Absence of hemolytic disease of fetus and newborn (HDFN) in a pregnancy with anti-Yka (York) red cell antibody

Abstract: The York antigen, assigned to the Knops system (KN5-ISBT 022005), is a high frequency antigen present in 90% of the Caucasian and 98% of the African-American population. No cases of anti-Yka in pregnancies have been published. No hemolytic diseases of the fetus and newborn have been observed previously. We report the first case of anti-Yka antibody found in a pregnant woman without fetal anemia, which was monitored by Doppler assessment of peak systolic velocity at the middle cerebral artery. A 36-year-old white woman, gravida 2, para 2 (1994 and 1996) was transfused with two units of packed red cells in 2009. On July 1, 2011 at 13 weeks of gestation of her third pregnancy, “type and screen” showed blood group O RhD positive and was found to have one IgG antibody that reacted against all panel red blood cells in the anti-human globulin phase by gel technique. The antibody was identified as anti-Yka and titer was 64. The patient’s phenotype was YK(a–). Peak systolic velocity at the middle cerebral artery, performed by Doppler, at weeks 25, 28, 32 and 34 of gestation did not show fetal anemia. At birth, the newborn was group O Rh (D) positive, Yk(a+) with direct Coombs test negative without anemia and hyperbilirubinemia. Our case contributes, as further evidence, to the clinically benignity of the anti-Yka antibody not been a cause of hemolytic disease of the fetus and newborn.

Keywords: Blood velocity middle cerebral artery; hemolytic disease of the fetus and newborn; Knops system.

Introduction

Antibody formation to the York (Yka) antigen was detected in 1965 [6] and much later was assigned to the Knops system, number 022 in the classification of the International Society of Blood Transfusion (ISBT) [1].

The antigens of the Knops system are located in the complement receptor type 1 protein (CR1, CD35) which is a transmembrane glycoprotein encoded by the CR1 gene on chromosome 1q32 [8]. The Yka antigen was first described to be absent in a Mrs. York who developed an antibody after a blood transfusion in 1963 [6].

Eight of the nine known antigens of the Knops system are linked to polymorphisms in exon 29. The absence of antigen Yka has not been reported as being caused by changes in exon 29 of CR1 [7]. Recently, Veldhuisen et al. [10] found that a mutation in exon 26 was linked to the absence of the Yka antigen. A change of threonine to methionine at position 1408 was shown to be the molecular basis of this antigen.

The York antigen is a high frequency antigen (HFA) present in 90% of the Caucasian and 98% of the African-American population [7], and was also shown to be inherited in a normal way as a Mendelian dominant character.

No hemolytic disease of the fetus and newborn (HDFN) has been observed previously. We report the first case of anti-Yka antibody found in a pregnancy without fetal anemia monitored by Doppler assessment of peak systolic velocity in the middle cerebral artery (MCA-PSV).

Case report

A 36-year-old white woman was followed-up in our hospital for her third gestation. She had two normal children in the past (1994 and 1996). Her transfusion history indicates she had spine surgery in 2009 and received two units of packed red blood cells with negative crossmatch and screening of immune antibodies was negative.

Our hospital Blood Bank performed a routine “type and screen” by gel technology (BioRad-DiaMed, Cressier,
FR, Switzerland) on July 1, 2011 at 13 weeks of gestation. Initial tests showed blood group 0 Rh (D) positive, indirect antiglobulin test (IAT) positive with negative autocontrol and direct antiglobulin test (DAT). Patient sera reacted to all red blood cells (RBCs) tested in screening panels (I, II, III) and the 11 red cells in the identification panel (Biorad-Diamed) with similar reactivity 2+ at 37°C in the same antiglobulin-Liss phase (panagglutination). An alloantibody to a HFA was suspected with these results. The 64 titer result along with the strength of reactivity suggested that the antibody could be of any antibodies formerly known as high titer low avidity (HTLA). Further characterization of the antibody was performed at the Immunohematology Reference Laboratory in Buenos Aires, Argentina (technicians were Deutsch G, Rey C and Torres O, MD). The results showed an alloantibody (IgG) anti-Yka (York KN5, ISBT 022005). No bind complement in vitro and it was not neutralized with pooled serum. It was reactive with papain treated cells and cord red cells (2+).

No other RBC alloantibodies were detected. Three YK(a–) cells were tested and were nonreactive. The patient phenotype was YK(a–).

Because IgG alloantibodies can cross the placenta, we investigated the possibility of fetal anemia by pulsed Doppler of the MCA-PSV at weeks 25, 28, 32 and 34 of gestation.

The values of MCA-PSV (cm/s) were plotted over the reference range for gestational age with a computer program (www.fetaltest.com) to calculate fetal hemoglobin and multiple of median values. The cut-off point of 1.5 times the median of MCA-PSV was found to correlate with the severity of fetal anemia. In our case, the average multiple of median (MoM) of MCA-PSV was 1.09 and 11.66 g/dL of hemoglobin.

Cesarean section due to lumbar arthropathy was performed at 39 weeks of gestation delivering a 3350 g, female baby with Apgar scores of 6 and 8 at 1 and 5 min, respectively. The newborn was group 0 RhD positive YK(a+) with negative DAT in gel technique (IgG and C3d) without anemia and hyperbilirubinemia.

Maternal serum reacted positive 2+ with cord RBCs in vitro similar to adult RBC panel. Antibody activity present in cord serum was weak (± or 1+).

**Discussion**

We report this case to show more evidence of clinical benignity of the anti-Yka antibody in pregnancy. No cases of anti-Yka in gestation have been published.

In 1982, Molthan [5] reported 304 patients referred to him since 1965. A total of 111 patients had anti-Yka and 5 had anti-Yka and Csa (Cost); 15 cases (10 women and 5 men) who received incompatible blood were presented; 7 patients had antibodies anti-Yka (2 men and 5 women) and 1 woman had anti-Yka and Csa (Cost).

Of these eight patients who received incompatible blood, three had extravascular hemolytic transfusion reactions (EHTRs), one had intravascular hemolytic reaction (IHTR), and there were two cases of probable successful transfusion.

The author concluded that alloantibodies against Yka were biologically significant in transfusion. A literature search revealed no cases of erythroblastosis fetalis (EF). The potential does exist, however, for mild cases of EF because the antibodies anti-Yka are IgG and the antigen is well developed in cord cells [5].

Some others antibodies to HFA are capable of causing HTR and HDFN [2, 3]. Such antibodies create a particular problem as compatible blood is often very difficult to find.

Antenatal screening for the presence of alloantibodies in pregnant women is a prerequisite for identifying a fetus at risk of developing HDFN. In one retrospective cohort study, serological findings of all pregnant women managed between January 1, 2001 and December 31, 2005 in the Transfusion Medicine Department of Social Security in Montevideo-Uruguay was reviewed [9]. Out of 14,860 pregnancies, 157 (1.05%) had anti-erythrocyte antibodies by gel technique (153 alloantibodies and 4 autoantibodies). No antibodies to HFA were found.

The IgG alloantibody anti-Yka can cross the placenta. Close fetal monitoring must be performed for diagnosis of fetal anemia with a noninvasive method.

Later, in 1995, Mari et al. [4] applied the measurement of MSV-PSV to determine fetal anemia in immunized pregnant women with anti-erythrocyte antibodies. In our case, the four determinations of MCA-PSV at 25, 28, 32 and 34 weeks of gestation did not show fetal anemia. The average value of MCA-PSV was 1.09 MoM and hemoglobin of 11.66 g/dL. The MCA-PSV is a simple method, noninvasive, with immediate results to follow-up pregnancies with anti-RBC antibodies.

This case report confirms that not all antibodies reacting in vitro at 37°C will cause in vivo red cell destruction. There are some antibody specificities such as anti-Yka that, although reactive at 37°C, usually by IAT, may not lead to red cell hemolysis. It could be that the maternal antibody does not bind to complement and does not cause fetal anemia [7]. The newborn with negative DAT does not have postnatal anemia or hyper-
bilibilirubinemia. The York antigen is well developed in
cord samples [6] and the strength of reaction is similar
to that found in adults. Maternal serum react positive
2+ with cord RBCs in vitro similar to adult RBC panel.
The antibody activity present in cord serum was weak
probably by low transplacental transport or by absorb-
ing anti-Yka antibodies in other cells such as leukocytes
[6, 7].

It is possible that subsequent pregnancies of this
mother with anti-Yka sensitization, the fetus or newborn
may or may not be affected.

Clinicians should still adhere to the use of compatible
transfusions whenever possible to prevent alloimmunization.

This is the first case report of anti-Yka antibody in
pregnancy. Also, it is the first case report of antibodies in
accordance to the Knops system in Uruguay with a popu-
lation of 3,241,003 individuals, of whom 93% are Cauca-
sian and 6% are African-American.

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References

Blood group terminology 2004; from the International
Society of Blood Transfusion committee on terminology
of red cell surface antigens. Vox Sang. 2004;87:
304–16.

Hemolytic disease of the newborn associated with anti-Jra
alloimmunization in a twin pregnancy: the first case report in

anti-Vel quantitative serologic monitoring with 2-ME serum
2010;26:8–10.

Ludomirsky A, et al. Diagnosis of fetal anemia with Doppler
ultrasound in the pregnancy complicated by maternal blood

and Knops alloantibodies. Rev Fr Transfus Immunohematol.

[6] Molthan I, Giles CM. A new antigen YK-a (York), and its


The C3b/C4b receptor is recognized by the Knops, McCoy,

[9] Pereira A, Silveira S, Hernandez C, Varela A, Gaggero M,
In: XXXI World Congress of the International Society of
Hematology (ISH), March 20–24, 2007 (abstract 186), Punta

der Shoot CE, et al. Molecular analysis of the York antigen of
the Knops blood group system. Transfusion. 2011;51:1389–96.

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