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A Rare Case of Failure to Thrive in An Infant Due to Aldosterone Synthase Deficiency Homozygous Cybp11b2 Gene Mutation

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Abstract

Objectives and Study: *We present a case of a 9-month-old male infant who was admitted to our Pediatric department because of failure to thrive, vomiting, and severe dehydration. Born on time, weight 4100 g, breastfed up to 5 months. Growth was normal until 5 months. When complementary feeding s introduced, the infant manifested episodes of constipation and repeated vomiting after feedings.*

Methods: *As the clinical presentation started with failure to thrive, all the possible and more common causes were addressed initially, such as cystic fibrosis, coeliac disease, allergies, etc. The situation worsened quickly, with the manifestation of severe dehydration, loss of 10% of the actual weight, and acid-base disturbances with metabolic alkalosis, critical hyponatremia, hyperkalemia, and hypochloremia. (pH 7.51; Na 116, K 6.5, Cl 87). Congenital adrenal hyperplasia (CAH) was ruled out with the 17-OH progesterone test.*

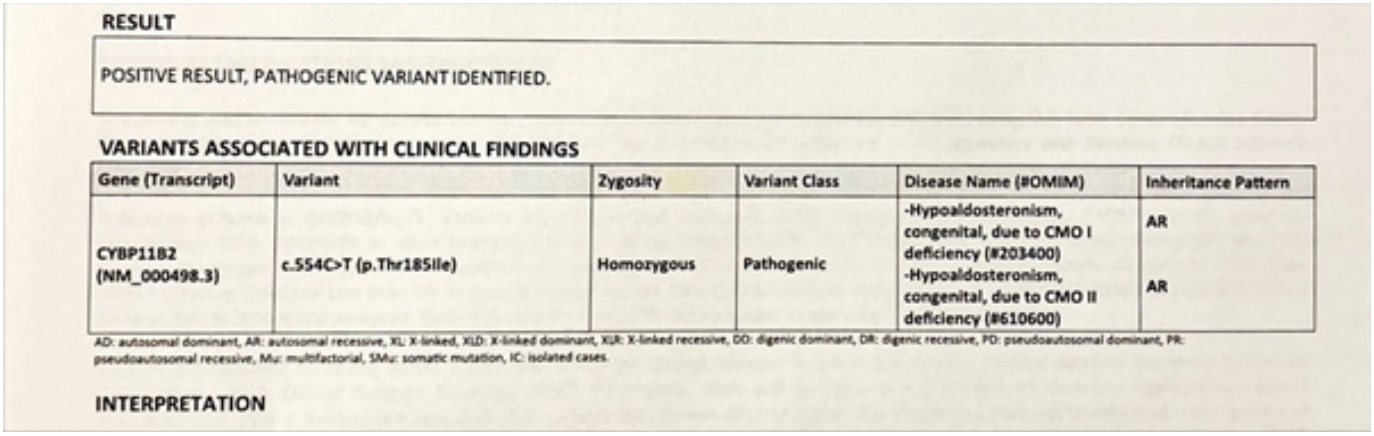
Results: *In the absence of clear evidence of gastrointestinal fluid losses or renal dysfunction, suspicion for other causes of salt wasting (SW) was addressed in further investigations. Next-generation sequencing of the infant's DNA revealed the pathogenic homozygous mutation (ACC-ATC) (c.554C>T) (p.Thr185Ile) in CYP11B2 (NM_00498.3) gene in the infant. Significant hypo aldosteronism due to aldosterone synthase deficiency can present in infancy with salt wasting, which can lead to dehydration, shock, and even death if not adequately treated. The treatment for patients with mineralocorticoid hormone deficiency is Fludrocortisone, accompanied by a high sodium intake through food.*

Conclusions: *Presenting symptoms of failure to thrive and later onset of salt wasting can be caused by Aldosterone Synthase Deficiency (ASD). Hypoaldosteronism is a rare, autosomal recessive syndrome that is a life-threatening disease. Coping in real life with this condition is challenging. Immediate treatment with mineralocorticoids is a must*

Case Presentation: *A 9-month-old male infant was admitted to the Pediatric Department of Acibadem Sistina Clinical Hospital with symptoms of failure to thrive, vomiting, and severe dehydration. He was born full-term, weighing 4100 grams, and was breastfed until 5 months of age. His growth was normal until the introduction of complementary feeding, at which point he developed constipation and recurrent vomiting. By the time of admission, he had lost 10% of his body weight and exhibited signs of severe dehydration, metabolic alkalosis, hyponatremia (Na 116 mEq/L), hyperkalemia (K 6.5 mEq/L), and hypochloremia (Cl 87 mEq/L). Initial investigations ruled out common causes of salt-wasting, such as cystic fibrosis and celiac disease. CAH was excluded based on normal 17-hydroxyprogesterone levels. Given the clinical presentation, we made a decision to perform genetic testing.*

Methods and Diagnostic Workup: *Next-generation sequencing (NGS) revealed a homozygous mutation in the CYP11B2 gene (c.554C>T; p.Thr185Ile), confirming aldosterone synthase deficiency. This mutation impairs aldosterone synthesis, disrupting sodium and potassium balance and resulting in severe electrolyte imbalances. Early genetic diagnosis is crucial for timely and effective treatment.*

Table 1: Genetic Mutation in Aldosterone Synthase Deficiency



RESULT

POSITIVE RESULT, PATHOGENIC VARIANT IDENTIFIED.

VARIANTS ASSOCIATED WITH CLINICAL FINDINGS

Gene (Transcript)	Variant	Zygosity	Variant Class	Disease Name (#OMIM)	Inheritance Pattern
CYBP11B2 (NM_000498.3)	c.554C>T (p.Thr185Ile)	Homozygous	Pathogenic	-Hypoaldosteronism, congenital, due to CMO I deficiency (#203400) -Hypoaldosteronism, congenital, due to CMO II deficiency (#610600)	AR AR

AD: autosomal dominant, AR: autosomal recessive, XL: X-linked, XLD: X-linked dominant, XLR: X-linked recessive, DO: digenic dominant, DR: digenic recessive, PD: pseudoautosomal dominant, PR: pseudoautosomal recessive, Mu: multifactorial, SMu: somatic mutation, IC: isolated cases.

INTERPRETATION

Treatment and Management

The infant was promptly started on fludrocortisone, a mineralocorticoid replacement therapy, along with dietary sodium supplementation. Fludrocortisone acts as a synthetic substitute for aldosterone, helping to restore sodium balance and correct electrolyte abnormalities. Over the course of treatment, the child's electrolyte imbalances were resolved, and he began to regain weight and hydration.

Follow-Up and Outcome

We followed the child's health multidisciplinary to ensure normal growth and development, minimize complications and to prevent complications. On the last check- up and follow up at 3 years and 6 months, the child's growth parameters had significantly improved, with a weight of 14.5 kg and a height of 103 cm. Clinical examination revealed no major developmental delays, although mild Harrison's sulci (a sign of rickets) were noted. His laboratory results remained stable, with aldosterone levels recorded at 3.75 ng/dL in February 2023 and 6.55 ng/dL in October 2023. While the child experienced occasional mild hyponatremia (Na 132 moll/L) during episodes of illness, no other complications were noted and no further interventions were necessary. The patient's family has another healthy 5-year-old sibling, who remains unaffected. Despite genetic counseling, the family has not pursued genetic testing. Our patient currently is scheduled for regular check-ups with no current treatment needed at the moment.

Discussion

Aldosterone synthase deficiency (ASD) is a rare genetic disorder caused by mutations in the CYP11B2 gene, which is responsible for aldosterone production. As a result, the adrenal glands produce insufficient aldosterone, leading to excessive salt loss, dehydration, and elevated potassium levels. ASD in infants can presents a diagnostic challenge, often mimicking more common conditions that result in electrolyte disturbances. This case highlights the importance of considering rare conditions in infants that are critically ill, such as ASD when evaluating infants with salt-wasting crises. The condition is caused by mutations in the CYP11B2 gene, leading to insufficient aldosterone production. Aldosterone is a hormone that helps the body regulate salt, potassium, and fluid levels. Insufficient aldosterone production can lead to serious health issues like dehydration and vomiting due to excessive salt loss, poor feeding and weight gain, hypotension, hyperkalemia.

These symptoms usually appear within the first few weeks of life and can quickly become dangerous if not treated. Given aldosterone's role and the importance of it early diagnosis and treatment are crucial. In the diagnostic approach, genetic testing can be very necessary and is critical for timely management. With fewer than 100 cases reported globally, Aaldosterone synthase deficiency is exceedingly rare, but it must be considered when infants present with failure to thrive, vomiting, and dehydration. Prompt mineralocorticoid therapy, including fludrocortisone, can correct electrolyte imbalances and support growth and development. Fludrocortisone, a synthetic mineralocorticoid, is used in children with ASD to increase sodium retention, promote potassium excretion, and maintain fluid balance. Treating an infant with fludrocortisone requires regular monitoring of electrolytes, blood pressure, and hydration to adjust dosing and avoid complications. Multidisciplinary follow-up is necessary to ensure normal growth and development of the child. Long-

term monitoring is crucial to ensure continued stability and to prevent complications such as hypertension and hyperkalemia [2-10].

Conclusion

Aldosterone Synthase Deficiency is a rare but potentially life-threatening condition that should be considered when diagnosing infants with electrolyte disturbances. This case highlights the importance of genetic testing in confirming the diagnosis and initiating appropriate treatment. With early intervention and long-term management, affected children can lead healthy, normal lives.

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