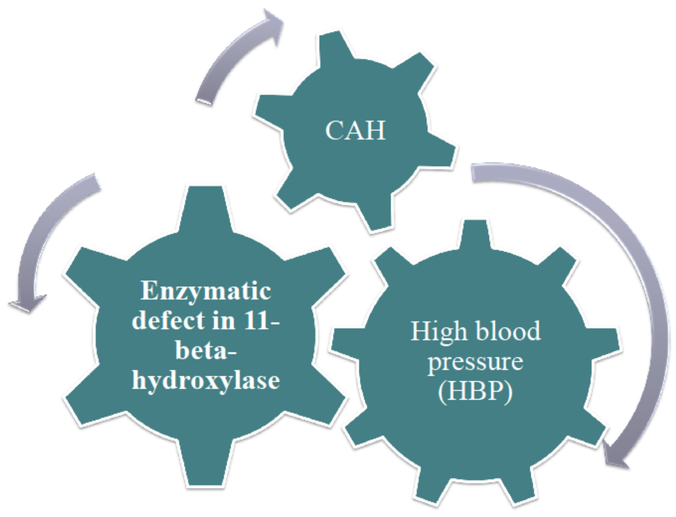
Severe High Blood Pressure with Renal Failure in a Neglected Case of 11β-Hydroxylase Deficient Congenital Adrenal Hyperplasia

Alina Daniela Belceanu[a], Mihaela Munteanu[b], Mariana Florea[c], Maria-Christina Ungureanu[a], George Zmau[a], Mirela Puiu[a], Ioana Armasu[a], Voichita Mogos[a] , Carmen Vulpoi[a]

[a]Endocrinology Department, Iasi, Romania; [b]Endocrinology Department, Bacau, Romania; [c]Cardiology Department, Iasi, Romania

Introduction

- **Congenital adrenal hyperplasia (CAH)**
  - a group of autosomal recessive disorders
  - characterized by impaired cortisol synthesis
- **11β-Hydroxylase Deficient Congenital Adrenal Hyperplasia**
  - an **enzymatic defect in 11-beta-hydroxylase**
  - the second most common variant of CAH (1)
  - accounts for approximately 5–8% of cases (1)
  - patients present with features of androgen excess (2)
  - approximately two thirds of patients also have high blood pressure (HBP), which is initially responsive to glucocorticoid replacement, but may become a chronic condition subsequently requiring standard antihypertensive therapy. (2)



11β-Hydroxylase Deficient CAH

- The management of CAH involves suppression of adrenal androgen production, in addition to treatment of adrenal insufficiency. (3)
- About 2/3 of patients with 11-beta-hydroxylase deficiency have early onset hypertension. (4)
- HBP is generally mild to moderate
  - 1/3 of cases, it has the greatest potential for long-term morbidity : left ventricular hypertrophy, retinopathy, and macrovascular events.(4)

Case Report

- **Patient** - A.P., female, 17 years

- **Medical history**:
  - the first child of a consanguineous couple
  - Family history of CAH (2 third-degree relatives)
  - diagnosed with CAH in the neonatal period
    - ambiguous genitalia : clitoral and vaginal reconstruction at the age of 2 years.
    - female genetic sex
    - Barr chromatin 17% positive

Daily treatment with glucocorticoids was initiated, but the medical follow-up and self-administered therapy were extremely irregular.

Several hospital admissions due to acute adrenal insufficiency

reported episode in April 2014, precipitated by an infectious disease,

she presented with
- severe hypertension
- hyperkalemia
- renal failure

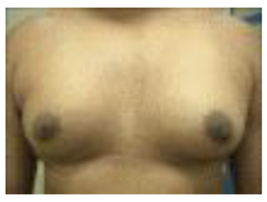


Fig.1: Breast development: Tanner stage III

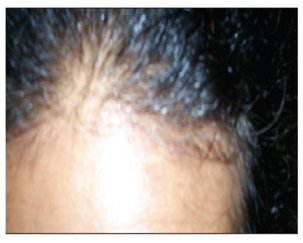


Fig.2: Male pattern baldness

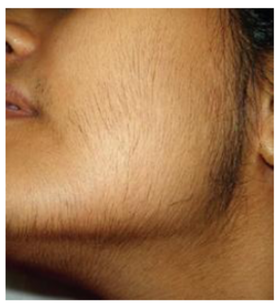


Fig.3: Hirsutism

Endocrinology department – further investigations
- H=142,5 cm (-3,7 SD), G= 40 kg, BMI=20 kg/m²
- Breast development: Tanner stage III (fig.1)
- Male pattern baldness was present (fig.2)
- Hirsutism (fig.3) was evaluated based on Ferriman-Gallwey score (result = 15)
- Deepening of the voice
- Amenorrhea
- Severe hypertension (maximum value 220/140 mmHg)

Complete baseline endocrine evaluation (before beginning steroid replacement) revealed **absolute cortisol deficiency, with elevated ACTH**

- **Laboratory findings and evolution:**

Date	ACTH (N:0-46)	Cortizol (8 AM: N:5-25)	17-OH-Progesteron (N:2-10)	DHEAS (N:0,95-11,67ug/dl)	Treatment
14/04/2014	>1250 pg/ml	5,56 µg/dl	27,60 ng/ml	16,20 umol/l	Prednison 15 mg/day Astonin 0,1 mg /day
02/07/2014	15,6 pg/ml	31,3 µg/dl	-	2,28 ug/dl	Prednison 15 mg/day Astonin 0,1 mg x2 /week
20/01/2015	16,7 pg/ml	5,22 µg/l	-	6,4 ug/dl	Prednison 15 mg/day Astonin 0,1 mg x3 /week

Inadequate stress adjustment of glucocorticoid dosage during acute infection

Irregular medical compliance

Poor medical fallow-up

Irreversible consequences:
- severe hypertension
- left ventricular hypertrophy
- stage IV renal failure.

Discussions

- The prevalence of cardiovascular risk factors in congenital adrenal hyperplasia (CAH) varies widely. (1)
- The association of CAH with hypertension was first noted in the 1950s. The hypertension is initially responsive to glucocorticoid replacement, but it may become a chronic condition subsequently requiring standard antihypertensive therapy. (2)
- The exact cause of the hypertension is unclear and is presumed to be due to excessive secretion of DOC (3)
- Possibly, the 18-hydroxy and the 19-nor metabolites of DOC, which are mineralocorticoids, may play an additional role.(3)

Conclusions

- Care of adolescents with congenital adrenal hyperplasia has unique challenges. (4)
- Children with rare congenital diseases are now living full, productive lives and the issue of effectively transitioning these children to adulthood is a major public health problem.
- This case illustrates that CAH due to 11 beta hydroxylase deficiency can progress to severe acute and chronic complications.
- While early treatment to prevent hypertension is mandatory in patients with CAH, once renal failure occurs, renal transplantation may be the best choice of treatment.
- Early recognition and compliance to treatment can prevent morbidity and mortality.

References:

(1) Reisch N, Högler W, Parajes S, Rose IT, Dhir V, Götzinger J, et al. A diagnosis not to be missed: Non-classic steroid 11ß-hydroxylase deficiency presenting with premature adrenarche and hirsutism. *J Clin Endocrinol Metab*. 2013 . (2) Davies E, Mackenzie SM, Freel EM, et al. Altered corticosteroid biosynthesis in essential hypertension: a digenic phenomenon. *Mol Cell Endocrinol*. 2008 .(3) White PC. Steroid 11 beta-hydroxylase deficiency and related disorders. *Endocrinol Metab Clin North Am*. 2001 Mar. 30(1):61-79. (4) DP Merke, DP Poppas. Management of adolescents with congenital adrenal hyperplasia. *Lancet Diabetes Endocrinol*. 2013; 1(4): 341–352.

ESPE 2015 604--P3
Adrenal
BELCEANU ALINA
DOI: 10.3252/pso.eu.54espe.2015
Poster presented at: 54th Annual Meeting 1-3 October ESPE 2015 BARCELONA European Society for Paediatric Endocrinology
PosterSessionOnline.com