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Salt-Wasting Form of Congenital Adrenal Hyperplasia: A Case Report and Literature Review

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ABSTRACT

Congenital adrenal hyperplasia is a set of autosomal recessive disorders characterized by enzyme abnormalities in the adrenal steroid genesis pathway, which cause impaired cortisol biosynthesis. Glucocorticoid, mineralocorticoid, and sex steroid production can all be altered in individuals, necessitating hormone replacement therapy. The symptoms might range from prenatal salt loss and abnormal genitalia to adult hirsutism and irregular menses. Screening for classic (severe) 21-hydroxylase deficiency, the most common type of congenital adrenal hyperplasia, is usually done in neonates with elevated 17-hydroxyprogesterone concentrations, but cosyntropin stimulation testing may be required to confirm the diagnosis or identify non-classic (milder) subtypes. Herein we report a case of congenital adrenal hyperplasia in a 7-year-old girl.

Keywords: Congenital adrenal hyperplasia (CAH), Cosyntropin, 21-hydroxylase deficiency (21-OHD)

INTRODUCTION

CAH is a set of autosomal recessives, monogenic illnesses in which cortisol production is reduced [1]. In most studies, the worldwide incidence varies from 1:14,000 to 1:18,000 births, based on newborn screening and national case registries [2]. CAH is caused in 95% of instances by mutations in the CYP21A2 gene, which codes for the adrenal steroid 21-hydroxylase [2]. The next common type is 11-hydroxylase (5%). Both are caused by enzymes that are only produced in the adrenal glands [3]. The salt loosing type is regarded the classic and most severe form of 21 hydroxylase deficiency, in which cortisol production is virtually absent and the aldosterone production is diminished leading to salt wasting, failure to thrive, and potentially fatal hypovolemia and shock [1]. Non-classic 21-hydroxylase deficiency refers to a situation in which partial 21-hydroxylase deficiency allows for a later onset, less intense hyperandrogenism, and milder clinical signs, if any at all [3] Serum 17-hydroxyprogesterone (17OHP) tests, most often with cosyntropin stimulation, remain the gold standard for confirming a diagnosis of CAH. In severely affected neonates, baseline values are >300 nmol/l (1000 ng/ml) compared to 3-6 nmol/l (10-20 ng/ml) in normal newborns. The availability of commercially available serum 21-deoxycortisol assays may make CAH carriers easier to identify. Retaining CAH patients after they've graduate from pediatric treatment is a key goal, and better mental health monitoring of those patients is also important [2]. In newborn females with classic or severe virilizing CAH, aberrant development of the external genitalia with varying degrees of virilization is a key characteristic. Missed diagnoses of salt-losing CAH are linked to an increased risk of early infant morbidity and mortality; therefore, newborn screening can help prevent these consequences [2]. Treatment is based on the principle of glucocorticoid and mineralocorticoid replacement in classic forms, as well as psychological support. The external genitalia of the majority of female patients will also require surgery [3]. In infants and children, hydrocortisone is the chosen glucocorticoid replacement and salt supplementation is indicated [3].

CASE REPORT

A 3 month-year-old girl was brought to the emergency due to altered mental status. The child had 5 episodes of vomiting and developed seizure-like activity in the form of rolling eyes upwards, jerky movement of left hand and fixed

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gaze lasting for 30 sec. Afterwards the baby became floppy, unresponsive and hence was rushed to the Emergency Room (ER) where her blood glucose level was undetectable. Further investigation showed hyponatremia, hypokalemia, hypoglycemia with raised renin activity, elevated adrenocorticotropic hormone (ACTH), low Dehydroepiandrosterone sulfate (DHEAS), low aldosterone and low cortisol but normal 17 hydroxy progesterone level. Ultrasound of the abdomen showed normal kidneys with normal corticomedullary demarcation and her brain scan was also normal. A diagnosis of congenital adrenal insufficiency was made and the patient was started on fludrocortisone and hydrocortisone.

DISCUSSION

The most common underlying problem in patients with CAH is 21-hydroxylase deficiency which is due to inadequate cortisol synthesis [1]. Insufficient cortisol synthesis causes the hypothalamus and pituitary to produce more corticotrophin releasing hormone (CRH) and ACTH. Adrenal glands become hyperplastic and begin to secrete excessive sex hormone precursors rather than cortisol as they do not require 21-hydroxylation for synthesis. These hormones are then converted to active androgens, such as testosterone and dihydrotestosterone, rather than estrogens, such as estrone and estradiol. The end result is prenatal virilization of girls and rapid somatic growth with early epiphyseal fusion in both sexes [2].

The baby we are reporting presented to the emergency with a typical presentation of salt losing crisis and later was confirmed to have congenital adrenal hyperplasia by laboratory variables showing hyponatremia, hypokalemia, hypoglycemia with raised renin activity. About three-quarters of patients, known as “salt wasters”, are unable to produce enough aldosterone to maintain sodium homeostasis. This puts them at risk of developing possibly fatal hyponatremic dehydration on a regular basis [2]. The disorder can be seen as a continuum from salt wasting to mild forms, but is divided into two categories for convenience: classical (C 21-OHD) approximately 67 % (“salt-losing”, “severe”, “ex-congenital”) and non-classical (NC 21-OHD) approximately 33 % (“non-salt-losing” or “simple-virilizing”, less severe, formerly known as late onset or cryptic) according to the degree of aldosterone deficiency [3,4]. Non-classic 21-hydroxylase deficiency (NC 21-OHD) with partial 21-hydroxylation deficiencies results in less significant hyper androgenemia and milder symptoms while classic results in severe symptoms [4].

CYP21, found on chromosome 6p, near the human leukocyte antigen (HLA) gene cluster is the gene for adrenal 21-hydroxylase. Specific mutations may be linked to a degree of enzymatic dysfunction and the clinical manifestation of 21-hydroxylase insufficiency (21-OHD) [5,6]. Patients with NC 21-OHD have minor mutations on both alleles, as well as one severe or mild mutation in the 21-OH gene (compound heterozygote) [3]. A retrospective cohort study conducted by Gidlöf [7] in Sweden found CYP21A2 genotype (conferring deficiency of 21-hydroxylase) in 81% of the patient and a slow rise in trend of salt-wasting form of congenital adrenal hyperplasia increased in both sexes reflecting improved diagnostic and treatment modalities. The baby we are reporting was diagnosed solely based on laboratory values and clinical findings. A study to perform CYP21A2 mutation tests combined with screening would mean physicians no longer need to wait for electrolyte problems in a newborn baby to determine the severity of their ailment sparing negative effect on further brain development. However, genotyping was not performed owing to adding financial burden to the patient.

The diagnosis of congenital adrenal hyperplasia can be done prenatally with amniocentesis or chorionic villus sampling and treatment involves dexamethasone administered at or before 10 weeks of gestation [8,9]. A study conducted by Carlson et al found that prenatal diagnosis and therapy of 21-OHD is safe and effective in lowering or eliminating virilization in the affected female, sparing the newborn female the repercussions of genital ambiguity, sex mis assignment, and gender confusion [10]. The baby is currently receiving dexamethasone. She is gaining adequate weight, reaching all developmental milestones and doing well in school.

CONCLUSION

Congenital adrenal hyperplasia is an uncommon illness that can be managed with dexamethasone, if detected and treated early can spare the children from the negative consequences of genital ambiguity, sex misassignment, and gender confusion.

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