Unexpected Non-Maternally Derived Anti-PP1P^k in an 11-Week-Old Patient

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Alloantibody formation at less than 4 months of age is rare. Most antibodies identified in these patients are maternally derived. Anti-PP1P^k was detected in an 11-week-old infant that was not maternally derived. A multidisciplinary team approach led to appropriate testing, diagnosis, and transfusion management in this critically ill infant. *(J Pediatr 2017;181:302-5).*

Transfusion practice in neonates and infants is driven by unique factors present in these populations and consequently differs from that of adults. Because of the immature immune system and described lack of red blood cell (RBC) alloantibody production, current AABB (formerly American Association of Blood Banks) Standards for Blood Banks and Transfusion Services allow for limited pretransfusion serologic testing in patients less than 4 months of age.[1] However, alloantibody formation after transfusion in this patient population has been reported.[2] We report an unusual case in which a non-maternally derived alloantibody was detected in a patient less than 4 months of age with no history of transfusion, and describe how multidisciplinary team communication was instrumental in making this novel diagnosis and for appropriate transfusion management.

Case Report

A previously healthy, nontransplanted, unimmunized 11-week-old female of Amish descent with acute respiratory failure was transferred from an outside hospital emergency department to the 21-bed pediatric intensive care unit (PICU) at our full-service children's hospital and academic medical center, equipped with a level III neonatal intensive care unit. History obtained on PICU admission revealed that her entire family had been sick recently with respiratory syncytial virus (RSV). The patient had been previously well until the day before presentation to the emergency department when she began coughing and was febrile (temperature 103.5°F/39.7°C). She was emergently intubated in the emergency department and arrived to the PICU on mechanical ventilation. On physical examination she was afebrile, with a pulse of 144 beats per minute and a blood pressure of 87/49 mm Hg. She appeared well-perfused and without petechiae or bruising. The patient was admitted to the PICU for management of respiratory failure secondary to suspected viral bronchiolitis. Blood cultures were drawn and the patient was started on ceftriaxone empirically. Ampicillin and oseltamivir were added the following day. Additional history revealed that this had been the mother's fifth pregnancy by the same father, resulting in an uncomplicated pregnancy and vaginal delivery of the patient at full term, with neither the infant nor the mother requiring transfusion.

On hospital day 1, her hemoglobin (HGB) concentration was 9.5 g/dL and white blood cell count and platelet count were within the reference ranges for her age. Laboratory test results are reported in **Table I**. On hospital day 2, her HGB level decreased to 7.7 g/dL with no obvious signs of bleeding on physical examination or imaging. Pretransfusion testing at this time identified the patient as ABO group O (back type testing of the patient's plasma revealed 3+ reactivity with both the A and B reagent cells), Rh positive with a positive antibody screen for unexpected RBC alloantibodies. A previous type and screen was not available for comparison because this patient had not been seen at our institution before and the outside hospital where she was born had not performed blood bank testing. Polymerase chain reaction testing for influenza B and RSV was positive (**Table I**).

The initial pretransfusion immunohematology evaluation revealed 3+ reactivity with all reagent RBCs tested using the column agglutination method (Ortho Clinical Diagnostics, Inc, Raritan, New Jersey) with a negative autocontrol. A direct antiglobulin test (DAT, Ortho Clinical Diagnostics, Inc) was performed owing to concern for immune-mediated hemolysis as an etiology for the anemia and was negative with polyspecific reagent. Lactate dehydrogenase, haptoglobin, and total and indirect bilirubin assays were performed to evaluate for hemolysis; all were within normal limits (**Table I**). The patient's

HGB	Hemoglobin
IRL	Immunohematology Reference Laboratory
PICU	Pediatric intensive care unit
RBC	Red blood cell
RSV	Respiratory syncytial virus

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Table I. Laboratory test results over time

Variables	Normal range	Hospital day 1	2	3	7*	11*
HGB (g/dL)	9.5-13.5	9.5	7.7	6.7	14.2	13.7
HCT (%)	29.0-41.0	30.6	23.1	19.9	41.5	40.6
WBC (10^9/L)	6.0-17.5	8.4	3.2	5.1	10.3	13.0
Platelets (10^9/L)	150-400	364	219	171	94	165
Reticulocyte (%)	0.5-2.0			2.2	1.7	
LDH (U/L)	153-538			275		
Haptoglobin (mg/dL)	30-200			175		
Bilirubin, total (mg/dL)	0.0-1.2	0.3		0.1		
Bilirubin, direct (mg/dL)	0.0-0.3			<0.1		
Alkaline phosphatase (U/L)	105-460	240		133		
AST (U/L)	7-54	128		146		
ALT (U/L)	10-60	149		173		
Total protein (g/dL)	4.6-7.0	6.7		4.1		
RSV PCR			Positive			
Influenza B PCR			Positive			
ABO group/Rh type			O positive			
Antibody screen			Positive			
DAT			Negative			

ALT, alanine aminotransferase; *AST*, aspartate aminotransferase; *DAT*, direct antiglobulin test; *HCT*, hematocrit; *LDH*, lactate dehydrogenase; *PCR*, polymerase chain reaction; *WBC*, white blood cell count.
*Post-transfusion.

immunohematology evaluation specimen was forwarded to the American Red Cross regional reference immunohematology laboratory, where the patient's plasma reacted with all PP1P^k reagent RBCs tested at immediate spin, room temperature, and in polyethylene glycol (Gamma PeG, Immucor, Inc, Norcross, Georgia) enhancement by the indirect antiglobulin test. The patient's plasma was nonreactive with 4 examples of PP1P^k-negative reagent RBCs at immediate spin, room temperature, and in polyethylene glycol by indirect antiglobulin testing. Owing to a limited sample, antibody titers were not performed. Serologic phenotyping of the patient's RBCs were negative for the PP1P^k antigen. Immunohematology Reference Laboratory (IRL) results are reported in **Table II**. With no history of prior transfusion, transplant, or pregnancy, these findings would be indicative of naturally occurring alloantibody anti-PP1P^k.

In patients of this age, however, the antibody or antibodies identified in the plasma are most likely maternally derived. Therefore, a maternal specimen was also forwarded to the regional American Red Cross reference laboratory for testing. The evaluation revealed that the mother was ABO group A, Rh negative, with a positive antibody screen. The antibody identification performed on the mother's plasma revealed an anti-D, consistent with a history of Rh immunoglobulin given postpartum, and an autoantibody with I specificity. These results are consistent with those obtained from outside hospital reports of previous immunohematology testing. Serologic phenotyping of maternal RBCs was positive for the PP1P^k antigen. Serologic phenotyping of paternal RBCs was also positive for the PP1P^k antigen (**Table II**). These findings support the conclusion that the anti-PP1P^k in the infant's plasma was not maternally acquired and is a naturally occurring alloantibody akin to ABO isohemagglutinins to RBC antigens that the patient lacks.

By hospital day 3, the patient's HGB had decreased even further to 6.7 g/dL (**Table I**). Pediatric hematology-oncology was consulted for evaluation of anemia with a positive antibody screen. The pediatric hematology-oncology team was concerned for bone marrow suppression owing to viral infection in addition to iatrogenic blood loss and advised RBC transfusion. Transfusion medicine was then contacted to make recommendations based on the immunohematology results and coordinate transfusion. Because of the rare availability of PP1P^k antigen-negative blood donors, RBC units for transfusion had to be acquired through the American Rare Donor Program. Therefore, 5 days after admission, the patient received full antihuman globulin cross-match–compatible PP1P^k antigen-negative RBCs in 2 separate 15 mL/kg transfusions. The patient tolerated the transfusions well and her HGB concentration increased from 6.1 to 14.2 g/dL. Blood cultures were negative and

Table II. IRL evaluation

	Plasma		Red Blood Cells
	PP1P^k positive test RBCs	PP1P^k negative test RBCs	PP1P^k phenotyping
Patient specimen	+ Immediate spin, room temperature, PEG/AHG	– Immediate spin, room temperature, PEG/AHG	Negative
Maternal specimen	Anti-D, autoanti-I		Positive
Paternal specimen	Not tested		Positive

AHG, anti-human globulin; *PEG*, polyethylene glycol.