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CORRESPONDENCE

A Case Report of a Rare Rh Phenotype: D—

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Introduction

Rh blood group (ISBT: 004) is the second major blood grouping system in addition to ABO, which was first described 60 years ago [1, 2]. Rh factor is an inherited blood protein or antigen on red blood cells [2]. This system includes at least 45 independent antigens from which D, C, c, E, and e are more important for transfusion medicine [3]. Among Rh antigens, e is the most common antigen (98.3%), followed by D (94.2%), C (88.11%), c (54.5%), and E (18.6%) [4]. Rh blood group antigens are highly complicated because of polymorphism in genes encoding them [5]. D and CE proteins/antigens in the Rh blood group system are encoded by RHD and RHCE genes stretching along a 75 kb sequence located on chromosome 1p36.11. Each Rh gene consists of 10 exons that are highly homologous with 93.8% amino acid identity, and RHAG protein on RBC surface is necessary for the expression of Rh antigens. Because of high immunogenicity, D antigen has been recognized as the most important Rh antigen that is used for Rh blood grouping [3]. One of the rare Rh phenotypes is D—, which was first described in 1950 by Race and Sanger. In this phenotype, RHCE proteins are not expressed on RBC membrane. After immune stimulus, individuals with D— phenotype produce an alloantibody known as AntiRh17 (AntiHr0) against CcEe antigens that can lead to the development of a hemolytic transfusion reaction (HTR) or hemolytic disease of newborn (HDN) [6–8]. Several genetic bases have been known to be responsible for this phenotype: (1) reduced transcription of CE gene, (2) RHCE deletion, (3) gene hybridization between RHD and RHCE genes because of their highly homologous nature. In the description of the last theory, studies showed that a hybrid gene only produced the D antigen [9, 10]. Immunoblotting techniques showed that the expression of D antigen and ICAM4 (LW) was increased whereas CD44 antigen and related blood group antigens were reduced [6]. Herewith, we have reported a case of a woman with rare D— phenotype.

Case presentation

A 39-year-old woman from Bam, Kerman, Iran with ovarian cancer was a candidate of blood transfusion due to anemia. She had a history of severe chronic hemolytic anemia, Hb levels as low as 5.5 g/dl with unknown etiology, and blood transfusion in her was followed by fever, chills, and hemolysis. Her blood was previously typed (back type method) as O, Rh (D) positive (CinnaGen Inc., Tehran, Iran) with incompatible crossmatch (3+ reaction) with all the blood units in hospital. Looking for compatible blood for this patient, her blood sample was referred to Kerman Blood Transfusion Center for identification of antibody.

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Table 1 Phenotypic evaluation of patient and her family

	Blood Group	D	C	c	E	e	Genotype
Patient	O+	3+	0	0	0	0	RHD, -/RHD,-
Brother 1	O+	4+	1+	2+	0	3+	RHD, RHCe/-, RHce
Brother 2	O+	3+	0	0	0	0	RHD, -/RHD,-
Brother 3	O−	0	0	4+	0	4+	-, RHce/-, RHce
Brother 4	O+	3+	0	0	0	0	RHD, -/RHD, -
Sister 1	O+	3+	0	4+	0	3+	RHD, RHce/-, RHce
Sister 2	O+	4+	2+	0	0	4+	RHD, RHCe/RHD, RHCe

The results of antibody screening (Immucor, Norcross, GA, USA) direct Coombs test, and antibody identification (Immucor, Norcross, GA, USA) tests indicated the presence of allo- and auto-antibodies in patient's serum, which were not reliable due to autoantibody interference. After a period of immunosuppressive therapy (4 months), the mentioned tests were repeated. Following a 3-cell antibody screening test, the presence of allo-antibodies in patient's serum was detected. Antibody identification test was done using eleven panels of red cells to identify the type of antibody. 3+ reaction at the cells positive for Rh antigens (except for D) showed that specific antibodies for E, e, C, and c antigens were present. Based on RBC phenotyping test, the patient red cells were typed as D+, C-, c-, E-, e -, K-, Fya-, Fyb-, M+, N-, S+, s+, Jka+. All the above tests were performed in duplicate for confirmation of results.

Patient's family members were invited for phenotypic evaluation. It was found that her two brothers had the same red cell phenotype as the patient. Patient and family's phenotypes and the most possible genotype of the individuals (according to phenotype and race) were shown in Table 1.

Discussion

Rh is one of the most important blood groups with highly immunogenic antigens that are indicative of its vital role in clinical transfusion medicine [2]. The five common Rh antigens (i.e. D, C, c, E, and e) are responsible for a majority of clinically significant antibodies in Rh system. Due to the importance role of Rh antigens in HDR and HDN, they are extremely important in blood type evaluation for transfusion and pregnancy [4, 11]. A few individuals have been recognized with a negative profile for RhCE antigens, so that the incidence rate of D— is very low. These patients are at risk of adverse transfusion reactions because they may produce antibodies against absent antigens of Rh system (CcEe) following pregnancy, childbirth or wrong transfusion [6]. In our case, the first transfusion was done according to ABO and Rh (D antigen) compatibility without RBC phenotyping. As a result, her immune system was stimulated and alloantibodies were produced. Faced with a rare blood group besides alloantibodies, it was difficult for us to find a compatible blood for the patient. Since the blood groups are inherited and Rh antigens are known to run in families, testing the patient's family members for finding a donor source was a good idea and we could find two donors for the patient. When these similar cases are identified, they must be encouraged to register themselves to blood banks so that they can be contacted in case of emergency. Cryopreservation process for rare donor units is also an option for such patients. If these programs are implemented for rare blood units, problems related to rare blood groups like this case can be solved in time of emergency. On the other hand, some studies suggested that autologous blood could be prepared and frozen if these patients were not anemic.

Conclusion

Finally, we can introduce this case as a significant one because it emphasizes the importance of detecting rare cases for safe blood transfusion.

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Compliance with Ethical Standards

Conflict of interest All authors have agreed the journals policy and authorship agreement. All authors explicitly declare no conflict of interest. Furthermore, informed consent was obtained from all individual participants included in the study.

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