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Rare Case of Haemolytic Disease of the Newborn Caused by Anti-Kidd (b) and Review of the Literature

Seltener Fall von hämolytischer Erkrankung des Neugeborenen, verursacht durch Anti-Kidd (b) und Literaturübersicht

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Summary:

We report on the very rare case of haemolytic disease of a newborn caused by diaplacental Anti-Kidd (b) from the mother. The second child of a 30 years old woman (two births, two pregnancies) developed a marked jaundice (maximal serum bilirubin 304.5 µmol/l). Other reasons for this jaundice could be excluded. Immunization was believed to stem from pregnancy, because the mother had never been transfused. In this context an overview is given on the literature concerning cases with haemolytic disease of the newborn due to Anti-Kidd (b). From this and from our case we conclude that antibody screening of pregnant women should be performed either with test erythrocytes of two donors with at least 2 methods (indirect antiglobulin test with albumin and one stage enzyme test) or one method (indirect antiglobulin test with albumin technique) with test cells from 3 donors. In unclear cases of HDN maternal serum should be cross matched against paternal red cells.

Keywords:

Haemolytic disease of the newborn — Phototherapy — Anti-Jk (b) antibody

Zusammenfassung:

Wir berichten über den sehr seltenen Fall eines Morbus haemolyticus neonatorum infolge von Anti-Jk (b). Das zweite Kind einer 30 Jahre alten Frau (2 Geburten, 2 Schwangerschaften) entwickelte einen deutlichen Ikterus (höchster Serum-Bilirubinwert 304,5 µmol/l). Andere Gründe des Ikterus konnten ausgeschlossen werden. Die Immunisierung war mit größter Wahrscheinlichkeit Folge der vorausgegangenen Schwangerschaft, da die Mutter zuvor nie Bluttransfusionen erhielt. Wir geben in diesem Zusammenhang eine Literaturübersicht über die bisher beschriebenen Fälle von Morbus haemolyticus neonatorum als Folge von Anti-Jk (b). Anhand dieser und unserem Fall ziehen wir den Schluß, daß der Antikörpersuchtest bei schwangeren Frauen entweder mit Testerythrozyten zweier Spender in mindestens zwei Testmethoden (indirekter Antiglobulintest mit Albumintechnik und Einstufenenzymtest) oder einer Methode (indirekter Antiglobulintest mit Albumintechnik) mit Testzellen von drei Spendern durchgeführt werden sollte. In unklaren Fällen von Morbus haemolyticus neonatorum sollte das mütterliche Serum gegen väterliche Erythrozyten gekreuzt werden.

Schlüsselwörter:

Morbus haemolyticus neonatorum — Phototherapie — Anti-Jk (b) Antikörper

Introduction

Since the discovery of the KIDD (Jk) blood group system, a considerable number of haemolytic transfusion reactions due to the corresponding antibodies especially to Anti-Kidd (a) have been reported (1, 10, 11). Haemolytic disease of the newborn (HDN) was observed only in a few cases. To our knowledge not more than ten cases of HDN caused by Anti-Kidd (b) have been published (4–7, 12, 15–18). All of those cases which were sufficiently well documented by immunhaematological diagnostics showed only a mild clinical course of HDN. Therefore we want to report on an additional case of haemolytic disease with marked hyperbilirubinaemia due to Anti-Kidd (b).

Case report

Family history

The mother (30 years) of the newborn (NB) had one pregnancy 8 years ago and no transfusions before. The first pregnancy was normal, but this child already showed elevated bilirubin levels shortly after birth (181.3 µmol/l). The cause could not be clarified, no immunohaematologic diagnostics was performed.

History of the case

The male child (V.S.-K.) was born spontaneously in february 1988 in the 37th week of an inconspicuous preg-

nancy. Several hours after birth the NB developed an increasing jaundice: bilirubin after 36 h 191.6 µmol/l. There was no change of the bilirubin level by phototherapy (PT) for 22 h. When the PT was stopped the bilirubin even raised up to 241.2 µmol/l. Therefore the PT was continued for 12 h more. As the clinical situation became worse, the NB was transferred to the children's hospital of the university of Marburg at day 6.

Clinical findings and laboratory data on admission

Well developed NB, distinct pallor, severe jaundice (bilirubin 304.5 µmol/l); physical and neurologic examination without any further pathological findings. Leukocytes 9400/µl, 81% lymphocytes, 18% polymorphnuclear cells, 1% bands; thrombocytes 416000/µl, hemoglobin (HB) 171 g/l, red cells (RBC) 4.9 mill/µl; normal concentrations of C-reactive protein, creatinine, glucose, potassium, sodium, calcium in serum, no pathological findings in urine analysis.

Immunohematologic results (For methods see 8, 10, 14)

NB: 0 Rhesus positive (CcDee), Jk(a+b+); direct antiglobulintest (DAT) negative with normal polyspecific antiglobulin serum (Ortho Diagnostics, Neckargemünd, FRG), but strongly positive (titer 1:32) with a high titer polyspecific antiglobulin serum (Antiglobulinserum forte®, Behringwerke, Marburg, FRG) and negative with monospecific antisera against IgG (Ortho), IgM (Behringwerke) and C3d (Ortho). The antibody screening (ABS) with serum against a panel of two test cells (Panogen®, Molter, Neckargemünd, FRG) which were heterozygous for Jk(a) and (b) was negative in a one stage enzyme test at 37°C (Bromelin®, Behringwerke) and in the indirect antiglobulintest (IAT) with albumin (Rinderalbumin 22%®, Ortho) as well as LISS (Enlist®, Baxter, Munic, FRG). The later control of ABS against two Jk (a−b+) test cells was positive in the enzyme test as well as with the two different methods of antiglobulin test using polyspecific antiglobulin serum (see above) but not with anti-IgG. The ether eluate (14) was negative in both methods of the ABS.

Mother: 0 Rh positive (CcDee), Jk (a+b−). The external ABS was negative in the 21st week of pregnancy. After delivery the ABS in our laboratory was only positive in the enzyme test when we used heterozygous Jk(a+b+) panel cells, but became positive with Jk(a−b+) red cells even in the antiglobulin test (albumin and LISS technique; polyspecific antiserum and Anti-IgG). In the identification panel (Resolve A®, Ortho) Anti-Jk(b) could clearly be demonstrated by the IAT with LISS as well as enzyme technique. In the one stage enzyme test 2 of 5 and in the IAT with albumin or polybrene none of the heterozygous Jk(a+b+) panel cells reacted positive. The antibody titer with Jk(a−b+) cells was in LISS-IAT 1:16 and in IAT with enzyme and albumin technique 1:4. Three months later the titer still was 1:8 in LISS-IAT.

Sister: The 8 year old sister was 0 Rh negativ (ccdee), Jk(a+b+).

Father: 0 Rh positiv (CcDee), Jk(a+b+). The cross match between the mothers's serum and the fathers's red cells was strongly positive in the enzyme test and IAT (albumin technique).

Clinical course

The child was submitted to the neonatal ward unit and treated again with PT in combination with 10% glucose solution (with sodium and potassium addition) as supportive therapy. After 12 h the bilirubin level fell to 165.9 µmol/l. Then the bilirubin concentration remained below the indication level for PT. Bilirubin at demission was 157.4 µmol/l.

Discussion

The reported case of HDN by anti-Jk(b) showed a rather severe hyperbilirubinaemia. Exchange transfusion could be avoided as PT had been started very early and was performed consequently. Most of the cases reported in the literature were less severe (Table 1). Only Kanner (1962) reported of a NB with anaemia and jaundice who died 2 days after birth (5). In the mother's serum anti-Jk(b) could be detected. Unfortunately the case is not well documented. In our case the origin of the antibody is not quite clear, since already the first child (1st pregnancy) developed hyperbilirubinaemia shortly after birth. In literature only one anti-Jk(b) (IgM) has been described as a natural antibody of the Kidd system (2). Additionally an autoantibody against Jk(b) was reported (10). Therefore, immunization probably occurred during the first pregnancy. Our case again demonstrates that there is not neccessarily a strong correlation between antibody

Tab. 1: Hemolytic disease of the newborn due to anti-Jk(b): Summary of available clinical and laboratory data

Number of pregnancy	Clinical findings: HCT (%)/HB (g/l) (time after delivery)	max. Bilirubin (µM/l) (time after delivery)	DAT	anti-Jk^b-titer (origin)	PT of the newborn	Ref.
3rd	−/120 (30 h)	171.6 (30 h)	+	1:32 (pregnancy)	−	6
2nd	−/152 (25 h)	153.9 (42 h)	+	1:16 (pregnancy)	−	4
3rd	death	−	−	− (pregnancy)	−	5
3rd	61/212 (cord)	83.8 (24 h)	+	1:8 (pregnancy)	−	17
4th	60.5/− (24 h)	143.7 (36 h)	+	1:32 (pregnancy)	−	18
7th	−/−	220.6 (24 h)	+	− (unknown)	+	12
2nd	48.8/171 (6 days)	304.5 (6 days)	+	1:16 (pregnancy)	+	authors

concentration and strength of hemolysis. Cytotoxicity against mononuclear cells seems to be more predictive in regard to clinical relevance (3). On the other hand the case showes clearly the need for adequate immunohematologic diagnostics in pregnant women and newborns. The ABS should be peformed both in IAT and one stage enzyme test. If only IAT is used ABS should be extended to 3 different panel cells in order to have homozygous test cells also for Jk. Then IAT can be performed with albumin. Despite the results in this case LISS-IAT cannot be recommended as a single method since this technique is not sufficiently sensitive to detect anti-K (8). In our experience the combination of the one step enzyme test and albumin IAT with two panel cells is even superior to a single ABS using 3 panel cells in IAT since various Rhesus antibodies can only be detected by enzyme tests.

In cases of unclear hyperbilirubinaemia and hemolysis in the NB the mother's serum should be tested against the father's red cells. If there is major ABO-incompatibility between them mother's serum can be neutralized by AB substance before. DAT should always be performed using two polyspecific antiglobulin sera one of which having a high titer. Finally adequate immunohematologic diagnostics should be carried out in all newborns and as early as possible in order to ensure proper clinical monitoring, and specific treatment (without unnecessary extended diagnostics).

References:

1. ALLEN, F. H. Jr., DIAMOND, L. K., NIEDZIELA, B.: A new blood-group antigen. Nature **167**, 482 (1951).
2. ARCARA, P. C., O'CONNOR, M. A., DIMMETTE, R. M.: A family with three Jk (a – b –) members. (Abstract) Transfusion **9**, 282 (1969).
3. GARRATTY, G.: Monocyte monolayer assay (MMA) – an efficient method for predicting the clinical significance of alloantibodies and the severity of hemolytic disease of the newborn. In KRETSCHMER, STANGEL, Transfusionsmedizin 1987, Beitr. Infusionsth., vol. 21, pp. 236–239 (Karger, Basel 1988).
4. GECZY, A., LESLIE, M.: Second example of hemolytic disease of the newborn caused by anti-Jk^b. Transfusion **1**, 125 (1961).
5. KANNER, J.: Anti-Jk^b in erythroblastosis fetalis. Am. J. Obstet. Gynecol. **83**, 1253 (1962).
6. KORNSTADT, L., HALVORSEN, K.: Haemolytic disease of the newborn caused by anti-Jk^b. Vox Sang. **3**, 94–99 (1958).
7. KORNSTADT, L.: New cases of irregular blood group antibodies other than Anti-D in pregnancy. Acta Obstet. Gynecol. Scand. **62**, 431–436 (1983).
8. KRETSCHMER, V., GERDES, R., BÄHR, E., KOSSMAGK, D.: Schnellkreuzprobe. Lab med. **11**, 53–58 (1987).
9. KRETSCHMER, V., MUELLER-ECKHARDT, C.: Relevanz verschiedener serologischer Untersuchungsmethoden bei Immunhämolysen. Lab.med. **6**, 133–138 (1982).
10. McGINNIS, M. H.: The ubiquitous nature of human blood group antigens as evidenced by bacterial, viral and parasitic infections. In: GARRATTY, G. (ed.) Blood Group Antigens and Disease. American Association of Blood Banks, Arlington VA, pp 33–43 (1983).
11. MOLLISON, P. L.: Blood Transfusion in Clinical Medicine, pp. 409–410. Blackwell scientific publications, Oxford, London, Edinburgh, Boston, Melbourne (1983)
12. PIERCE, S. R., HARMAN, J. T., STEELE, S., BECK, M. L.: Hemolytic disease of the newborn associated with anti-Jk3. Transfusion **20**, 189–191 (1980).
13. PLAUT, G., IKIN, E. W., MOURANT, A. E., SANGER, R., RACE, R. R.: A new blood-group antibody, anti-Jk^b. Nature **171**, 431 (1953).
14. RUBIN, H.: Antibody elution from red blood cells. J. Clin. Path. **16**, 70 (1963).
15. SCHELLONG, G., SANDMANN, G., FISCHER, K., POSCHMANN, A.: Hamolytische Neugeborenen-Erkrankungen durch Blutfaktoren-Unverträglichkeit außerhalb der Rh (D)- und ABO-Inkompatibilität. Dtsch. Med. Wochenschr. **101**, 1595 (1976)
16. SIMMONS, R. T., GRAYDON, J. J., JAKOBOWICZ, R., SANTAMARIA, J., GARSON, M.: Immunization by the blood-group antigen Kidd (Jk^b) in pregnancy and in blood transfusion. Med. J. Aust. **2**, 933 (1957).
17. WAGMAN, E., BOVE, J.: Hemolytic disease of the newborn caused by anti-Jk^b. Am J. Clin. Path. **41**, 481 (1964).
18. ZODIN, V., ANDERSON, R. E.: Hemolytic disease of the newborn due to anti-Kidd (Jk^b) Case report and review of the literature. Pediatrics **36**, 420–422 (1965).

Anschrift des Verfassers:

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