CASE REPORT

CONGENITAL ADRENAL HYPERPLASIA (CAH): PRESENTATION WITH AMBIGUOUS GENITALIA

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INTRODUCTION

Congenital adrenal hyperplasia (CAH) is a disorder of steroid genesis due to deficiency of enzymatic activities necessary for its synthesis. It is a recessively inherited disorder and has an average incidence of 1:5000, the most common of these is 21-hydroxylase deficiency that accounts for 95% of involved cases[1]. Females with classical 21-hydroxylase deficiency, being exposed to excess androgens prenatally, are born with virilized external genitalia[2,3]. By associating the genotype with phenotype will enable the clinicians to predict the clinical outcome in affected patients.

CASE REPORT

A 5-day-old child was brought to out patient department of Paediatrics, Military Hospital (MH), Rawalpindi, Pakistan with ambiguous genitalia since birth. Her parents were consanguineous. There was history of taking contraceptive pills by the mother during first trimester due to ignorance about her pregnancy. The mother also gave the history of death of a daughter at the age of 3 months who had similar complaints. Rest of the history and general physical examination were unremarkable. The genital examination revealed hyperpigmented genital fold, prominent phallus and single uro-genital opening. The gonads were not palpable; rest of the systemic examination did not reveal any abnormality. Radiologically, bone age was normal. Ultrasonographic study showed female internal genital tract and gonads. The patient karyotype was 46XX. The laboratory investigations revealed hyperkalemia, hyponatremia with markedly high 17 hydroxyprogesterone (17-OHP), ehydroepiand-rostenedione sulphate (DHEA – S) and low Serum Cortisol. These findings were consistent with salt losing form of CAH.

The patient was prescribed tab Fludrocortisone 0.05 mg BD and tab Hydrocortisone 20 mg/m2/day. The parents were informed about the different treatment modalities and were counseled regarding curative surgical procedures. She was assigned female gender. Her vaginoplasty was carried out in June 2002. No issue was reported by the parents following the reconstructive surgery. She was discharged with advice to continue hormone replacement treatment and regular visits in child OPD, Military hospital Rawalpindi.

After treatment, serum DHEA-S levels were within reference range. There was improvement in serum: sodium and potassium, urinary: sodium and potassium. However, the level of serum 17 Hydroxy progesterone was still high mainly due to non compliance of the patient. No issue regarding the complications of medical treatment reported. The patient is currently on tab hydrocortisone 20 mg/m2/day and tab fludrocortisone 0.1 mg OD and is regularly being followed up in Child OPD Military Hospital Rwp.

DISCUSSION

Congenital adrenal hyperplasia (CAH) is a very rare disease. Patients may either present with ambiguous genitalia at birth or have late onset features[4]. 21- hydroxylase deficiency is the most common cause of CAH. The gene responsible for this disorder is located at the short arm of chromosome 6 (6p21.3)[5]. In Pakistani population, the prevalence of CAH is expected to be high due to the high frequency of parental consanguinity among the population[3]. In our population, the gene(s) frequency for CAH is probably common[3].

CAH is presented in 3 forms. Classical salt-losing form, classical non-salt losing form and non-classical late-onset form. In first two

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Table-1: Laboratory investigations results

Test	Result	Reference range
Blood Counts:		
Haemoglobin	15.1	12-15 g/dL
Total leukocyte count	5.2	4.0-10.0 x 10^9 /L
Neutrophils	52%	40-80%
Lymphocytes	40%	20-40 %
Monocytes	2%	2-10 %
Eosinophils	3%	1-6%
MCV	78.3	76-96 fL
Platelets	139	150-400 x 10^9 /L
ESR	6	0 – 15 mm at 1st hr
Serum Cortisol	2.5	5-25 µg/dL
Serum 17 OHP	> 36.0	0.1-2.7 nmol/l
Serum DHEA-S	490	45 – 430 µg/dl
Liver function tests		
Serum total Bilirubin	3.1	0- 0.11 µmol/L
Serum ALT	31	0-35 U/l
Serum ALP	319	0-645 U/l
Plasma Glucose (Random)	3.5	3.3-11.1 mmol/l
Serum Urea	3.2	1.8- 6.4 mmol/l
Serum Creatinine	21	18 - 46 µmol/l
Serum Sodium	128	136 – 149 mmol/l
Serum Potassium	5.8	3.5 – 5.0 mmol/l
Serum Calcium (total)	2.50	2.15 – 2.55 mmol/l

ESR: Erythrocyte sedimentation rate; 17 OHP: 17 hydroxy progesterone; DHEA-S: Dehydroepiandrostenedione sulphate

Table 2: Laboratory investigations: Follow up (Sep – Dec 2008)

Test	Result	Reference range
Serum 17 OHP	> 36.0	0.1 – 2.7 nmol/L
Serum DHEA-S	56.1	45-430 µg/dL
Serum Sodium	137	136 – 149 mmol/L
Serum Potassium	3.7	3.5 – 5.0 mmol/L
Urinary Sodium	43	40-220 mmol/24 hr
Urinary Potassium	26	25-125 mmol/24 hr
Serum Prolactin	257	40 – 530 miU/L
Plasma Glucose (Random)	4.0	3.3-11.1mmol/L

t with ambiguous genitalia and marked virilization of the newborn with female karyotype often causing uncertainty in assignment of sex[8]. Late-onset CAH presents as precocious puberty in later childhood. This form may also become evident at puberty or adulthood with signs of androgen excess conditions, boys may present with precocious puberty and the girls with ambiguous genitalia[6]. The non-classical late onset type usually presents with hirsutism, clitoromegaly and amenorrhea[6]. Other clinical presentations include vomiting, shock and failure to thrive[7].. The basis of diagnosis is elevated serum 17- Hydroxy progesterone level. In salt-losing type, hyperkalemia and hyponatremia are usually common[6].

A milder simple virilizing form may presen

including acne, advanced bone age, tall stature, hirsutism, amenorrhea or infertility[8,9]. Studies have shown variable incidence of non-classic 21-OH deficiency in children presenting with an early onset of puberty as well as with hirsutism in adult females[10]. Majority of children having male karyotype present with salt wasting early on and precocious puberty at later ages. Patients having female karyotype mostly present early with either or both of salt wasting and simple virilizing form of CAH[3].

The standard therapy for CAH is steroids replacement (tab: hydrocortisone, prednisone or dexamethasone), fludrocortisone (given in salt losing type), and clitoroplasty and vaginoplasty in virilized females, if indicated[6].. Neonatal screening or prenatal diagnosis and treatment are advisable to the high-risk groups[3]. Such neonates should be investigated by serum 17-OHP analysis some days postnatally to rule out the 25% risk for CAH[3]. The main aim of treatment is to correct the visible anatomical abnormalities, creating an appearance coinciding the gender and making an individual to lead a normal life, including sexual function and if possible, reproduction.

Clitoral reduction is a procedure which often leaves the glans clitoral keeping the tactile sensation intact[11]. The technique of cliteroplasty is modified depending upon the size of phallus. Good cosmetic and tactile results may be achieved by selective lateral clitoral and corpora cavernosa excisions, preserving the glans and neurovascular bundle[12].

In patients with CAH, depression and stress are often reported, particularly weight gain is associated with steroid replacement

therapy[13]. The management is thus based on multidisciplinary care with endocrinology, gynaecology and psychology expert teams[4].

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