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A SHORT REVIEW ON CONGENITAL ADRENAL HYPERPLASIA

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Abstract

Congenital adrenal hyperplasia describes a group of hereditary genetic disorders affecting adrenal glands. The two main types of CAH are classic and non-classic is diagnosed at birth and non classic is typically diagnosed during adolescence. Symptoms are life threatening associated with CAH , may include vomiting, diarrhoea, hypotension and hypoglycaemia .both males and females may have infertility or adrenal crisis with CAH. Treatment goals are to reduce excessive hormones and replace deficient ones.

***Keywords*:** Congenital adrenal hyperplasia, hereditary genetic disorders, adrenal glands.

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Introduction

Group of autosomal recessive disorders characterised by impaired cortisol synthesis. The most common types are 21-hydroxylase deficiency (21-OHD) due to mutations in the 21-hydroxylase (*CYP21A2*) gene, 3β-hydroxysteroid dehydrogenase and 11β-hydroxylase deficiencies associated with mutations in the 3β-hydroxysteroid dehydrogenase (*HSD3B2*) and 11β-hydroxylase (*CYP11B1*) genes. These specific enzyme deficiencies are aetiological factors. 21-hydroxylase deficiency (21-OHD) is the most common type among the three. Depending on the severity of the enzyme deficiency, 21OHD is defined as classic (severe form) or nonclassic (mild form).Approximately 75% of patients who have the classic form also have salt wasting due to inadequate aldosterone production, further subdividing the classification into classic simple virilizing and classic salt-wasting forms.

The earliest description of presumed classic 21-OHD CAH dates to 1865, when an Italian pathologist, Luigi De Crecchio, described the autopsy of a man with a 10-cm phallus, hypospadias, empty scrotum, vagina, uterus, fallopian tubes, ovaries and enlarged adrenals [1].

Epidemiology

Congenital Adrenal Hyperplasia (CAH) is an autosomal recessive disorder with an incidence ranging from 1:10,000 to 1:20,000 births [2-9].The screen positive rate of CAH among a cohort of 104,066 babies screened at birth in India was 1 in 5762 as per a recent report [10]. The overall incidence of CAH due to 21OHD is approximately 1 in 16,000, with variations seen in different ethnic and racial groups.CAH resulting from 11β-hydroxylase deficiency (11β-OHD) is the second most common cause of CAH, accounting for 5-8% of all cases [11]. In Moroccan Jews, for example, the disease incidence was initially estimated to be 1 in 5,000 live births [12]. In the Ashkenazi Jewish population, 1 in 3 is carriers of the allele, and 1 in 27 is affected with the disorder.

Pathophysiology

Adrenal steroidogenesis occurs in three major pathways:
1) glucocorticoids
2)mineralocorticoids
3) Sex steroids.

The adrenal gland architecture suggests that the adrenal acts as three separate glands: zonaglomerulosa, zona fasciculate, zonareticularis (3). The hypothalamic-pituitary-adrenal feedback system is mediated through the circulating level of plasma cortisol by negative feedback of cortisol on CRF and ACTH secretion. Therefore, any CAH condition that results in a decrease in cortisol secretion leads to increased ACTH production, which in turn stimulates (4) excessive synthesis of adrenal products in those pathways unimpaired by the enzyme deficiency and

(5) a build-up of precursor molecules in pathways blocked by the enzyme deficiency.

In first step of adrenal steroidogenesis, cholesterol enters mitochondria via a carrier protein called steroidogenic acute regulatory protein. ACTH stimulates cholesterol cleavage, the first and rate limiting step of adrenal steroidogenesis. The five enzyme required for cortisol production are cholesterol side chain cleavage enzyme, 17α-hydroxylase, 3β-hydroxysteroid dehydrogenase (3βHSD2), 21-hydroxylase, and 11β-hydroxylase.

Signs and symptoms

- Excessive androgen production.
- Hyperpigmentation of skin creases and genitalia may be early signs of adrenal insufficiency
- hyperandrogenism in childhood include early appearance of axillary and pubic hair, acne, and adult body odour.
- tall and muscular features in early childhood.
- Decreased activity/fatigue
- Altered sensorium/unresponsiveness
- Poor feeding/weak suck
- Dry mucous membranes
- Abdominal pain
- Vomiting
- Hyponatremia
- Hyperkalemia
- Hypoglycemia
- Virilisation , an elongated clitoris with a phallic-like structure is seen [2]
- Metabolic acidosis.
- Hypothermia.
- Hypotension.
- Dehydration.
- Lack of weight gain

DIAGNOSIS

Hormonal Diagnosis

Potential diagnosis of CAH must be suspected in infants born with atypical genitalia. The diagnosis should rely on genetic sex, hormonal determination of specific deficient enzyme, patients potential for future sexual activity and fertility. Physical characteristics of CAH in newborns. biochemical evaluation of hormones can be done. hormonal diagnosis is also done by corticotropin stimulation test [6].

Prenatal diagnosis of 21OHD-

In 1965, Jeffcoate et al first reported a successful prenatal diagnosis of 21OHD, based on elevated levels of 17-ketosteroids and pregnanetriol in the amniotic fluid [7]. Hormonal diagnosis is used rarely.

Non-invasive prenatal diagnosis of CAH-

Virilization of the genitalia in a female fetus affected with CAH owing to 21OHD and 11B-OHD can be treated prenatally with dexamethasone administered to the mother. Treatment with dexamethasone must begin before the 9th week of gestation, yet chorionic villous sampling can only be done at the 9-11th week, with karyotype and DNA results available 2-3 weeks later. Non-invasive prenatal diagnosis would eliminate unnecessary treatment and invasive procedures such as CVS and amniocentesis.

Preimplantation diagnosis

Preimplantation genetic diagnosis (PGD) identifies genetic abnormalities in preimplantation embryos prior to embryo transfer, so only unaffected embryos established from IVF are transferred. PGD is being used for a growing number of genetic diseases [8].

Prenatal diagnosis and treatment of 11beta- OHD CAH-

The ideal method to diagnose 11β-OHD CAH in the fetus is by Advances in genotyping of the *CYP11B1* gene have made molecular genetic studies of fetal DNA extracted from maternal blood.

Treatment

The goal of therapy in CAH is to both correct the deficiency in cortisol secretion and to suppress ACTH overproduction. hydrocortisone (or its equivalent) for the treatment of classical 21-OHD form of CAH is about 10-15 mg/m^2/day divided into 2 or 3 doses per day and for non-classical 21-OHD 5-8 mg/m^2/day divided into 2 or 3 doses per day. A small dose of dexamethasone at bedtime (0.25 to 0.5 mg) is usually adequate for androgen suppression in non-classical adult patients. salt-retaining 9α-fludrocortisone acetate should be given to Patients with salt wasting CAH dose of 0.1mg daily. Growth hormone therapy, in conjunction with a GnRH analogue, has been shown to be effective in improving final adult height [13].

In adrenal crisis an immediate bolus of hydrocortisone 100mg/m2/day given is recommended in IV or IM given In continues infusion or divided at least every 6 hours. Hypoglycemia may require dextrose bolus and an initial bolus of 0.5-1 gram/kg of dextrose can be given intravenously at 2-3 ml per minute. cardiac monitoring should be done to monitor for EKG changes in hyperkalemia.

Management of adolescents with congenital adrenal hyperplasia

Management of adolescents with congenital adrenal hyperplasia (CAH) is especially challenging because changes in the hormones during puberty can lead to inadequate suppression of adrenal androgens, psychosocial issues often affect adherence to medical therapy, and sexual function plays a major part in adolescence and young adulthood [14]. Common issues for these patients include urinary incontinence, vaginal stenosis, clitoral pain, and cosmetic concerns; for males with classic congenital adrenal hyperplasia, common issues include testicular adrenal rest tumours.

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