Severe ABO-hemolytic disease of fetus and newborn requiring exchange transfusion- three neonatal cases.

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Disclaimer

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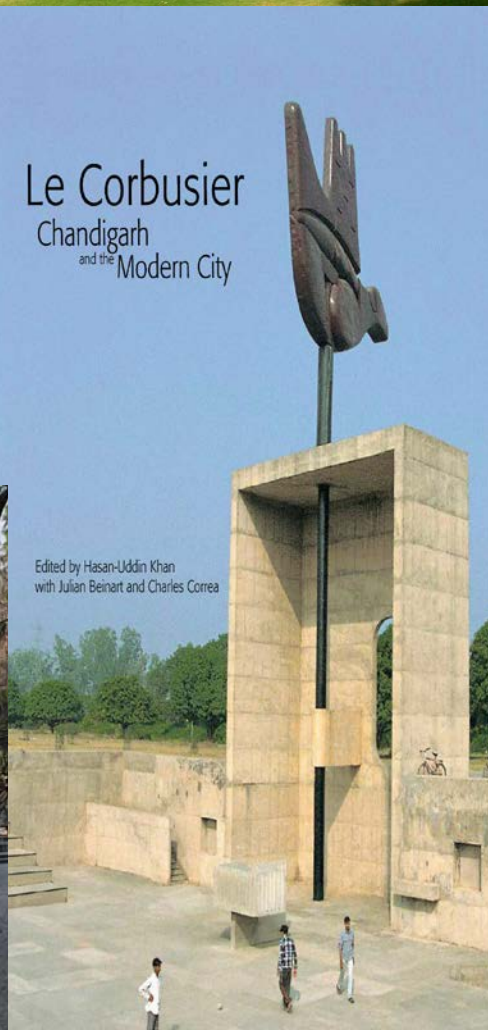

Introduction

- Hemolytic disease of fetus and newborn (HDFN)- transplacental passage of maternal antibodies leading to immune hemolysis of neonatal red cells, is an important cause of neonatal morbidity and mortality

- ABO incompatibility and other alloantibodies- emerged as a significant cause of HDFN

Basu et al AJTS 2011;5:3-7

- Quite common & frequently benign in its clinical course

- Delay may lead to significant hyperbilirubinemia requiring intervention.

Patients and Methods

- We report three cases of severe HDFN due to ABO incompatibility who were referred to our Institute, a tertiary care center in the region
- These cases were managed with exchange transfusions to decrease the high serum bilirubin levels.
- Packed red blood cell (PRBC) units reconstituted in AB plasma.
- The compatibility testing with maternal serum and neonatal direct antiglobulin test (DAT)- Gel technique (LISS-Coombs AHG cards, Biorad, Switzerland).

Report of cases

Case 1-

- Three-day old female (birth weight- 2.5 kg)
- Diagnosis- neonatal jaundice (NNJ) with encephalopathy
- Requisition for Blood group and DAT, and two PRBC units for double volume exchange transfusion (DVET)
- First child in the family.

Immunohematology Work-up

	Onset of jaundice	TSB	Blood Group of neonate	DAT(gel technique;LISS Coombs)	Blood Group of the mother	Blood group of the father	Mother's ABO antibody titer	Mother's antibody screen	Elution on baby's sample(heat elution)
Case-1	Day 3 of birth	22 mg%	A RhD positive	Positive (2+) IgG.	O RhD positive	A RhD positive	Anti-A Titer IgM-1:32 IgG-1:512	Negative	Positive with A_{cells} (gel technique)

Management

- DVET- Two O RhD positive PRBC units compatible with mother's and baby's blood sample at AHG phase.
- Patient was discharged next day with TSB value of 9.8 mg%.

Case 2

- Second case-Four-day old boy (birth weight- 3.5 kg)
- Diagnosis - NNJ.
- Blood requisition for DVET.
- History of jaundice in elder sibling (blood group not known). Onset of jaundice- Day three of birth, phototherapy given.

Immunohematology Work-up

	Onset of jaundice	TSB	Blood Group of neonate	DAT(gel technique;LISS Coombs)	Blood Group of the mother	Blood group of the father	Mother's ABO antibody titer	Mother's antibody screen	Elution on baby's sample(heat elution)
Case-2	Day 3 of birth	27 mg%	A RhD positive	Positive(1+), IgG, IgG_1 and IgG_3	O RhD positive	-	Anti-A Titer IgM-1:256 IgG-1:1024	Negative	Positive with A_{cells} (gel technique)

Management

- Two DVETs done at the interval of 24 hours with O RhD negative PRBC unit as O RhD positive unit was not available.
- Post DVET, DAT was weak positive.

Case 3

- Four-day old neonate, female (birth weight- 2.5 kg)
- Hemoglobin level- 5g%, hematocrit-15%.
- Peripheral blood film (PBF)- microcytosis and spherocytosis.
- There was no history of jaundice in elder sibling (boy, two years of age, blood group O RhD positive) at birth.

Immunohematology Work-up

	Onset of jaundice	TSB	Blood Group of neonate	DAT(gel technique;LISS Coombs)	Blood Group of the mother	Blood group of the father	Mother's ABO antibody titer	Mother's antibody screen	Elution on baby's sample(heat elution)
Case-3	Day 3 of birth	25 mg%	A RhD positive	Positive (2+) IgG, IgG_1 and IgG_3,	O RhD positive	A RhD positive	Anti-A Titer IgM-1:256 IgG-1:1024	Negative	Positive with A_{cells} (gel technique)

Management

- Post DVET, serial 8 hourly TSB values were – 20 mg%, 15, mg% 11mg% and 10 mg%.
- Post DVET, DAT was weak positive.

Discussion

- HDFN due to non anti-D antibodies is on rising trend due to increasing awareness among the clinicians regarding the screening of Rh'D' negative antenatal patients and use of anti-D prophylaxis

- ABO hemolytic disease is relatively lesser recognized entity as
  - routine antenatal screening for high titer anti-A and anti-B is not recommended due to poor reproducibility
  - HDN due to ABO antibodies is rarely severe

- The reported incidence of ABO incompatible pregnancies is 15-25% in India

Contd…

- In a study by Bhat et al, ABO incompatibility was seen in 17.3%(151/878) of pregnancies out of which 50.4% were O-A and 49.6% were O-B incompatible pregnancies.
- Forty six (30.4%) required phototherapy, none required exchange transfusion

Bhat et al Ped Int Child Health 2012;32:93-96

- In another study by Usha and Sulochna including 100 antenatal O group mothers, ABO HDN was encountered in 3 neonates

Usha et al Ind J Pediatr 1998;65:863-65

Contd…

- In the present case series, all three cases of ABO HDN required exchange transfusion due to severe hyperbilirubinemia.
- All the three cases were of O-A incompatible, DAT positive with IgG as the antibody specificity.
- IgG subclass was found to be IgG_1 and IgG_3 in two of the cases.
- Antibody screen on maternal serum was negative ruling out non-ABO antigen system antibodies

Contd…

- It is advocated that lysis of red blood cells (RBCs) in ABO incompatible HDN is extravascular mediated by macrophages and complement is not activated

- It is due to low level of A and B antigenic expression on neonatal red cells and low complement levels in serum

Brouwersm et al Br J Hematol 1988;68:363-66

Contd…

- The clinical severity in ABO-HDN varies from mild to moderate hyperbilirubinemia that can be managed by phototherapy in most of the cases
- Rarely, exchange transfusions may be required
- The extent of involvement depends upon the amount of antibody that crosses the placenta.

Literature Review

Authors	Case report	Outcome
Deng et al	Significant ABO-HDN presenting with severe anaemia in a neonate with a cis-AB phenotype born to a group O mother	Good with phototherapy, intravenous immunoglobulin (IVIG) and recombinant human erythropoietin (rhEPO)
Haque et al	Severe HDN in a neonate with A_1B blood group (mother's blood group B RhD positive)	Good with two exchange transfusions
McDonnell et al	Hydrops fetalis due to Significant ABO-HDN	
Goraya et al	Hydrops fetalis due to Significant ABO-HDN	

Contd…

- A high index of suspicion is required for early diagnosis of ABO HDN

- According to Procianoy et al, DAT in cord blood, elution test and evidence of hemolysis (rise in bilirubin concentration, anemia, reticulocytosis and spherocytosis on PBF), may help in early diagnosis.

Contd…

- Sarcini et al determined prospectively the critical serum total bilirubin level to predict significant hyperbilirubinemia and severe hemolytic disease in healthy term newborns with ABO incompatibility

- They concluded that bilirubin levels of 4 mg/dL and 6 mg/dL at the sixth hour of life predicts the development of significant hyperbilirubinemia and severe hemolytic disease of the newborn respectively

Pediatrics 2002;109

Conclusions

- ABO HDN, usually a mild condition, has been implicated in complications like neonatal cholestasis if not diagnosed appropriately
- If maternal and neonatal ABO incompatibility is present, red cell transfusions should be compatible with both maternal and neonatal serum
- Transfusion of red cells identical only to neonate can lead to hemolysis due to stronger ABO antigen expression on adult donor cells.

To Conclude

- *There is a need to sensitize the clinicians towards ABO HDN for optimizing care in terms of early diagnosis and adequate monitoring.*
- *A high-risk approach should be adopted if there is a history of ABO HDN in previous pregnancies or if there is ABO incompatibility between the partners.*

Thank you

Contd…

- In the present case series, ABO HDN led to severe hyperbilirubinemia (serum bilirubin >20 mg/dl) that required exchange transfusions.
- Other treatment modalities include IVIg and rhEPO.
- The efficacy of IVIg in ABO HDN has been found to be variable.
- More randomized clinical trials are required to standardize the dose and the dosing schedule of IVIg and to study its cost effectiveness.
- Its potential benefits should be weighed against the potential risks especially necrotising entercolitis, thrombosis and IVIG-mediated hemolysis from anti-A and anti-B antibodies found in IVIG.