Neonatal jaundice: Is it hereditary spherocytosis?

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ABSTRACT
A full term baby developed indirect hyperbilirubinemia within first 12 hours of life. Hence, capsule phototherapy was started and investigations were done to find out the cause. There was a history of death of previous sibling apparently due to neonatal jaundice. Mother’s blood group was A positive, baby’s blood group was A negative and DCT was negative. Reticulocyte count was 34%. The baby had low hemoglobin and high MCHC. Hence, diagnosis of neonatal non-immune hemolytic jaundice was considered. Most likely causes were G-6 PD deficiency and hereditary spherocytosis. With capsule phototherapy indirect hyperbilirubinemia was under control with peak TSB level of 22.6 mg/dl on 3rd day of life, dropping to 8.5 mg/dl on 12th day of life. In addition, single volume exchange blood transfusion was carried out on 5th day. The baby remained clinically well throughout hospital stay and was taking breastfeeding well. The baby had bronze grayish color of skin, which could be due to component of direct hyperbilirubinemia present as a result of excessive hemolysis. G-6 PD quantitative test was normal. Peripheral smear done on 4th day showed moderate anisopoikilocytosis with spherocytosis and polychromasia with frequent presence of NRBCs. The percentage of spherocytes were 8% of red cells. In view of above clinical picture and laboratory findings, diagnosis of hereditary spherocytosis was considered.

In hereditary spherocytosis, there is alteration of red cell membrane due to genetic defect causing deficiency of cell membrane protein and reducing their deformability1. It affects about 1 in 2000 in Europe and North America. Most cases are autosomal dominant and are mild to moderate in severity with small number of cases being autosomal recessive and having severe form of the disease. Our case probably belongs to autosomal recessive type in view of severe clinical symptoms, family history of sibling who died of severe jaundice in the neonatal period and history of consanguinity between the parents (they were cousins).

Keywords: Hereditary Spherocytosis, Neonatal presentation, Autosomal recessive
INTRODUCTION
Severe neonatal unconjugated jaundice requiring exchange blood transfusion can be caused by either immune mediated or non-immune mediated hemolytic jaundice. Immune mediated hemolysis could be either isoimmune or less commonly autoimmune. In immune mediated hemolysis, direct coomb’s test is usually but not always positive. The more common causes of non immune mediated severe neonatal unconjugated hyperbilirubinemia are G-6 PD deficiency and hereditary spherocytosis (HS). Hereditary spherocytosis (HS) is an uncommon disorder inherited either by autosomal dominant or recessive mechanism and varies in severity from mild to severe variety. Without typical family history, HS is difficult to diagnose in the neonatal period. We present one similar case of neonatal presentation of HS and discuss its clinical implications.

CASE REPORT
The newborn baby was born in our hospital on 2/7/14 by normal vaginal delivery. He was noted to have icterus at 5 hours of age. Hence, baby’s total and indirect bilirubin levels were sent. Mother’s blood group was A positive where as baby’s blood group was A negative, ruling out ABO and Rh blood group incompatability. Baby’s total serum bilirubin (TSB) level was 11.3 mg/dl with indirect component of 10.3 mg/dl. Hence, he was admitted to the NICU and was started on capsule phototherapy. Baby was further investigated for the cause of pathologic indirect hyperbilirubinemia. There was a history of previous sibling death in the neonatal period apparently due to jaundice. The exact cause was not known. Also, parents were cousins suggesting history of consanguinity. Direct Coomb’s test (DCT) was negative, reticulocyte counts were 34% and complete blood count showed hemoglobin of 11.5 gm/dl, MCV- 114, MCHC-36%, Platelet count of 150,000/cmm. In view of the negative DCT, evidence of hemolysis and absence of major blood group incompatibility, diagnosis of non-immune mediated hemolytic jaundice was made. The common causes of severe unconjugated hyperbilirubinemia due to non-immune mediated hemolysis are G-6 PD deficiency and HS. Hence, G-6 PD test and peripheral blood smear examination was requested. G-6 PD quantitative test showed level of 20 U/g of Hb, which is normal. Peripheral blood smear showed moderate anisopoikilocytosis with spherocytosis and polychromasia with frequent presence of NRBCs. Percentage of spherocytes were 8% of red cells. In view of clinical picture and laboratory findings including MCHC value on the upper range of normal, diagnosis of HS was strongly suspected. With capsule phototherapy, TSB level decreased to 9.3 mg/dl at 48 hours of age. TSB level at 60 hours of age, 12 hours after stopping phototherapy, was 22.6 mg/dl with direct component of 2.2 mg/dl. Hence, capsule phototherapy was restarted and exchange blood transfusion was contemplated. Due to unavailability of fresh A negative blood exchange blood transfusion could not be done on 3rd day, but was done on 5th day of age. Baby’s skin appeared bronze grayish in color since 4th day of age. This could be due to effect of phototherapy on direct component of bilirubin, which was slightly high in our case. This was probably a result of excessive hemolysis. With capsule phototherapy, TSB level dropped to 18.4 mg/dl with direct component of 2.6 mg/dl on 5th day of age. Due to availability of single bag of blood group A negative whole blood, single volume exchange blood transfusion was done at this time. Post-exchange blood transfusion, TSB level dropped to 13.6 mg/dl with direct component of 2.1 mg/dl. With capsule phototherapy, TSB level further dropped to 6 mg/dl (direct bilirubin of 1.5 mg/dl) by 8th day of age. At this stage capsule phototherapy was stopped and TSB levels were repeated over next few days. It remained in the normal range and then showed downward trend. Baby remained clinically well throughout the NICU stay and was on full oral feeds. Baby was discharged on 12th day of postnatal life and advised to follow up. On last enquiry,
baby was 2.5 months old and was following up with hematology department of government hospital in Sharjah. He required blood transfusion once after discharge in view of severe anemia. Further blood tests are planned 3 months after last blood transfusion to establish the diagnosis.

DISCUSSION
Hereditary spherocytosis is a familial hemolytic disease in which genetic mutation leads to abnormality in red cell membrane protein making it more rigid\(^2\)\(^-\)\(^4\). These cells are then trapped in spleen and destroyed. The mode of inheritance is either autosomal dominant or autosomal recessive\(^2\)\(^-\)\(^4\). HS varies in clinical severity and is divided in to mild, moderate and severe type\(^2\)\(^-\)\(^4\). Mild type generally presents in adult life with cholelithiasis or anemia secondary to aplastic or hemolytic crisis. They may not present until seventh to ninth decade of life\(^4\). Moderate variety may present with mild to moderate anemia, jaundice requirement of intermittent blood transfusion or splenomegaly\(^4\). Severe variety of disease generally requires frequent blood transfusions, may present in neonatal period with severe jaundice or present in an early childhood period with anemia, jaundice or splenomegaly and generally requires partial or total splenectomy for cure\(^2\)\(^-\)\(^4\). Neonatal presentation does not always mean a severe clinical course in the future\(^3\). Severe variety usually has an autosomal recessive inheritance\(^4\). In patients with typical family history, presence of hemolytic anemia, reticulocytosis, high MCHC, negative DCT and presence of spherocytes on peripheral smear establishes the diagnosis of HS\(^4\). In cases without typical family history further tests are required. These tests are cryohaemolysis test, the osmotic gradient ektacytometry and the EMA binding test\(^4\). In neonates without typical family history, diagnosis may be delayed up to 6 months of age, by then the cellular morphology is more typical\(^4\).

REFERENCES