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Case Report

Paediatrics Section

Congenital Adrenal Hyperplasia Presenting as Life Threatening Hyponatremic Dehydration: A Tale of Missed Diagnosis

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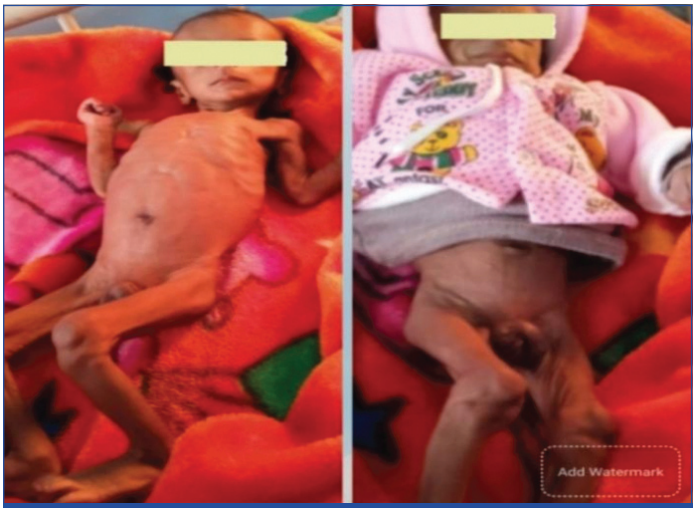
ABSTRACT

Congenital Adrenal Hyperplasia (CAH) is a group of autosomal recessive disorders that occur due to defects in steroid synthesis. It is characterised by a deficiency of adrenocortical hormones and an excess of steroid precursors. A deficiency of 21-hydroxylase is the most common type, constituting 90% of the cases. The authors hereby, report a case of a one-month-old baby who presented to the Paediatric Emergency Department with typical features of the salt-wasting form of CAH. The diagnosis was confirmed with elevated levels of 17-hydroxyprogesterone and a Cytochrome P450 Family 21 Subfamily A Member 2 (CYP21A2) gene mutation. The child was managed with hydrocortisone, fludrocortisone and salt supplementation, along with symptomatic and supportive care. The child is still under regular follow-up and is doing well.

Keywords: Autosomal recessive disorder, 21-hydroxylase, 17-hydroxyprogesterone

CASE REPORT

A one-month-old male baby presented to Paediatric Emergency services with complaints of progressive weight loss, multiple episodes of vomiting that were non projectile and non bilious and fever for the past two days. He was born at 38 weeks of gestation via elective caesarean section, with a birth weight of 3 kg. The baby cried immediately after birth and was started on exclusive breastfeeding, being discharged on day three of life. The family history revealed similar complaints in an elder sibling who expired at the age of 1.5 months. Upon examination, the patient was emaciated and exhibited signs of severe dehydration. There was generalised hyperpigmentation, particularly in the genitalia [Table/Fig-1].



[Table/Fig-1]: One-month-old male with Congenital Adrenal Hyperplasia (CAH) showing generalised hyperpigmentation moreso in genitalia.

His weight was 2.2 kg, indicating a loss of 800 grams since birth. He was febrile (Temperature: 100.6°F) and his vitals showed a heart rate of 138 beats per minute, a respiratory rate of 42 breaths per minute and an SpO_2 of 90% on room air. Systemic examination revealed no significant abnormalities.

Investigations conducted on day 1 of admission showed a negative sepsis screen along with dyselectrolytemia. His blood urea was 48 mg/dL, serum creatinine was 0.5 mg/dL, serum sodium was 112.7 mEq/L and serum potassium was 6.3 mEq/L. His random blood sugar was 38 mg/dL. Blood gas analysis indicated a pH of 7.281, partial Pressure of Carbon Dioxide (PCO_2) of 28.4, Bicarbonate (HCO_3) of 11.6, with a base deficit of -13.7. Repeat investigations showed persistent hyponatremia and hyperkalemia [Table/Fig-2]. Due to a high suspicion of CAH, 17-hydroxyprogesterone levels were sent on day 7 of admission, which returned positive (>200 ng/mL). Genetic testing conducted at a later date (due to financial constraints) confirmed the diagnosis of CAH with a positive result for the CYP21A2 gene.

Laboratory investigations	Day 1	Day 2	Day 3	Day 5	Day 10 (Post-treatment)	Day 12 (Post-treatment)
PH	7.281	7.366	7.418	7.467	7.401	7.420
PCO_2	28.4	34.7	24.4	28.4	34.3	35.8
HCO_3	11.6	20.1	24.3	23.4	22.1	22.3
Base	-13.7	-5.5	0.5	-1.2	-2.6	-2.0
Na^+	112.7	115.2	128.8	124.7	133	137
K^+	6.33	5.61	5.42	5.81	4.48	4.30

[Table/Fig-2]: Trend of electrolytes from day of admission till discharge.

Initially, the patient was managed with intravenous fluids, including dehydration correction, salbutamol nebulisation and intravenous antibiotics. After confirmation of the diagnosis, the patient was started on hydrocortisone (15 mg/m^2/day) and fludrocortisone (100 mcg/day). Salt supplementation (2 grams/day mixed in expressed breast milk) was added later after consultation with a paediatric endocrinologist. The parents were counselled regarding dose modification during intercurrent illnesses and were advised to double the dose of hydrocortisone in case of febrile illness. They were also informed of the need for immediate follow-up in emergencies if danger signs appeared. The infant improved remarkably following the initiation of treatment and has consistently gained weight according to his age without signs of steroid toxicity. A repeat 17-hydroxyprogesterone (17-OHP) test conducted after three months yielded a result of 40 ng/mL. Follow-up at one year of age indicated an appropriate weight gain of 9.8 kg and age-appropriate developmental milestones [Table/Fig-3]. Parental consent was obtained for publication purposes, as the patient is a minor.

[Table/Fig-3]: Follow-up at one year of age shows appropriate weight gain of 9.8 kg and age appropriate developmental milestones.

A comparative analysis of studies published in the past alongside the present case report is presented in [Table/Fig-4] [10,11]. The patient was managed with hydrocortisone, fludrocortisone and salt supplementation, along with supportive care [12]. The present case responded favourably to the recommended treatment. The patient continues to have regular follow-ups and is doing well.

CONCLUSION(S)

The present case highlights that 21-hydroxylase deficiency should be considered in all infants with failure to thrive, hyponatremia, hyperkalemia and/or ambiguous genitalia. A raised 17-hydroxyprogesterone level is diagnostic of 21-hydroxylase deficiency. Salt supplementation is essential for all infants with the salt-wasting form of 21-hydroxylase deficiency. The glucocorticoid dose should be increased during periods of stress and patients should be closely monitored for common side-effects, including hypertension, throughout their treatment.

S. No.	Case report	Year	Symptom	Investigation	Treatment	Recovery
1.	Twayana AR et al., [10]	2022	Vomiting and seizure like activity	Hyponatremia, hypoglycemia, hyperkalemia with raised 17-hydroxyprogesterone levels. Genetics test (CYP21A2) not done due to financial constraint	Hydrocortisone, Fludrocortisone and salt supplementation	Yes
2.	Canlas JF and Ponmani C [11]	2019	Poor feeding, lethargy and life threatening arrhythmia	Metabolic acidosis, hyponatremia, hyperkalemia, CYP21A2 (+)	Hydrocortisone, Fludrocortisone and salt supplementation	Yes
3.	Present case report	2024	Progressive weight loss, vomiting with severe dehydration and hyperpigmentation over genitalia	Hyponatremia, hypoglycemia, hyperkalemia with raised 17-hydroxyprogesterone levels (>200 ng/mL). Genetics test (CYP21A2) positive	Hydrocortisone, Fludrocortisone and salt supplementation	Yes

[Table/Fig-4]: Comparative analysis of similar cases [10,11].

DISCUSSION

The CAH is an autosomal recessive disorder that is present at birth, characterised by hyperplasia of the adrenal glands [1]. In most cases, there is a deficiency of cortisol, which triggers the production of Adrenocorticotropic Hormone (ACTH), resulting in hyperplasia of the adrenal glands [2]. A deficiency in 21-hydroxylase (21-OHD) is the most common type of CAH, accounting for 90% of the cases [3]. CAH is divided into two categories: classical (which includes salt-wasting and simple virilising types) and non classical [4]. The incidence of classical CAH is estimated to be 1:10000 to 1:20000 individuals [5].

Common clinical features include failure to thrive, vomiting, lethargy, abnormal genital appearance and shock [6]. Females with classical CAH present with ambiguous genitalia due to exposure to excess androgens prenatally [7]. Males typically have normal genitalia but may present with signs of dehydration, dyselectrolytemia and shock [8]. In the index case, the patient presented with progressive weight loss, vomiting, lethargy and increased pigmentation around the genitalia. CAH is primarily diagnosed based on typical clinical features, dyselectrolytemia and hormonal and genetic testing [9]. The index case exhibited typical clinical features and electrolyte abnormalities (hyponatremia, hyperkalemia and hypoglycemia), elevated 17-OHP levels and a positive CYP21A2 gene test, confirming the diagnosis.

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