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Non-classical Congenital Adrenal Hyperplasia: the challenge of an accurate diagnosis

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1 Abstract

We present the case of a 24 year-old lady with mild congenital adrenal hyperplasia (CAH) who presented with infertility, hirsutism and clitoromegaly and increased 17 alpha hydroxy progesterone serum levels. She was treated with hydrocortisone, cyproterone acetate and estradiol valerate. We present this case in view of its complexity in making an accurate diagnosis, its rarity, low level of suspicion and hospital diagnosis due to stigmatization and lack of education/counseling concerning such medical pathologies.

2 Introduction

Congenital adrenal hyperplasia [CAH] is an endocrine disorder comprising of a group of inherited autosomal recessive anomalies that cause a deficiency in an adrenal enzyme, resulting in altered cortisol and aldosterone secretion. The loss of negative feedback inhibition by cortisol leads to increased hypothalamic-pituitary-adrenal axis activity and subsequent hyperplasia of the adrenal gland[1]. CAH due to 21-hydroxylase deficiency [21-OHD] is the commonest variant, and accounts for over 95% of all affected cases [1,2]. Non-classical forms of CAH are characterized by milder enzyme deficiency and manifests commonly in adolescence or adulthood. This partial enzyme deficiency of the steroidogenic enzyme 21-hydroxylase produces mild to moderate hyperandrogenemia, hirsutism, polycystic ovaries, oligomenorrhea or amenorrhea, insulin resistance, male

pattern baldness and subfertility[3].

Classic congenital adrenal hyperplasia is generally recognized at birth or in early childhood because of ambiguous genitalia, salt wasting, or early virilization. Non-classic adrenal hyperplasia is generally recognized at or after puberty because of oligomenorrhea or virilizing signs in females[2].

3 Case Report

A 24 year-old single lady presented to the out-patient department of the National Obesity Centre of the Yaoundé Central Hospital on account of amenorrhea. She has never been sick or admitted before and consulted about 4 years prior to this present consultation for the same reason. She was placed on Hydrocortisone 20mg per day which she discontinued 3 months later for lack of finances. It is important to note that during the 3 months of treatment, she had her menses normally.

She reported good health with no history of chronic headaches, galactorrhea or syncope. She has no family history of amenorrhea or other endocrine pathology. There was no menarche and her puberche was around 13 years.

On physical examination, she is well-looking, oriented with an abnormal facial hair distribution. Vital signs included a blood pressure of 114/79 mmHg, pulse rate of 80 beats/minute, respiratory rate of 20 breaths/minute and weight of 80 kg. Her body mass index was 29.1 kilograms/meter square. She also presents with hirsutism, Tanner 2 for the mammary glands, Tanner 5 for the pubic hair distribution, clitoral hypertrophy with a total diameter of 2 cm. The remainder of the physical examination was uneventful.

Laboratory investigations revealed: Hormone profile:- estradiol 215.66 pg/mL, follicle stimulating hormone 2.81 mUI/mL, progesterone 6.88 ng/mL, 17 alpha hydroxyl-progesterone 180.7

ng/mL, testosterone 1.69 ng/mL. Total leukocyte count 7 150/uL (differential count – neutrophils: 48%, eosinophils: 3%, basophils: 0%, lymphocytes: 47%, monocytes: 2%), hemoglobin 13.9 g/dL, platelets 225 000/ul. Blood glucose 80 mg/dL, natremia 146.4 mmol/L, kalemia 3.3 mmol/L, chloremia 112.3 mmol/L, calcemia 98 mg/L, magnesemia 26mg/L, total bilirubin 13.9 mg/L, conjugated bilirubin 5.36 mg/L, non-conjugated bilirubin 8.54 mg/L, aspartate-amino transferase 16 IU/L, alanine-amino transferase 6 IU/L.

Abdominal ultrasound showed a hypotrophic uterus measuring 43 x 27 x 23 (mm) with the endometrium not visible, dystrophic ovaries measuring 41 x 26 x 27 (mm) right and 39 x 21 x 23 (mm) left.

Abdominal CT Scan with injection of contrast medium revealed a bilateral adrenal hypertrophy. The rest of the abdominal organs were morphologically normal.

4 Discussion

CAH usually affects both sexes with equal frequency. However, because accumulated precursor hormones or associated impaired testosterone synthesis impacts sexual differentiation, the phenotypic consequences of mutations or deletions on a particular gene differ between the sexes[4].

Ambiguous genitalia, salt wasting or early virilization generally recognizable at birth or early childhood are indicative of classical congenital adrenal hyperplasia. Non-classical adrenal hyperplasia is generally recognized at or after puberty because of oligomenorrhea or virilizing signs in females. This milder form of enzyme deficiency was termed non-classical 21-hydroxylase deficiency (NC21OH) in 1979 and is diagnosed by serum elevations of 17-alpha hydroxyl-progesterone (17-OHP) and should typically be confirmed with molecular genetic analysis[2]. Women with non-classical CAH usually will present with symptoms of androgen excess, such as hirsutism, temporal baldness, delayed menar-

che, menstrual irregularities, and infertility[5].

After literature review, this case fits best the description of non-classical congenital adrenal hyperplasia based on the clinical presentation and the elevated 17-alpha hydroxyl-progesterone serum level. Molecular diagnosis being absent in our setting is call for a high level of clinical suspicion amongst physicians.

5 Conclusion

Congenital adrenal hyperplasia should be considered in females who present with signs of virilization and infertility in our setting and clinical presentation and hormonal analysis are hallmarks for appropriate diagnosis in resource low settings devoid of molecular analysis.

6 References

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