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Case Report

Correlation of hyperprolactinemia, Subclinical hypothyroidism with Polycystic Ovary Syndrome and infertility

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Abstract

Background: Polycystic ovarian syndrome (PCOS) is a hyperandrogenic condition characterized by polycystic ovarian morphology and chronic oligo-anovulation. When it is combines with hypothyroidism and hyperprolactinemia, this condition can have severe consequences, may even lead to infertility.

Case Presentation: This case study illustrates the complexity of PCOS and the significance of a multidisciplinary approach to its diagnosis and therapy. The patient is a 24-year-old non diabetic nonsmoker female with PCOS who has been attempting to conceive for seven years. The patient presented to the hospital with irregular menstrual cycles and a desire to become pregnant. The patient had previously been unsuccessfully treated with Clomid and letrozole. The patient's BMI was determined to be 23. 3 and a pelvic scan indicated PCO ovaries. Laboratory results revealed hyperprolactinemia (53 ng/ml) and subclinical hypothyroidism (TSH 12.6 uIU/ml, T4 0.54 ng/dL- TPO antibodies:187 IU/mL, Anti thyroglobulin antibodies 235 IU/mL), but a pituitary gland MRI was normal. Thyroid US features going with Hashimoto thyroiditis. The patient's PCOS symptoms were initially managed with metformin and Duphaston, and then Cabergoline was introduced to address hyperprolactinemia. The patient became pregnant shortly following hyperprolactinemia medication. Prenatal screenings revealed elevated fasting glucose levels and gestational diabetes. The patient's blood sugar was initially controlled by Metformin, but she later required multiple insulin doses to maintain control. The patient was scheduled for induction of labor at 38 weeks, but a lower segment emergency cesarean surgery was performed due to fetal distress.

Conclusion: Regular monitoring and management of both PCOS and related conditions such as hypothyroidism and hyperprolactinemia are crucial to ensure the best outcome for the patient. Additionally, we suggest Metformin, Duphaston, Cabergoline to treat PCOS patient having subclinical hypothyroidism and hyperprolactinemia.

Keywords: Polycystic ovarian syndrome, subclinical hypothyroidism, hyperprolactinemia, gestational diabetes.

Introduction

Polycystic ovary syndrome is a prevalent endocrine disorder that affects 15-20% of women of reproductive age. The condition is characterized by hyperandrogenism, irregular menstrual cycle, oligo-anovulation, and hyperandrogenism[1]. Hyperandrogenemia, or an excess of male hormones, is a common finding in women with PCOS and can be caused by disruptions in normal adrenal and ovarian function, excess deposition of fatty tissue, and excessive androgen formation[2]. Additionally, a lot of women having PCOS experience decreased levels of FSH and increased levels of luteinizing hormone [3]. This hormonal imbalance can lead to amenorrhea or oligomenorrhea, the presence of numerous small cysts on the ovaries, and other symptoms such as virilization, hirsutism, and infertility [4]. Hirsutism has been reported in 70 percent of the cases of women with PCOS and is a reliable indicator of hyperandrogenism[2]. Other observed clinical features of this syndrome include alopecia, acne, and acanthosis nigricans. However, it's crucial to remember that young girls frequently experience acne, thus this condition shouldn't be mistaken for a sign of PCOS [5].

Besides Hyperandrogenemia and decreased FSH levels, Insulin resistance is a common endocrine irregularity in PCOS. Over half of the people with PCOS develop metabolic syndrome, weight gain, hyperglycemia, and insulin resistance [6]. These symptoms are also shared by hypothyroidism, which is characterized by hyperglycemia, raised levels of sex hormone-binding globulin (SHBG), and dyslipidemia[7]. Both conditions have different causes, but thyroid disorders are more frequently observed in PCOS patients [8]. Additionally, hypothyroidism, due to increased "thyrotropin releasing hormone" (TRH), can alter the "FSH/LH ratio" and raise "DHEA-S" levels. The excess TSH can stimulate the FSH receptor[9]. This condition can also lead to infertility, hyperglycemia, weight gain, and dyslipidemia. Even mild or asymptomatic cases of Subclinical hypothyroidism or hypothyroidism may lead to or worsen various metabolic and

hormonal functions in women with PCOS[10]. It has been suggested that complicated alterations brought on by obesity and IR in PCOS contribute to the coexistence of hypothyroidism and PCOS, albeit this association is not yet proven.

Moreover, hyperprolactinemia is a disorder characterized by increased blood levels of prolactin, which may have physiological, pathogenic, or idiopathic causes[11]. Women are more likely to develop "prolactin-secreting pituitary adenoma" (prolactinoma) and "idiopathic hyperprolactinemia"[12]. The additional less frequently observed causes include intake of drugs, pituitary and hypothalamic tumors, and primary hypothyroidism that compresses the pituitary stalk [13]. Hyperprolactinemia in females is characterized by amenorrhea, galactorrhea, and infertility[14]. It is also important to note hyperprolactinemia can be triggered by hypothyroidism in patients having PCOS[15]. However, the exact mechanism is not known.

The current case report discusses the complex case of a patient with PCOS who was unable to find relief from her symptoms for several months. Upon further examination, it was discovered that the patient had both hyperprolactinemia and subclinical hypothyroidism, which were found to be the underlying causes of her PCOS symptoms.

Case Presentation:

A 24-year-old non diabetic nonsmoker female patient with a known diagnosis of PCOS presented to the hospital with a history of irregular menstrual cycles, and a desire to conceive. The patient has been married for 7 years and has a history of irregular menstrual cycles, periods every 2-3 months. The patient reported a family history of hemophilia in two of her brothers. The patient had been previously treated with Clomid and letrozole for several months with different gynecologists without success.

Physical examination: The patient's obstetric history was P0+A0, and her BMI was 23.3. The patient's last menstrual period (LMP) was on 03/01/2022. A pelvic ultrasound revealed PCO ovaries.

Laboratory results: Laboratory work revealed hyperprolactinemia (53 ng/ml) and subclinical hypothyroidism (TSH 12.6 uIU/ml, T4 0.54 ng/dL). The patient's LH and FSH levels were 8.51 IU/L and 4.95 IU/L, respectively, and her estradiol level was 30.09 pg/ml. An MRI of the pituitary gland findings was within normal limits.

Treatment: The patient was initially treated with metformin and dydrogesterone to manage her PCOS symptoms. However, due to the presence of hyperprolactinemia, Cabergoline was later added as a treatment for hyperprolactinemia. Ovulation tracking revealed late ovulation. The patient became pregnant immediately after treatment for hyperprolactinemia and her estimated due date (EDD) by early scan was 22/10/2022. Antenatal screening tests revealed high fasting blood glucose (FBG) and the patient was unable to tolerate a 75-gram glucose tolerance test (GTT) which may indicate gestational diabetes. The patient was planned for induction of labor at 38 weeks and delivered by emergency lower segment cesarean section (LSCS) due to fetal distress. The baby weighed 3.2 kg at birth.

Figure 1: Ultrasound showed small gestational sac.

Follow-up: The patient was started on levothyroxine 50 mcg per day, which was later increased to 75 mcg per day for treatment of hypothyroidism. Both the patient and the baby were discharged in good condition. The patient was advised to follow up with her endocrinologist and gynecologist for regular monitoring and management of her diabetes and hypothyroidism, respectively.

Discussion

This case report discusses the case of a female PCOS patient who presented to a hospital with a complaint of irregular menstrual cycles, and a desire to conceive. The patient also developed hyperprolactinemia and hypothyroidism along with this condition. Polycystic ovary syndrome is a common endocrine disorder that affects women of reproductive age. PCOS is characterized by hyperandrogenism (elevated levels of male hormones) and anovulation (absence of ovulation), as well as other metabolic disturbances[16]. These changes can have long-term health implications for those affected. The sign and symptoms include missed periods, irregular periods, ovarian cysts, hirsutism, weight gain, infertility, and acne issues[17]. Our patient also had irregular periods and problems with infertility. In addition, she also gained weight as her BMI was 23.3.

Studies indicate that women with PCOS should be screened for hypothyroidism and hyperprolactinemia, as these conditions can worsen the symptoms of PCOS. Hyperprolactinemia, which is characterized by high levels of the hormone prolactin, can lead to amenorrhea (absence of menstruation), galactorrhea (milk production in the absence of breastfeeding), and infertility. Hyperprolactinemia can occur before menarche (first menstruation) and can cause primary amenorrhea, or later in life, leading to oligomenorrhea (infrequent menstruation) and eventually to amenorrhea[11]. Our patient presented with a complaint of infrequent menstruation, periods every 2-3 months. She was also facing problems with fertility.

On the other hand, hypothyroidism, which occurs due to decreased formation of thyroid hormones, can also affect the reproductive system function and development. In females, hypothyroidism can cause delayed onset of puberty, anovulation, amenorrhea, irregular menstruation, and an increased risk of spontaneous abortion[18]. The effects of hypothyroidism on reproductive function are believed to be caused by changes in the level of "thyroid-stimulating hormone" (TSH), which has overlapping functions with other hormones such as FSH, LH, and prolactin[19]. Our patient also developed hyperprolactinemia and subclinical hypothyroidism as her prolactin levels were found to be elevated at 35.11 ng/ml, while T4 0.54 ng/dL levels were found to be very low. The patient's LH and FSH levels were 8.51 IU/L and 4.95 IU/L, respectively, and her estradiol level was 30.09 pg/ml.

It has been believed that there exists a strong relationship between hyperprolactinemia and hypothyroidism. The connection between hypothyroidism and hyperprolactinemia has also been explored by researchers Ansari and Almalki, who have proposed that an elevation in "thyrotropin-releasing hormone" (TRH) in hypothyroidism can stimulate the "dopamine-secreting cells" of the pituitary gland, resulting in hyperprolactinemia[20]. Similarly, other studies have also documented increased prolactin levels in PCOS patients. A change in pyodermic-dopaminergic tone has been hypothesized to explain this result[21]. However, recent investigations have shown prolactin rise in these patients is temporary and most likely due to underlying stress, the use of offending medications, or hypothyroidism[22]. In our case, the patient was also diagnosed with hyperthyroidism. Similarly, in another study, women with PCOS phenotypic and elevated prolactin levels had an underlying reason such as pituitary adenoma, hypothyroidism, oral contraceptive use, or the use of an offending drug[23]. Therefore, the authors concluded that hyperprolactinemia is not a clinical indication of PCOS and that any considerable prolactin rise in patients suspected of having PCOS warrants additional investigation.

Furthermore, prolactin is a potent stimulant for ovarian androgen formation because hyperprolactinemia causes "luteal phase" defect and subsequent "two-cell theory-defective ovarian steroidogenesis" (defective conversion of androstenedione from the theca cell to estrogen in the granulosa cell). Defective ovarian steroidogenesis causes an increase in ovarian androgen, primarily testosterone and androstenedione resulting in a worsening of PCOS symptoms[18]. This can explain the infertility and menstrual issue our patient was having despite several months of treatment for PCOS. Since she was receiving treatment but still, was unable to conceive.

Additionally, pregnant women with PCOS have a three times greater risk of developing gestational diabetes than patients without PCOS [24]. Therefore, management with metformin has been recommended. Treatment with the drug metformin, which is commonly used to treat type 2 diabetes, can reduce the risk of miscarriage and gestational diabetes in these women[25]. It has been suggested that metformin may protect against early pregnancy loss in women with PCOS by reducing plasma androgen levels, likely as a result of decreasing insulin levels. Additionally, despite the ongoing debate about its long-term use, metformin is commonly prescribed to pregnant women with PCOS to address metabolic imbalances and hyperinsulinemia as well as endocrine disruptions, specifically by decreasing LH and sex-hormone binding globulin levels[26].

However, the report notes that further research in the form of randomized clinical trials with large participant groups, appropriate placebo controls, and blinding is necessary to confirm the benefits of metformin in PCOS patients. Additionally, as metformin has no known teratogenic effects and minimal adverse effects, it may be a safe option for PCOS patients who are at a higher risk of developing type 2 diabetes due to impaired glucose tolerance, which is prevalent in approximately 33% of PCOS cases[27]. In our case, the patient was initially treated with metformin and Dydrogesterone to manage her PCOS symptoms, and later Cabergoline was added as a treatment for hyperprolactinemia.

The clinical implications of this case report are that in women with PCOS, it is important to screen for hyperprolactinemia and subclinical hypothyroidism, as these conditions can worsen the symptoms of PCOS and affect the patient's fertility. Hyperprolactinemia can lead to amenorrhea, galactorrhea, and infertility, and subclinical hypothyroidism can cause delayed onset of puberty, anovulation, amenorrhea, irregular menstruation, and increased risk of spontaneous abortion.

Conclusion

In conclusion, this case highlights the complexity of PCOS and the importance of a multidisciplinary approach to its diagnosis and management. Regular monitoring and management of both PCOS and related conditions such as hypothyroidism and hyperprolactinemia are crucial to ensure the best outcome for the patient. In our case, the patient was initially treated with metformin and Dydrogesterone to manage her PCOS symptoms and later Cabergoline was added as a treatment for hyperprolactinemia.

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