NON-CLASSICAL CONGENITAL ADRENAL HYPERPLASIA WITH INCIDENTAL ADRENAL ADENOMA: A CASE REPORT

Sadia Salman,[1] Abida Pervaiz,[2] Zahid Jamil[3]

ABSTRACT

A 33 years old female was referred to endocrinology clinic of Jinnah hospital, Lahore for the assessment of hirsutism and secondary amenorrhea. Her Ferriman-Gallwey scale for hirsutism was 29; however, there was no clitoromegaly or genital ambiguity. She had already undergone CECT of adrenals glands by her physician which was suggestive of bilateral adrenal enlargement with small right adrenal tumor. Her 17-hydroxy progesterone levels were raised on ACTH stimulation testing. An initial diagnosis of adrenal hyperlpasia (NCCAH) in association with adrenal incidentiloma was made and patient showed a good response to prednisolone in close follow up.

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Androgen excess underlies as one of the potential pathologies of female infertility in disorders like polycystic ovarian syndrome, Non-classical congenital adrenal hyperplasia (NCCAH), and adrenal and ovarian malignancies. NCCAH is one of the disorders that are characterized by the defect in the enzymatic pathway of various hormones produced in the steroidogenesis pathway. As a result of deficient cortisol production, a rise in CRH (corticotropin releasing hormone) and ACTH (Adrenocorticotropic hormone) levels occur that leads to hyperplasia of adrenal glands.[1] In NCCAH, enzymatic activity of 21 alpha hydroxylase is mildly impaired and it presents at a later stage of life probably near puberty. Females with NCCAH presents with acne, excessive hairs growth and menstrual irregularities. Diagnosis is mainly made by detection raised 17-OH-Progesterone (17OHP) especially in proper clinical context and ACTH stimulation testing.[2] Sometimes raised 17-OH-Progesterone concentration beyond 100nmol/l can be due to adrenal tumors. Patients with 17-OHP have mutations of genes CYP21A2 which can be used to confirm CAH cases in case of intermediate response to ACTH stimulation and tumor morphology.[3] Treatment is individualized patient to patient in the form of anti-androgen or combined hormone replacement therapy along with topical treatments. We report a case of female patient with her informed consent for publication.

1,2. Department of Endocrinology, JHL/Saira Memorial Hospital, Lahore.
3. Department of Medicine, LGH
Correspondence:
Dr. Zahid Jamil, *Assistant Professor, Department of Community Medicine, AMC/LGH. Email: hudaarshad@yahoo.com*

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CASE PRESENTATION

A 33 years old female patient presented to Endocrinology clinic, Jinnah hospital, Lahore with complaints of excessive hair throughout her body along with secondary amenorrhea.

She achieved menarche at the age of 15 years followed by monthly withdrawl bleeding for 5 years with the use of OCPs(oral contraceptive pills). Later due to her own wishes, she discontinued treatment and experienced secondary amenorrhea for the past 12 year. In the interim, she gained 5 kilograms of weight, became lethargic and diagnosed as having sub-clinical hypothyroidism and started on thyroxine replacement in a dose of 25 mcg per day but her symptoms did not alleviate, and she developed hirsutism.

She was examined thoroughly, and it was recorded that there was male hair pattern and her Ferriman-Gallwey scale for hirsutism was 29. She had frontal recession along with male pattern of alopecia. However, her external genitalia were normal female

looking with no evidence of clitoromegaly and breast development was Tanner 3.

Patient underwent investigations including FSH: 4.04 Miu/ml (NR: 1.38- 9.58 miu/ml), LH: 6.62 Miu/ML (0.83-15.5 Miu/ML), serum Testosterone: 269.90 ng/ml (15-70 ng/ml), serum Prolactin: 10.3 ng/ml (5.2-27.0), 17-OH-Progesterone: 51.53 ng/ml (0.3-1.4), and 159.3 after ACTH stimulation, serum Anti-TPO: > 100.00 IU/Ml, TSH: 7.21 (0.4-4.5 Uiu/ml), Serum DHEAS: 361.9 ug/ml (98.90-340.0), serum cortisol: 7.9 ug/dl (intermediate ranges). CECT abdomen with adrenal protocol showed bilateral bulky body of adrenal glands with size of 9.5 mm and 7.8 mm of right and left gland respectively and a focal lesion in the medial limb of right adrenal gland with a small sized uterus. She was successfully treated for NCCAH with escalating dose of spironolactone and OCPs with monitoring of serum potassium levels along with laser treatment for facial hairs and close follow up. She was advised for low doses of prednisolone 5mg per day for NCCAH and counseled for future reproductive health.

DISCUSSION

We presented a case of 33 years old female with hirsutism and secondary amenorrhea with a diagnosis of NCCAH. Due to limitation of resources and diagnostics, CY212A2 mutation testing was not carried out. However, the rise in 17-OH progesterone value was well above the confirmatory target in ACTH stimulation testing. CECT (contrast enhanced computed tomography) showed bilateral adrenal hyperplasia along with small right sided adrenal nodule. Since testosterone levels were elevated markedly in our patient, an adrenal androgen or ovarian androgen producing tumor was also a differential diagnosis.

Patients with NCCAH tend to present in adolescence, especially females with excessive hair growth, acne, and menstrual irregularities. Treatment is aimed to reduce the symptoms with use of steroids, OCPs, and anti-androgen therapy.[4] Patients have variable response with available therapies. A study showed that patients, who had a poor response to steroid therapy, were later on found to be having ovarian or adrenal malignancies and improved with adrenalectomy.[5]

CYP21A2 mutation testing should be done for all patients having raised 17-OHP levels and adrenal nodules morphology on incidental imaging. It is important to offer genetic testing to the partner to assess the risk of disease transmission in the offspring. The prevalence of 17-OHP secreting tumors along with CAH/NCCAH is very rare and elevation of basal 11-deoxycorticosterone and 11-deoxycorticosterol may be the reason of such adrenal appearance.[6]

Female infertility had a huge impact in our society along with repeated fertility procedures with a high cost. Endocrinologist should evaluate and advised 17-OHP levels with cosyntropin stimulation as a workup of female infertility. If 17-OHP tends suggestive, genetic testing should be offered.

CONCLUSION

There is a need for genetic mutations testing in patients having NCCAH's clinical and biochemical features but an incidental imaging suggestive of adrenal tumor. A close follow up is of paramount importance in such cases to not miss a sinister pathology.

Ethical Approval:

The ethical order was obtained vide order no. ERB185/7/18-03/S1 ERB

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Author's Contribution

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