Case Report

Postmenopausal Ovarian Hyperthecosis

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ABSTRACT

Ovarian hyperthecosis has variable clinical importance. It can cause hyperandrogenism, particulary in premenopausal women, and may be a rare cause of androgenic alopecia in postmenopausal women. The physiological level of androgens secreted by ovarian stromal cells is greatly increased with hyperplastic or neoplastic transformation leading to possible clinical consequences. We report a case of postmenopausal ovarian hyperthecosis.

KEY WORDS: hyperandrogenism, postmenopausal

INTRODUCTION

The term hyperthecosis refers to the presence of nests of luteinized theca cells in the ovarian stroma due to differentiation of the ovarian interstitial cells into steroidogenically active luteinized stromal cells.

The nests or islands of luteinized theca cells are scattered throughout the stroma of the ovary, rather than being confined to areas around cystic follicles as in the polycystic ovary syndrome. The result is greater production of androgens. It is not clear why hyperthecosis occur. Bilateral ovarian stromal hyperthecosis occasionally causes virilization in premenopausal women[1]. However, a previous review article found only two previously reported cases of stromal hyperthecosis in postmenopausal women[2].

CASE REPORT

A 54-year-old Kuwaiti female, reaching menopause at the age of 50 years with no significant postmenopausal symptoms, was first seen in endocrine clinic with three years history of hirsutism and frontal hair loss. She was known to have type 2 diabetes and hypertension, had menarche at age 13 and described that she had oligomenorrhea since menarche and infertility, but had two successful pregnancies after clomiphene treatment. On October 2010, she had partial gastrectomy due to stomach cancer followed by chemotherapy and currently, the patient is in remission.

Physical examination revealed temporal and anterior baldness and increase facial hair on her sideburns and chins. She was overweight with body mass index of 28 kg/m^2. Examination of the chest, heart, abdomen and pelvis were otherwise normal.

Initial investigation showed normal full blood count, lipid profile, renal and liver function tests. Her fasting blood sugar was 9.1 mmol/l. Hormonal profile revealed raised serum total testosterone 401 nmol/l (0.3 - 3.0), with sex hormone binding globulin 15 nmol/l (20 - 118), dehydroepiandrosterone sulfate 7.4 nmol/l (0.9 - 11.7) and androstenedione 22.4 nmol/l (1.6 - 9.4). The gonadotrophins which are luteinizing hormones and follicular stimulating hormone (FSH) were in the postmenopausal range, whereas the serum estradiol level was slightly elevated for postmenopausal state (340 pmol/l). Thyroid function tests were normal.

The results of further diagnostic tests were as follows: morning serum cortisol after overnight dexamethasone suppression test (1 mg) was normally suppressed (20 nmol/l). Short synacthen test (250 micrograms cortisone intravenously) was done to exclude the diagnosis of late onset congenital adrenal hyperplasia (Table 1).

A significant decrease in dehydroepiandrosterone (1.6 nmol/l), but only partial suppression of testosterone (2.8 nmo/l) followed low dose dexamethasone therapy (0.5 mg 4 times a day for 5 days). Ultrasound examination of adrenals and transvaginal ultrasound

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Table 1: Short synacthen test (250 micrograms cortisone intravenous) to exclude the diagnosis of late onset congenital adrenal hyperplasia

Time	Cortisol nmol/l	17 hydroxyprogesterone nmol/l
0	323	1.6
30	683	14
60	763	14

of ovaries were normal. Magnetic resonance image of abdomen and pelvis was normal.

In view of these clinical and biochemical observations, a diagnosis of ovarian hyperthecosis (severe variant of polycystic ovary syndrome) was made.

The patient subsequently received spironolactone and metformin treatment. At the same time, she started laser therapy with improvement in her hirsutsim.

DISCUSSION

We describe a case of postmenopausal hyperthecosis, a severe variant of polycystic ovary syndrome who presented with hirsutism and responded well to antiandrogen therapy.

Ovarian hyperthecosis is characterized by significantly increased stromal tissue with luteinized theca cells[3]. It is an uncommon disorder with androgen overproduction. Ovarian hyperthecosis shares many clinical features with polycystic ovary syndrome including hirsutism, acne and menstrual irregularities. However, it tends to be more likely associated with virilisation[4]. Most women with ovarian hyperthecosis are obese, with long standing history of hirsutism. The hirsutism is usually severe and most of the women shave daily. Many also have clitoral enlargement, temporal balding, deepening of the voice and a male habitus. Most have amenorrhea and the remaining have irregular anovulatory cycles. Acanthosis nigrican is suggestive of severe insulin resistance.

Despite marked hyperandrogenism as in our case, mainly testosterone is elevated in most cases and postmenopausal ovarian hyperthecosis generally presents as a non-neoplastic, functional disorder, which result from abnormal regulation of ovarian steroidogenesis[5].

Unlike polycystic ovary syndrome, which occurs only during the reproductive years, hyperthecosis of the ovaries can occur in postmenopausal women. Severe hirsutism and virilization in postmenopausal women are more often due to ovarian hyperthecosis than virilizating ovarian tumor[6], which is an ovarian tumor made up of hormone secreting cells due to excessive male hormone (androgen) production. Previous reports suggest that ovarian hyperthecosis occurs mainly in association with insulin resistance that manifest with central obesity, hypertension, hyperlipidemia, hyperinsulinemia and type 2 diabetes or impaired glucose tolerance[7,8], as was the case in our patient .

Imaging is required to rule out ovarian neoplasm and to measure endometrial thickness, as there is an association between ovarian hyperthecosis and endometrial cancer[9]. As described in a previous study, it is likely to be related to increased androgen production by the luteinized theca cells, which then serve as precursors for estrogen production[[0-12]. Sonographic features of ovarian hyperthecosis are variable. The most frequent finding is a normal ovary, as was the case in our patient. A small percentage of affected ovaries may have co-existing morphological features of polycystic ovary syndrome and infrequently a small solid mass may be seen[13]. Treatment of hyperthecosis should include weight reduction, insulin sensitizing agents such as metformin and thiazolidinedies. However, hirsutism can be controlled by antiandrogen therapy that includes spironolactone and gonadotropin releasing hormone agonists. If patient is in the reproductive age, oral contraceptive pills can be used or clomiphene, if she seek fertility.

CONCLUSION

Although ovarian hyperthecosis is a recognized cause of premenopausal virilization, it should also be included as an unusual cause of postmenopausal virilization. The demonstration that this syndrome can develop in the postmenopausal period, as in our patient, strongly suggest that it is a distinct entity and not a late stage of polycystic ovary syndrome, as has been suggested.

REFERENECES

1. Goldman JM, Kapadia LJ. Virilization in postmenopausal women due to ovarian stromal hyperthecosis .Postgrad Med J 1991; 67:304-306.
2. Van Heyningen C, MacFarlane IA, Diver MJ, Muronda C, Tuffnell D. Virilization due to ovarian hyperthecosis in a postmenopausal women. Gynecol Endocrinol 1988; 2:331-338.
3. Rajput R, Bhansali A, Singh A. Ovarian hyperthecosis and response to antiandrogens: An uncommon presentation of a common disorder. J Obstet Gynaecol 2008; 28:249-250.
4. Ashaweah K, Aghilla MM, Randeva HS. Androgenic alopecia in postmenopausal ovarian hyperthecosis. J Obstet Gynaecol 2011; 31:351-352.
5. Krug E, Berga SL. Postmenopausal hyperthecosis functional dysregulation of androgenesis in climacteric ovary. Obstet Gynecol 2002; 99:893-897.

6. Efstathiadou Z, Tsatsoulis A. Long-term remission of ovarian hyperandrogenism after short-term treatment with a gonadotropin-releasing hormone agonist. Fertil steril 2001; 75:59-62.
7. Nagamani M, Dinh T, Kelver ME. Hyperinsulinemia in hyperthecosis of the ovaries. Am J Obstet Gynecol 1996; 154:384-387.
8. Barth JH, Jenkins M, Belchtz PE. Ovarian hyperthecosis, diabetes and hirsutes in postmenopausal women. Clin Endocrinol 1997; 46:123-128.
9. Clement PB, Kurman RJ. Non-neoplastic lesion of the ovary. Blaustein's Pathology of the Female Genital Tract 2002; 5:675-728.
10. Sasono H, Fukunaga M, Silverberg SG. Hyperthecosis of the ovary. Int J Gynecol Pathol 1989; 96:311-320.
11. Ronnett BM, Zaino RJ, Ellenson LH, Kurman RJ. Endometrial cancer. In : Kurman RJ, Editor. Blaustein's Pathology of the Female Genital Tract 5th ed. New York: Springer 2002; 5:501-559.
12. Jongen VH, Hollema H, van der Zee AG, Santema JG, Heineman MJ. Ovarian stromal hyperplasia and ovarian vein steroid levels in relation to endometroid endometrial cancer. BJOG 2003; 110:690-695.
13. Brown DL, Henrichsen TL, Clayton AC, *et al*. Ovarian stromal hyerthecosis: Sonographic features and histological association. J Ultrasound Med 2009; 28:587-593.