CASE REPORT

Two neonates with Bartter syndrome

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Abstract

Bartter syndrome is an autosomal recessive disorder caused by gene mutations that involve hypokalaemia, hypochloraemia and metabolic alkalosis along with raised serum renin, hyperaldosteronism and normal blood pressure. We report two cases of neonatal Bartter syndrome. Case 1 was a product of non-consanguineous marriage and mother had unexplained polyhydramnios in pregnancy while case 2 was a product of consanguineous marriage. Both cases were diagnosed based on hypokalaemia, hypochloraemia and metabolic alkalosis along with elevated serum renin and aldosterone levels. Case 1 positively responded to indomethacin while case 2 had Protein C and S deficiency and sepsis as co-existing diseases and thus could not be given indomethacin and expired. Regular antenatal visits can help in diagnosis of the syndrome particularly if unexplained polyhydramnios is investigated.

Keywords: Neonatal Bartter syndrome, serum renin, serum aldosterone, polyhydramnios

Introduction

Bartter syndrome is a rare autosomal recessive chronic tubular disorder characterized by hypokalaemic, hypochloraemic metabolic alkalosis and involves polyuria, salt wasting and hyperaldosteronism with normal blood pressure.[1] It has five types and all of them involve mutations in the genes responsible for these symptoms.[2] Occurrence of neonatal Bartter syndrome is a rare phenomenon (1.2 cases per million) and is divided into type 1 and 2. Type 1 is caused by mutations in Na-K-2Cl co transporter of thick ascending loop of Henle that causes defective reabsorption of potassium and chloride. In type 2 there are mutations in ROMK gene that encodes for ATP sensitive potassium ions and absorb them back to lumen causing defective absorption of potassium, chloride and water and hence causing hypokalaemia, hypochloraemia and polyuria.[3]

Delay in diagnosis can result in increase morbidity and mortality owing to a large number of complications. It becomes difficult to diagnose neonatal Bartter syndrome if the antenatal visits are not regular and if there is coexisting sepsis or any other disease. We hereby report two cases of neonatal Bartter syndrome. One baby had co-existing sepsis and protein C and S deficiency.

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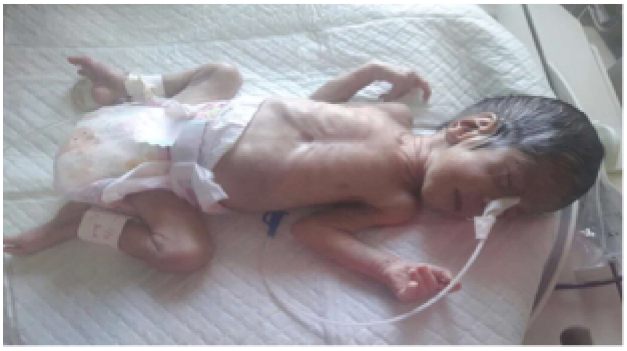

Figure-1: Male baby with neonatal Bartter syndrome.

Case 1

A male baby weighing 1.9 Kg was born at 35 weeks gestationvia emergency Caesarean section due to foetal distress. Baby was a product of non-consanguineous marriage. Mother had unexplained significant polyhydramnios in all pregnancies and also had undergone amniocentesis in this pregnancy in a private hospital. However, due to irregular antenatal check-ups, no significant diagnosis was available. The baby was admitted in December 2017 in the nursery of Children's Hospital, Pakistan Institute of Medical Sciences, Islamabad due to episodes of apnoea. In spite of intravenous fluid therapy, baby remained dehydrated. Laboratory investigations showed hypokalaemia (2.5 Meq/L), shypochloraemia (64 Meq/L) and metabolic alkalosis. Since there was history of unexplained polyhydramnios along with hypokalaemia, hypochloraemia and metabolic alkalosis,neonatal Bartter syndrome was suspected. For confirmation of the disease, laboratory analyses for serum renin and aldosterone were carried out. Serum renin was >500μIU/L and serum aldosterone was >200 ng/dl. Thus, diagnosis of neonatal Bartter syndrome was made (photograph 1). Potassium was continuously replaced in intravenous fluids. Baby was given aldosterone antagonist

and angiotensin converting enzyme inhibitors. However, the baby did not improve and serum potassium did not rise. Baby was then started on indomethacin (2mg/kg/day). The baby gradually started improving and potassium levels increased. On discharge the baby was stable, taking oral feeds and serum biochemistry was normal. Oral sodium and potassium supplements were continued.

Case 2

The second case was of a baby born to a primigravida mother at term via emergency Caesarean section due to non-reactive cardiotocography of the baby. Mother had irregular antenatal visits. Baby was a product of consanguineous marriage. The case was referred from another hospital to the Children's Hospital, Pakistan Institute of Medical Sciences, Islamabad in June 2017 with complaints of difficulty in breathing, bluish discoloration of the entire right arm extending up to the chest and severe dehydration. We suspected severe neonatal sepsis with thrombotic complication. However, protein C and protein S deficiency was also considered.

Baby was initially investigated, rehydrated and intravenous antibiotics were started. Blood culture showed Klebsiella sepsis. Total leukocyte count, platelet count and haemoglobin gradually dropped for which blood products were repeatedly transfused. PT and APTT were also deranged. C-Reactive Protein and procalcitonin were positive. Purpura fulminans on the arm started resolving. Laboratory investigation yielded deficiency of Protein C (18 U/mL) and protein S (30 U/mL). Inspite of intravenous fluids, baby repeatedly became extremely dehydrated with polyuria. Laboratory investigations revealed hypokalaemia (2.8 Meq/L), hyponatraemia (120Meq/L) and hypochloraemia (80Meq/L) along with metabolic alkalosis. Repeated laboratory investigations revealed the same trend. Thus neonatal Bartter syndrome was suspected. The suspicion was confirmed with elevated level of serum renin (>500 μIU/L)and serum aldosterone (>200ng/dl). Indomethacin could not be started because baby was suffering from Klebsiella sepsis and platelet count was very low. Aldosterone antagonist and potassium sparing diuretic were given. Potassium was also replaced continuously with intravenous fluids. However baby's condition deteriorated and baby had to be placed on the ventilator and later expired.

Discussion

Bartter syndrome is named after Fredrick Bartter who first described a case of hypokalaemic metabolic alkalosis along with hyperaldosteronism and normal blood pressure. It results from mutations in the NKCC2 and ROMK gene that causes defective absorption of sodium, potassium and chloride in the thick ascending loop of Henle and hence increased loss of these ions. Bartter syndrome can be diagnosed by elevated levels of serum renin and aldosterone.[4] In both cases under report, we suspected neonatal Bartter syndrome due to persistent laboratory findings of hypokalaemia, hypochloraemia and metabolic alkalosis and the diagnosis was confirmed after finding high serum levels of renin and aldosterone. Confirmation through genetic analysis could not be made as facility was not available in the country.

Bartter syndrome can be suspected antenatally if there is unexplained polyhydramnios and later growth restriction is seen in the baby. High chloride levels in amniotic fluids are regarded as diagnostic.[5] In our case 1, there was history of unexplained polyhydramnios which could not be diagnosed due to irregular antenatal visits of the mother. Bhat et al[6] and Narayan et al[7] concluded that Bartter syndrome could be a cause of unexplained polyhydramnios. However, polyhydramnios was not seen in mother of case 2.

In case 1, baby improved and potassium levels increased after the initiation of indomethacin therapy. Earlier studies[8,9] have also shown to have positive effect of prostaglandin inhibitors like indomethacin in improving electrolyte balance and improve growth and development. Indomethacin inhibits prostaglandin synthesis and it helps in weight gain and increase in sodium and potassium levels.[10] Management of Bartter syndrome should also include proper hydration, replacement of potassium in fluids, aldosterone antagonists and potassium sparing diuretics.

There is no evidence of association between neonatal Bartter syndrome and protein C and S deficiency, thus in case 2, these were probably two independent diseases.

Conclusion

We report here two cases of neonatal Bartter syndrome with the diagnosis based on hypokalaemia, hypochloraemia and metabolic alkalosis along with elevated serum renin and aldosterone levels. In uncomplicated case, indomethacin therapy proved

effective. Regular antenatal visits of expecting mother can assist the physician in earlier diagnosis. Antenatal polyhydramnios without any apparent cause may be investigated for Bartter syndrome.

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