CASE REPORTS

A RARE CASE OF SLC4A1 MUTATION WHICH PRESENTED AS NEONATAL HEMOLYTIC ANEMIA AND DEVELOPED DISTAL RTA BY TODDLER AGE GROUP

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ABSTRACT

Distal renal tubular acidosis (dRTA) is an uncommon condition resulting from impaired hydrogen ion secretion in the distal nephron, leading to metabolic acidosis. Mutations in the SLC4A1 gene are known to cause dRTA and may also be associated with hemolytic anemia due to its expression in erythrocytes. We describe a 21-month-old male child, born to consanguineous parents, who presented with acute generalized weakness, excessive urination, and irritability. He had a prior history of neonatal jaundice, anemia, and hepatosplenomegaly requiring transfusion. Laboratory evaluation revealed severe hypokalemia and metabolic acidosis. Genetic analysis identified a homozygous missense mutation in the SLC4A1 gene (c.2573C>A; p.Ala858Asp). The child responded well to potassium replacement and alkali therapy. This case underlines the importance of considering genetic etiologies in children with electrolyte disturbances and previous hematological abnormalities.

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Hypokalemia, Anemia, Hypotonia, Acidosis.

Introduction

Renal tubular acidosis encompasses a group of disorders characterized by defective renal acid-base regulation, leading to persistent metabolic acidosis despite preserved glomerular function.[1] Distal RTA (type 1) arises due to the inability of the distal nephron to adequately excrete hydrogen ions.

Inherited forms of dRTA are commonly linked to mutations in genes such as SLC4A1, ATP6V1B1, and ATP6V0A4.[2] The SLC4A1 gene encodes the anion exchanger protein (AE1), which plays a role in bicarbonate transport in both renal tubular cells and red blood cells. Consequently, mutations in this gene may present with both renal tubular dysfunction and red cell abnormalities, including hemolytic anemia.[3]

We report a child with dRTA due to an SLC4A1 mutation presenting with acute hypokalemic weakness and a background of neonatal hemolytic anemia.

Clinical Description

A 21-month-old boy, born of a second-degree consanguineous marriage, presented with sudden onset weakness involving all four limbs along with neck muscle involvement. The illness was accompanied by increased thirst, frequent urination, and irritability.

The child had a significant neonatal history of prolonged jaundice, anemia, and hepatosplenomegaly requiring blood transfusion. At that time, a diagnosis of hereditary spherocytosis was considered based on genetic testing, although osmotic fragility testing was negative.

On examination, his anthropometric parameters were between -1 and -2 Z scores. Neurological evaluation revealed generalized hypotonia with muscle strength graded at 2/5 in all limbs, while deep tendon reflexes were intact.

Laboratory investigations demonstrated metabolic acidosis (arterial pH 7.21, bicarbonate 12 mmol/L) and severe hypokalemia (1.8 mmol/L). Peripheral smear showed normocytic hypochromic red blood cells. Renal function tests, thyroid profile, and abdominal ultrasonography were within normal limits. Urine pH was inappropriately high at 7.5.

Further genetic evaluation using whole exome sequencing revealed a homozygous missense variant c.2573C>A (p.Ala858Asp) in the SLC4A1 gene, which was categorized as likely pathogenic.

The child was managed with intravenous potassium supplementation along with fluid support and alkali therapy. Gradual improvement in muscle strength was observed over the course of treatment. He was subsequently transitioned to oral potassium citrate and calcium supplements prior to discharge. At follow-up, the child remained asymptomatic with complete resolution of motor weakness.

Discussion

Distal renal tubular acidosis (dRTA) is a disorder of impaired hydrogen ion secretion in the distal nephron, leading to persistent normal anion gap metabolic acidosis. It is typically associated with hypokalemia and an inability to acidify urine appropriately.[1,4] If untreated, dRTA can result in growth failure, nephrocalcinosis, and bone disease in children.

In this case, the child presented with acute flaccid weakness due to severe hypokalemia. Potassium depletion in dRTA occurs as a result of increased distal sodium delivery and secondary hyperaldosteronism, causing renal potassium loss. Severe hypokalemia may manifest as muscle weakness or paralysis, as observed in this patient.[5]

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The identification of an SLC4A1 mutation explains the combined renal and hematological features. The SLC4A1 gene encodes the anion exchanger 1 (AE1), which facilitates chloride-bicarbonate exchange in both renal tubular cells and erythrocytes. In the kidney, AE1 dysfunction leads to defective acid secretion, while in red blood cells it contributes to membrane instability, resulting in hemolytic anemia.[6]

The patient's history of neonatal jaundice, anemia, and hepatosplenomegaly supports an underlying congenital hemolytic disorder associated with this mutation.[3,8] The p.Ala858Asp variant has been reported in association with dRTA, though clinical manifestations may vary. Neuromuscular presentations such as hypokalemic paralysis are less commonly described.[7]

Consanguinity in this case suggests an autosomal recessive inheritance pattern and highlights the importance of genetic testing for confirmation and counseling. Management includes prompt correction of hypokalemia and long-term alkali therapy to maintain acid-base balance and prevent complications.[9]

This case highlights the need to consider dRTA in children with unexplained hypokalemia and weakness, especially when there is a history of hemolytic anemia. Early recognition and treatment are essential to improve outcomes.

Conclusion

In children with congenital hemolytic anemia, the possibility of associated renal tubular disorders should be considered. Early identification of genetic causes of dRTA enables timely treatment and helps prevent long-term complications. Genetic counseling plays a vital role in families with consanguinity.

Compliance with Ethical Standards

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