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Incidence of a Type AB Infant Born to a Type O Mother

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Abstract

Routine cord blood testing may include ABO, Rh, Direct Antigen Testing (DAT) and Indirect Coombs testing (IDC), among other testing, but varies widely from blood bank to blood bank. In this case, the routine testing revealed that an AB infant was born to an O mother. It is not routine to find an AB infant born to an O mother, as the mother carries an O,O type and would have to pass an O to the infant, leaving the possibilities of O,O; A,O; or B,O type for the infant, depending on the father's blood type. Because of the rarity of an AB infant being born to an O mother, several troubleshooting steps were taken prior to the release of test results. It is important to investigate whenever there is a discrepancy discovered during laboratory testing. An AB and O couple producing an AB child cannot be explained in terms of the usual inheritance patterns. One would not expect the cord blood result to be AB when the mother is type O, however, in very rare instances, such as the *cis*-AB blood type, it is possible. Extensive troubleshooting revealed the infant to have this very rare *cis*-AB blood type.

The incidence of the *cis*-AB blood type is very rare. By chance this remarkable blood type was encountered during routine ABO typing of a newborn cord blood specimen. Routine cord blood testing may include ABO, Rh, direct antigen testing (DAT), and indirect Coombs testing (IDC), among other testing, but varies widely from blood bank to blood bank.[1] The testing performed on the cord blood in this instance revealed the infant to be AB positive. This would not normally be a major cause for concern; however, routine cord blood ABO testing is performed on infants born to type O mothers. The results in this circumstance led to concern of the possibility of an error—clerical, procedural, or perhaps some other unusual situation. Ultimately, the infant's blood was tested by polymerase chain reaction–restriction fragment length polymorphism (PCR-RFLP) and gene sequencing and found to possess a rare *cis*-AB allele.[2]

Methods

Routine cord blood testing varies from blood bank to blood bank.[1] This testing took place at Saint Francis Medical Center (SFMC) in Grand Island, Nebraska. SFMC requires ABO testing on the infant's cord blood in the instance that the mother is blood type O. If the infant's cord blood is then determined to be type A or B, the DAT is performed with the intent of monitoring hemolytic disease of the newborn (HDN) which could be caused by the ABO incompatibility.[1] In other words, the type O mother lacks A and B antigens on her erythrocytes and produces both A and B antibodies. Depending on the infant's blood type (A has only A antigen present on RBCs, B has only B antigen present) the mother's antibodies may attach to the infant's RBC's and cause HDN. Indirect Coombs testing is also performed to indicate whether the mother is carrying an unexpected antibody and to determine which maternal antibody (-ies) may be attached to the infant's cells. Upon discovery of a positive DAT or IDC, the amount of bilirubin present in the cord blood specimen is determined to aid in monitoring HDN.

For further investigation, the cord blood, a heelstick collection from the infant, and both the mother and father's specimens were submitted to the ARC Molecular Laboratory in Philadelphia for PCR-RFLP testing and genomic DNA sequencing of the ABO transferase genes.

Results

The mother in this circumstance was type O, and the infant's cord blood type was AB positive. **Table 1** documents the cord blood test results. An AB and O couple producing an AB

Table 1_Principal Laboratory Findings

Test	Cord Blood Result	"Normal" Reference Range
ABO Newborn		
Anti-A	4+	
Anti-B	4+	
Rh	4+	
Rh Control	0	
Interpretation	AB Positive	
Direct Antigen Testing (Direct Coombs)		
DAT IS	1+	0
DAT Interpretation	Positive	Negative
Anti-IgG	1+	0
IgG Interpretation	Positive	Negative
Anti-C3 IS	0	0
Anti-C3 5 min	0	0
Anti-C3 Check Cells	2+	
Anti-C3 Interpretation	Negative	Negative
Indirect Antiglobulin Testing (Indirect Coombs)		
A1 Cells AHG	2+	0
B Cells AHG	2+	0
Screening Cells I	0	0
Screening Cells II	0	0
Screening Cells III	0	0
Anti-A Interpretation	Positive	Negative
Anti-B Interpretation	Positive	Negative
AB Screen Interpretation	Negative	Negative

child cannot be explained in terms of the usual inheritance patterns.[3] One would not expect the cord blood result to be AB when the mother is type O; however, in very rare instances, such as the *cis*-AB blood type, it is possible. Typically, an O mother would produce either an A, B, or an O infant. **Table 2** outlines the usual transmission to an infant born to an O mother and an AB father.

Table 2_Routine Genotype Transmission – O Mother, AB Father

Mother	Father: A	Father: B
O	A,O	B,O
O	A,O	B,O

The infant born to this couple would have a 50:50 chance of inheriting type A or B. The infant in a routine case such as this would not inherit type AB.

Table 3_Genotype Transmission in This Family

Mother	Father: A_1	Father: cis-AB
O	A_1,O	cis-AB, O
O^{1var}	A_1,O^{1var}	cis-AB,O^{1var}

The circled genotype represents the infant in this case.

Discussion

It is always important to investigate whenever there is a discrepancy discovered during laboratory testing. Because of the rarity of this circumstance, several troubleshooting steps were taken prior to the release of test results. Initially, it was thought that the cord blood had been mislabeled, and that it was actually another infant's specimen. After speaking with the nurse responsible for the collection, labeling, and transport of the specimen, it was determined that it was the correct specimen and had been labeled properly. There was also concern that there had been a clerical error of the mother's blood type, either during transfer into the hospital's computerized information system, or during the initial documentation into the mother's chart in the clinic. Upon verification of the mother's blood type between the clinic chart and the computer system, the next concern was a procedural error made during the testing of the cord blood specimen. The same technologist repeated testing on the same cord blood specimen. A second technologist retested the cord blood specimen and confirmed the results.

A subsequent concern was an error in the initial testing of the mother's specimen. Since the testing had been performed by another facility, it was nearly impossible to review the results or consult with the person responsible for the initial testing. It was also impossible to repeat testing on the original specimen. A new specimen was collected from the mother and a new heelstick specimen was collected from the infant for testing. The mother's blood type was confirmed by this testing to be O positive, and the infant again typed AB positive.

It was established through record verification and discussion with the nurses involved in the delivery of the infant that there was no possibility that the infant belonged to another mother. Other uncommon circumstances were also ruled out through discussion with the mother's physician, such as surrogacy and unusual circumstances, such as an extremely rare in-vitro fertilization error. Upon consultation with the American Red Cross, a specimen was collected from the father, and the father's specimen typed AB negative. The ARC Molecular Laboratory in Philadelphia reported that the infant carried a *cis*-AB blood type that had been transmitted to the infant by the father. **Table 3** summarizes the genetic transmission by the mother and father in this rare occurrence.

Blood group alleles are inherited and can be identified by specific nucleotides present. In this circumstance, the ABO PCR-RFLP and gene sequencing results were used to confirm that this child was produced by these 2 individuals and was also used to identify their ABO genotypes. Usually group AB individuals carry the A gene on one chromosome and the B gene on the other, each being co-dominant; however, there have been families in which both the A and B have been shown to be inherited from one parent (*cis*-AB), which was the case in this situation.[4] The infant inherited an ABO gene, *cis*-AB, from the father that can produce both A and B antigens. The *cis*-AB phenotype, first described in 1964, corresponds to a special ABO allele encoding a glycosyltransferase that is capable of synthesizing both A and B substances.[5] Two possible genetic mechanisms have been reported: unequal chromosome crossing over and structural mutation in the blood group glycosyltransferase.[6,9] Structural mutation in either the A or B gene produces a single enzyme with bifunctional activity.[7] In a previous study, 2 unrelated *cis*-AB individuals of the genotype cis-AB/O were found to have *cis*-AB alleles that were identical to one another while different from the A_1 allele by nucleotide substitutions, one previously reported in A_2 alleles and the second substitution responsible for the *cis*-AB phenotype.[8,9]

Conclusion

The incidence of *cis*-AB throughout the world is very rare. The majority of *cis*-AB cases are found in Japan, especially Shikoku Island, but some have been found in other areas of the world such as the United States, Korea, Poland, France, Belgium, Romania, and Germany.[9,10] The ratio of *cis*-AB to total AB (A_1B and A_2B) in Japan proves that the *cis*-AB type is extremely rare; it was estimated to be approximately 0.012%, and the gene frequency of the *cis*-AB was found to be about 1.1×10^{-5}.[10] It is by this example that we are led to believe that the incidence in the United States would be more uncommon.

Although cord blood testing can vary from blood bank to blood bank, there is some consistency to the testing performed. The majority of blood banks screen for ABO incompatibilities to monitor HDN. The necessity for proper identification and labeling specimens is obvious in this example as is the necessity of the ability to troubleshoot rare circumstances. An AB infant born to an O mother was

questioned. After extensive troubleshooting, the infant was determined to be a unique *cis*-AB blood type, inherited from the father. LM

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