

Severe hemolytic disease of the fetus due to anti-Kpa antibody

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ABSTRACT

Introduction: Anti-Kpa antibodies are an uncommon cause of hemolytic disease of the fetus and newborn (HDFN). Screening for antibodies to low frequency antigens such as Kpa is not routine, so detecting them can present a challenge. **Case Report:** We report a case of hydropic HDFN due to anti-Kpa antibodies discovered incidentally with direct antiglobulin testing of a fetal blood sample in the course of work-up and treatment for presumed acute parvovirus B19 induced hydrops fetalis. Six intrauterine red blood cell transfusions and one simple neonatal red blood cell transfusion were required. **Conclusion:** The cause of fetal anemia needs to be properly diagnosed in order to provide appropriate clinical care in affected pregnancies. Sensitization from uncommon antigens is more difficult to diagnose due to the lack of routine screening. This case illustrates the importance of performing direct antiglobulin testing on fetal blood before intrauterine transfusion in any case

of fetal anemia despite presumed alternative etiologies.

Keywords: Anti-Kpa antibody, Hemolytic disease of the fetus and newborn (HDFN), Direct antiglobulin test (DAT), Hydrops fetalis, Alloimmunization

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INTRODUCTION

Antibodies to the Kell antigens are a well-known source of potentially severe hemolytic disease of the fetus and newborn (HDFN). There are 24 antigens in the Kell blood group. Antibodies to the K antigen are most frequently associated with HDFN [1, 2]. Less common antigenic incompatibilities in the Kell blood group system such as anti-Kpa are infrequently reported to be associated with HDFN. Approximately, 2% of Caucasians and less than 0.01% of African-American express the Kpa antigen. A review of literature found one other case of prenatal diagnosis of severe HDFN due to maternal anti-Kpa and four reports of babies diagnosed after birth and requiring treatment for HDN due to anti-Kpa [3–7]. A review of a database of all alloimmunized pregnancies evaluated with serum screening at the authors' institution from 1959 through 2011 did not identify any other cases of anti-Kpa. The incidence of HDFN is estimated to be 0.15–1.1% from

non-RhD antibodies and 1–2% from antibodies to RhD (Rhesus disease) [8]. Our case illustrates the potential for severe HDFN due to anti-Kpa and the importance of routine direct antiglobulin testing in any case of fetal anemia that could be caused by uncommon antibodies. The local institutional review board approved the publication of this case report.

CASE REPORT

A 27-year-old Caucasian female presented for a routine fetal anatomical ultrasound at 25 weeks and 2 days gestation in her third pregnancy. Using standard hemagglutination tests, no antibodies were detected in the maternal serum using MTS gel cards (Ortho Clinical Diagnostics, Raritan, NJ) and all antibody screens during previous pregnancies were also negative. The patient had negative antibody screens in the current and past pregnancies. Her previous pregnancies were conceived with the same partner and she had not received blood transfusions in the past. Her first pregnancy was uncomplicated and delivered at term, the second pregnancy ended in a first trimester spontaneous abortion and the current pregnancy was otherwise uncomplicated.

Fetal hydrops fetalis was diagnosed during this routine ultrasound. Middle cerebral artery peak systolic velocity (MCAPSV) ultrasound measurement was greater than 1.5 multiples of the mean, a finding consistent with fetal anemia. The presumed etiology was parvovirus B19 because the patient was an elementary school teacher with a known recent exposure to a child with parvovirus (Fifth disease).

Prompt fetal blood sampling via cordocentesis confirmed severe fetal anemia (hemoglobin 3.0 g/dL, hematocrit 9.2%, reticulocyte count 10.4%, absolute reticulocyte count $6.66 \times 10^4 / \mu\text{L}$, 139 nucleated red blood cells). The fetal blood was tested by the tube method and found to be type O RhD positive with a 1+ direct antiglobulin test (DAT). Maternal serology and polymerase chain reaction (PCR) study of the amniotic fluid were negative for parvovirus. Amniotic fluid analysis yielded a delta OD 450 high in zone IIA, evidence of a hemolytic process in the fetus. In addition, maternal serum rubella, herpes simplex, and cytomegalovirus serologies were unrevealing.

Maternal plasma was tested against a panel of five red blood cells positive for low incidence antigens (V, CW, Kpa, Jsa, and Lua) using the tube method because of the positive fetal DAT. A maternal Kpa antibody with a titer of 32 was detected. The father was tested and found to be Kpa/Kpb antigen positive. Maternal sensitization was thought to be caused by exposure to the Kpa antigen in a former pregnancy. The fetus was then identified as Kpa antigen positive by testing of the amniocyte deoxyribonucleic acid (DNA). A karyotype returned as normal male.

Six intrauterine red blood cell transfusions with compatible (Kpa antigen negative) red blood cells were performed over the next eight weeks of pregnancy. Fetal

anemia should be corrected by transfusing a maximum of 25% of the estimated fetal blood volume, so the first three intrauterine transfusions were performed every three days to gradually increase the fetal hemoglobin from 3.9–14.1 g/dL [9]. Based on an estimated decline in fetal hematocrit of 1% per day due to circulating maternal antibodies, the fourth and fifth intrauterine transfusions were then performed every two weeks. Based on the likely cumulative effect of multiple transfusions with Kpa negative red blood cells, the sixth and final transfusion was performed after a three-week interval. Elective delivery was then performed four weeks later at 37 week 2 day gestation. The newborn did not have jaundice, but required one simple red blood cell transfusion with at one month of life when the hemoglobin fell to 8.0 g/dL.

DISCUSSION

Clinical management of pregnancy with fetal anemia will be different based on the cause of the anemia. In such a case correct diagnosis is valuable to the managing physician. Parvovirus infection during pregnancy can result in acute fetal anemia that may require one or two fetal blood transfusion or may gradually resolve without transfusions [10]. The alternative diagnosis of maternal red blood cell alloimmunization is often managed with repeated transfusions until delivery, and perhaps as a neonate, due to the continued fetal exposure to maternal antibodies. The diagnosis of maternal alloimmunization as the cause of fetal anemia also impacts the management of future pregnancies [9].

There are several potential etiologies for fetal anemia, but the most common is alloimmunization involving red blood cell antibodies resulting in HDFN. The K antibody is particularly important incompatibility because anti-K alloimmunization can cause severe HDFN through hemolysis and suppression of fetal erythropoiesis. The K antibody is detected by routine serum antibody screening [1–2]. This case and others in literature illustrate the possibility of HDFN from less common Kell antigens such as Kpa and Kpb that are not routinely screened for [4–7].

Due to the low frequency of the Kpa antigen, many commercially available screening kits do not contain a Kpa antigen positive cell, possibly causing maternal antibodies to be missed on routine prenatal screening. Given the low antigen frequency of Kpa and maternal history of exposure, parvovirus was an alternative explanation for the fetal anemia in this case. Direct antiglobulin testing of the fetal blood sample before the first intrauterine blood transfusion led to the correct diagnosis and appropriate fetal and neonatal surveillance and treatment in this case [11].

CONCLUSION

The American Association of Blood Banks recommends routine maternal antibody screening against red blood

cell antigens commonly implicated in hemolytic disease of the fetus and newborn. Extended testing against low incidence red blood cell antigens is necessary to detect the rarer incompatibilities when the fetal or neonatal direct antiglobulin test is positive.

Even in cases where an alternative etiology seems likely, direct antiglobulin testing of a fetal blood sample before intrauterine transfusion is always indicated. Antibody identification in this case allowed for better management and advice for care of future pregnancies

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Author Contributions

Karen Q Rossi – Conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Critical revision of the article, Final approval of the version to be published

Scott Scrape – Drafting the article, Critical revision of the article, Final approval of the version to be published

Christopher Lang – Drafting the article, Critical revision of the article, Final approval of the version to be published

Richard O'Shaughnessy – Conception and design, Acquisition of data, Analysis and interpretation of data, Drafting the article, Critical revision of the article, Final approval of the version to be published

Guarantor

The corresponding author is the guarantor of submission.

Conflict of Interest

Authors declare no conflict of interest.

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