. Transfusion aroused the "sleeping antibody" and this results in a transfusion reaction of greater or lesser degree.[3, 5, 8]

Rh antibodies may on rare occasions be "naturally" occurring but they are usually of immune origins, and have a thermal optimum of 37°C. They may be pure or mixed, e.g. (anti-c + anti-E). These antibodies may be of the complete or incomplete. Incomplete forms are detectable by albumin, enzyme and, antiglobulin (Coombs) techniques.[2,4,6]

All the Rhesus antibodies can cause hemolytic transfusion reactions and hemolytic disease of the newborn. Some of them have also been found as auto-immune antibodies in acquired hemolytic anemias, e.g. patients of type CDe/cde R_1r with anti-e in the serum.

In the Rh system, c antigenicity is second to D and anti-c may be a cause of H. D. N. B. as serious as anti-D. The total c antigen frequency is almost 80 % in Caucasians, and almost all Rh negative individuals have the cde/cde genotype with an approximately 99 % or higher frequency. That is approximately 20 % individuals who lack c antigen (CDe/CDe (R_1 R_1)) are susceptible to the production of anti-c due to Rh negative blood transfusion.

Thus, physicians and especially obstetricians should remember that the random transfusion of Rhesus negative blood is not without risk of immunising the patient to the antigen c, and such a former injection or transfusion is an important factor in hemolytic disease of the newborn, especially in the first pregnancy.

Antibodies in the Kidd system have only been found as immune antibodies.[2, 4, 6] Jk^a is a comparatively poor antigen in man. Anti-Jk^a has been found as a cause of hemolytic disease of the newborn and 16 cases of materno-fetal Kidd isosensitization have been reported.[1] Also anti-Jk^a has been reported as a cause of transfusion reactions. It has also been found in approximately one in 30.000 routine compatibility tests. The antiglobulin test is the most efficient method for detection of anti-Jk^a. Some anti-Kidd sera may give enhanced reactions with a combined enzyme-antiglobulin test.

Since anti-c and anti-Jk^a are both immune, the mild transfusion reactions in the first transfusion in this case, suggest that isoimmunization had occurred before, due to former transfusions in the city hospital, and probably transfusion of a Rh negative blood which is quite common in general practice in Turkey.

Summary

An isoimmunization and hemolytic transfusion reaction case is presented. Isoimmunization was considered as a result of former blood transfusions. Two differenet antibodies with the specificity of anti-c and anti-Jk^a were identified and some practical aspects of blood transfusions are discussed.

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