Case Report

Abdelazim and Sakiyeva endocrinopathy associated with polycystic ovary syndrome: Case reports

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Abstract

Polycystic ovary syndrome (PCOS) is a multiple endocrine disorder associated with significant reproductive and metabolic manifestations. A genetic variation at the level of aromatase enzyme gene (CYP19 gene) and/or androgen receptors with subsequent increased ovarian androgen was suggested in PCOS. Recently, researchers noted that 56% of the PCOS women had evidence of hypothyroidism and this report represents three case of PCOS with hypothyroidism and hyperprolactinemia (Abdelazim and Sakiyeva endocrinopathy associated with PCOS) to highlight the hypothyroidism and hyperprolactinemia as a common endocrinopathy associated with PCOS. PCOS women should be screened for the endocrinopathy associated with PCOS especially the hypothyroidism and hyperprolactinemia because the undiagnosed endocrinopathy aggravates the PCOS symptoms.

Keywords: Abdelazim, disorders, endocrine, PCOS, Sakiyeva

Introduction

Polycystic ovary syndrome (PCOS) is a multiple endocrine disorder associated with significant reproductive (anovulation, infertility, and hyperandrogenism) and metabolic manifestations [insulin resistance (IR) and glucose intolerance].[1-3]

The prevalence of PCOS is about 15–20% when the European Society for Human Reproduction and Embryology and the American Society for Reproductive Medicine (ESHRE/ASRM) diagnostic criteria used.[1] PCOS is a multifactorial disorder, involving interactions between certain genes, environmental factors, pituitary and hypothalamic dysfunction.[2]

A genetic variation at the level of aromatase enzyme gene (CYP19 gene) and/or androgen receptors was suggested in PCOS.[4,5] Aromatase enzyme gene (CYP19 gene) and/or androgen receptor variation lead to aromatase deficiency or reduced activity with subsequent increased ovarian androgen.[5]

Nath *et al.*, noted that 56% of the PCOS women had evidence of hypothyroidism and the long-standing hypothyroidism increases the severity of PCOS symptoms due to anovulation.[6]

This report represents three case of PCOS with hypothyroidism and hyperprolactinemia (Abdelazim and Sakiyeva endocrinopathy associated with PCOS) to highlight the hypothyroidism and hyperprolactinemia as a common endocrinopathy associated with PCOS.

Case Reports

Case 1

A 18-years-old unmarried girl presented with menstrual disturbance diagnosed as PCOS based on; PCO ultrasound picture, oligo/hypomenorrhea, biochemical hyperandrogenism

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(elevated total testosterone 91.5 ng/dl (normal 6–86 ng/dl), elevated free testosterone 4.5 pg/ml (normal 0.7–3.6 pg/ml), and elevated androstenedione 3.9 ng/ml (normal 0.7–3.1 ng/ml). Her thyroid stimulating hormone (TSH) was 6.3 mIU/ml (normal 0.4–4.1 mIU/ml) and prolactin was 820 mIU/ml (normal <614 mIU/ml).

Case 2

A 26-years-old infertile woman presented with infertility, oligo/hypomenorrhea and diagnosed as PCOS based on; PCO ultrasound picture, biochemical hyperandrogenism (elevated total testosterone 99.2 ng/dl, elevated free testosterone 5.2 pg/ml, and elevated androstenedione 4.6 ng/ml). Her TSH and prolactin were 7.5 and 795 mIU/ml; respectively.

Case 3

A 23-year-old unmarried girl referred from the dermatology clinic due to acne and hirsutism and diagnosed as PCOS based on; PCO ultrasound picture, oligo/hypomenorrhea, biochemical hyperandrogenism (elevated total testosterone 95.7 ng/dl, elevated free testosterone 4.8 pg/ml and elevated androstenedione 4.9 ng/ml). Her TSH and prolactin were 6.8 and 980 mIU/ml; respectively.

PCOS defined by the ESHRE/ASRM criteria as presence of two of the following criteria; (1) polycystic ovaries (PCO), (2) oligo/anovulation, and/or (3) clinical or biochemical evidence of hyperandrogenism after exclusion of other causes of hyperandrogenism as late onset congenital adrenal hyperplasia (CAH), androgen secreting ovarian or adrenal tumors and Cushing`s syndrome.[2]

The studied cases evaluated for Day 2-3 hormonal profile including; follicle stimulating (FSH) and luteinizing hormones (LH), prolactin, TSH, total and free testosterone, androstenedione, dehydroepiandrosterone (DHEA) and 17-hydroxy progesterone (17-OH progesterone).

Ultrasound diagnosed criteria of PCO means (≥10 small follicles measuring 2-8 mm in both ovaries).[1-3]

FSH, LH, prolactin, TSH, total and free testosterone, androstenedione, DHEA and 17-hydroxy progesterone measured by using the enzyme-linked immunosorbent assay (ELISA).[7]

Elevated hormonal profile (androgen and/or TSH or prolactin) confirmed by two laboratory results 8 weeks apart.

Women with prolactin level twice the normal [normal value <29 ng/mL (<614 mIU/ml)] evaluated for pituitary micro and/or macroadenoma using the pituitary magnetic resonance imaging (MRI) according to the hospitals protocol. CAH as a cause of excess androgen excluded by the measurement of the 17-OH progesterone level (normal value <200 ng/dl or <6.06 nmol/).

According to hospitals protocol women with elevated total testosterone >200-250 ng/dl, screened for the ovarian or adrenal androgen secreting tumors using the pelvi-abdominal MRI. Androgen secreting adrenal tumors suspected when the DHEA-sulphate (DHEA-s) is high with >200–250 ng/dl total testosterone. Androgen secreting ovarian tumors suspected when the total testosterone >200–250 ng/dl with normal DHEA-s. Dexamethasone suppression test with 24-hours urinary cortisol done for the cases with suspected Cushing`s syndrome as a cause of excess androgen (Cushing`s syndrome diagnosed when serum cortisol remains high at 8 AM after 1 mg of dexamethasone suppression dose at 11 PM).[2]

Discussion

TSH and prolactin were significantly high in the studied three PCOS cases. Nath *et al.*, noted that 56% of the PCOS women had evidence of hypothyroidism and they explained this association by the prevalence of iodine deficiency worldwide (WHO estimated 2 billion with iodine deficiency worldwide).[6]

Abufaza *et al.*, found 10–40% of PCOS women are obese and 40–90% are overweight.[2] The association between PCOS and hypothyroidism can be explained by the obesity and increased body mass index (BMI) of the PCOS women which produce relative deficiency of the thyroid hormone (sub-clinical hypothyroidism). The non-diagnosed sub-clinical hypothyroidism of the PCOS women converted to clinical hypothyroidism by the time and increased BMI of the PCOS women. Long-standing hypothyroidism increases the severity of PCOS symptoms due to anovulation.[6]

The association between hypothyroidism and hyperprolactinemia explained by Ansari and Almalki, and they mentioned that the elevated thyrotropin-releasing hormone (TRH) in hypothyroidism has a stimulatory effect on the dopamine secreting cells of the pituitary gland with subsequent hyperprolactinemia.[8]

Prolactin is a potent stimulus for ovarian androgen production because hyperprolactinaemia produces luteal phase defect with subsequent defective ovarian steriodogessis of the two-cell theory (defective conversion of androstenedione from the theca cell to estrogen in the granulosa cell). The defective ovarian steriodogessis leads to elevated ovarian androgen mainly androstenedione and testosterone with subsequent increased severity of PCOS symptoms.

The testosterone (both free and total testosterone), and the androstenedione were high in studied three cases. Similarly; Lerchbaum *et al.*, found that free testosterone and androstenedione are the main androgens elevated in PCOS.[9] Mostafa *et al.*, reported manifestation of hyperandrogenism in 70% of PCOS women.[4] Mostafa *et al.*, in another study reported excess androgen in 50% of PCOS women and they suggested the use of free and total testosterone to detect excess ovarian androgen production in PCOS.[10]

To the best of our knowledge this is the first report mentioning and explaining the association of hypothyroidism and hyperprolactinemia with PCOS (Abdelazim and Sakiyeva endocrinopathy associated with PCOS). Large prospective study is going on to confirm the association of hypothyroidism and hyperprolactinemia with PCOS.

Conclusion

PCOS women should be screened for the endocrinopathy associated with PCOS especially the hypothyroidism and hyperprolactinemia because the undiagnosed endocrinopathy aggravates the PCOS symptoms.

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Conflicts of interest

There are no conflicts of interest.

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