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Ovarian Leydig cell tumour in a postmenopausal woman with alopecia

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Summary

Hyperandrogenism in females usually results from ovarian and/or adrenal pathology. A rapid progression of clinical manifestations, such as hirsutism, male-pattern hair loss, and clitoromegaly can strongly suggest androgen-secreting neoplasm. The authors describe a case of a postmenopausal 64-year-old woman, presented with advanced androgenic alopecia and progressive hirsutism arising over three years. The patient suffered from many internal disorders. Hormonal tests revealed high total levels of testosterone and estradiol. A solid tumour of the right ovary measuring 15×13×16 mm with strong enhancement was observed in pelvic dynamic MRI. Total abdominal hysterectomy, bilateral salpingo-oophorectomy, and partial omentectomy were performed. Histology revealed a 2.5-cm right ovary containing a 1.8-cm sized beige-yellow tumour, identified as Leydig cell ovarian tumour with positive result of inhibin staining. Postoperatively, testosterone level returned to normal with a gradual regression of clinical symptoms..

Key words: Hyperandrogenism; Adrenal glands; Hirsutism; Ovarian Leydig cell tumour.

Introduction

The postmenopausal ovary remains hormonally active, secreting significant amounts of androgens and estrogens for many years after menopause [1]. An imbalance among estrogens and androgens, decrease in sex hormone-binding globulin (SHBG) concentrations and high luteinizing hormone (LH) stimulation may result in hyperandrogenic syndrome in postmenopausal women [2]. The polycystic ovary syndrome, ovarian hyperthecosis, and congenital adrenal hyperplasia due to chronic course, are the most frequent causes of hyperandrogenism in both reproductive-aged and postmenopausal women [3, 4]. However, the development of true hirsutism (defined as the presence of excessive terminal hair in androgen-dependent areas), acne, male-pattern alopecia, deepening of the voice, clitoromegaly, and other signs of masculinization should not be regarded as normal and the search for ovarian and/or adrenal pathology [4, 5]. A rapid progression of clinical manifestations, especially symptoms of virilisation, can strongly suggest rarer causes such as androgen-secreting neoplasms [6].

The authors describe an ovarian Leydig cell tumour in a postmenopausal woman with advanced and rapidly progressive symptoms of hyperandrogenism.

Case Report

A 64-year-old Caucasian woman presented with advanced male-pattern baldness and progressive hirsutism occurring over three years was referred to the Department of Gynecological Endocrinology of Medical University of Warsaw, in 2015.

The patient suffered from abdominal obesity, type 2 diabetes mellitus, hypertension, ischemic heart disease, asthma, atrial fibrillation treated with acenocumarol, hyperuricemia, and non-alcoholic fatty liver disease. Her menarche occurred at the age of 13 and menopause at the age of 38 years. She became pregnant three times (two labours, one miscarriage). She underwent myomectomy and bariatric surgery. On physical examination, she had an advanced, diffuse male-pattern alopecia, especially located around the frontotemporal areas (Ludwig pattern) and hirsutism (score 26, Ferriman-Gallwey scale). Cushingoid body habitus was not found, and her BMI was 34.6 kg/m^2. Gynecological examination revealed no features of postmenopausal bleeding, virilisation, and palpable adnexal masses.

Endocrine evaluation revealed markedly increased total serum testosterone (10.75 ng/ml, reference value < 0.58 ng/ml) and estradiol concentrations (59.0 pg/ml, reference value < 10 pg/ml). Serum levels of androstenedione (A), dehydroepiandrostenedione sulphate (DHEAS), SHBG, 17-hydroxyprogesterone (17-OHP), cortisol, prolactin, and thyroid-stimulating hormone (TSH) were in the normal ranges (Table 1). The laboratory, hormonal parameters were measured with chemiluminescent immunoassay using an enzyme linked fluorescent assay VIDIA technique. Transvaginal pelvic ultrasound was normal (7.5 MHz vaginal probe). Pelvic MRI disclosed: left ovary – 19×15 mm and right ovary 21×15 mm. A solid tumour of the right ovary measuring 15×13×16 mm with strong enhancement was observed in dynamic MRI (Figure 1). Total abdominal hysterectomy, bilateral salpingo-oophorectomy, and partial omentectomy were performed. Histology revealed a 2.5-cm right ovary containing a 1.8-cm seized beige-yellow tumour, located at central part of the gonad, surrounded by unchanged stroma identified as Leydig cell ovarian

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Table 1. — *Hormonal parameters.*

Hormonal parameters	Levels	Reference value
Total serum testosterone	10.75 ng/ml	< 0.58 ng/ml
Estradiol	59.0 pg/ml	< 10.0 pg/ml
Androstenedione	2.6 ng/ml	0.3−3.30 ng/ml
Dehydroepiandrostenedione sulphate (DHEAS)	1.56 umol/L	1.5–7.7 umol/l
Sex hormone-binding globulin (SHBG)	97.5 nmol/L	19.9−155.2 nmol/l
17-hydroxyprogesterone (17-OHP)	0.97 ng/ml	0.2−0.9 ng/ml
Cortisol	8:00 a.m. 15.0 ug/dl 11:00 p.m. 2.79 ug/dl	8:00 a.m. 3.7−19.4 ug/dl 11:00 p.m. < 7.0 ug/dl
Prolactin	10:00 p.m. 11.90 ng/ml 2:00 a.m. 35.69 ng/ml 6:00 a.m. 34.31 ng/ml	5−35 ng/ml
Thyroid-stimulating hormone (TSH)	0.42 uIU/ml	0.35−4.94 uIU/ml

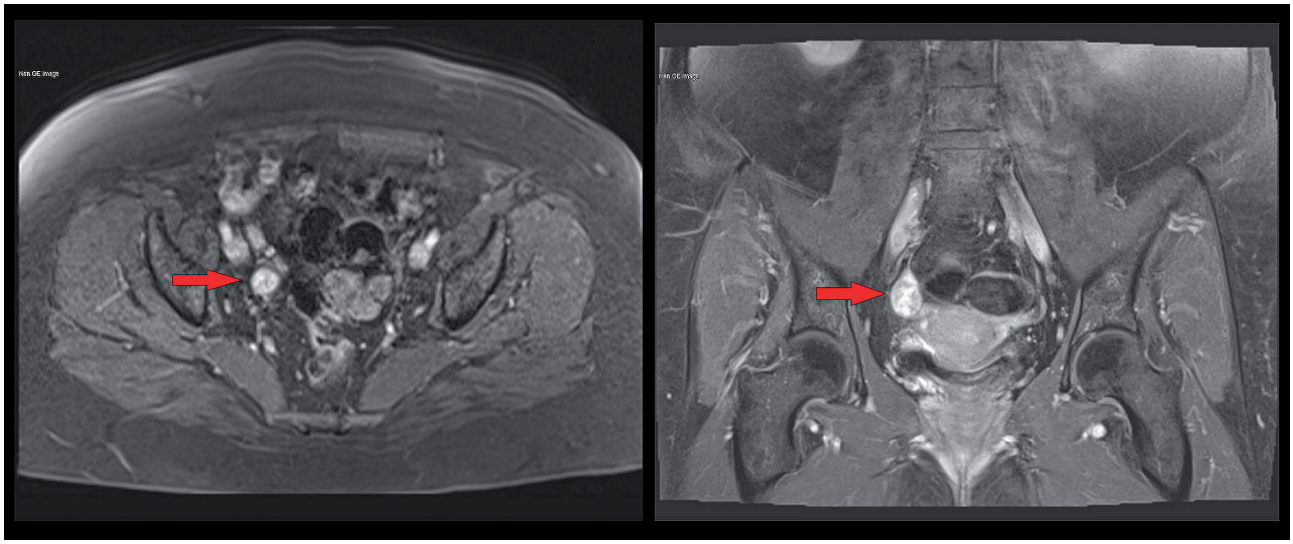

Figure 1. — MRI showing a 15×13-mm solid tumour of the right ovary.

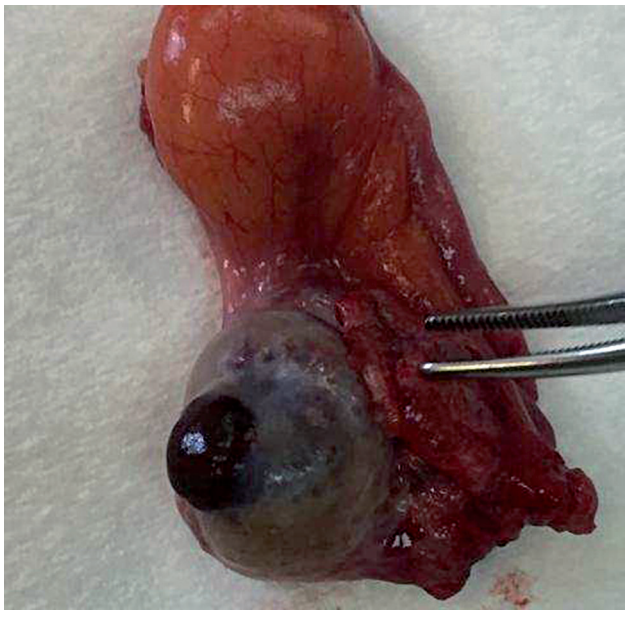

Figure 2. — An image of the right ovarian tumour of the patient.

tumour with positive result of immunohistochemical test for inhibin (Figures 2 and 3). Postoperatively, testosterone level returned to normal with a gradual regression of clinical symptoms.

Discussion

The androgen-secreting ovarian tumors arise from the sex cord-stromal cells and are extremely rare in women (5 - 8% of all ovarian neoplasms) [6, 7]. The Sertoli-Leydig cell tumors (androblastomas) account for less than 0.5 % of all ovarian neoplasms. These tumors are relatively large size, generally unilateral. Pure Leydig cell tumors are mostly androgen-secreting, whereas pure Sertoli cell tumors (0.1% of all ovarian neoplasms) secrete estrogens. The characteristic microscopic feature of Leydig cells is abundant eosinophilic cytoplasm, a central-located round nucleus, and positive inhibin α-subunit staining [7, 8]. Ovarian androgen-secreting tumours like the hilus cell (0.02 %) and granulosa cell tumours should be also extremely rare in postmenopausal women.

The diagnostic approach toward postmenopausal alope-

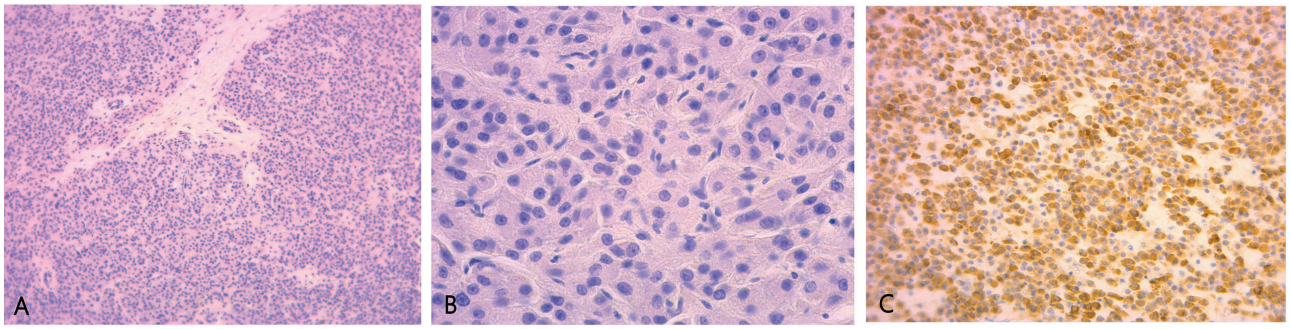

Figure 3. — Histological images of the right ovary pathology. (A) Ovarian stroma with lobulated cell groups, consisting of Leydig cells. (B) The Leydig cells are characterized by abundant eosinophilic cytoplasm with a central nucleus with a nucleolus. (C) The Leydig cells have a positive inhibin staining.

cia and hirsutism can be challenging and often requires a multidisciplinary approach. Quantification of serum testosterone, DHEAS and 17-OHP enables identification and differentiation of adrenal causes. Based on the results, imaging studies (ultrasonography, CT, and/or MRI) should be performed to assess the pituitary gland, adrenals, and/or ovaries. Adrenal androgen-secreting neoplasms are usually large and aggressive carcinomas with a fatal outcome [2]. The imaging studies often fail to show small hormone producing ovarian tumours, as these tumours do not generally lead to obvious ovarian enlargement or aberrant appearance [1, 3]. In such cases adrenal and ovarian venous catheterization and sampling may be helpful in delineating the source of androgen hypersecretion, although the success rate of the procedure is as low as 26-45% [6, 7].

A detailed clinical history and physical examination were essential for the correct management of the present patient. Obesity, diabetes, and probably premenopausal polycystic ovary syndrome promoted the occurrence of hyperandrogenic syndrome and the anticoagulants therapy might prolong the telogen effluvium of hair [4, 9].

In the present patient, very high serum testosterone level (total testosterone 10.75 ng/ml) may suggest an androgen-secreting ovarian neoplasm. However, both ovaries were normal in appearance and size in transvaginal ultrasonography. Catheterization of ovarian veins was not conducted due to the potential complications in an elderly, obese patient with cardiovascular history.

After the visualization of ovarian tumor (pelvic MRI), bilateral salpingo-oophorectomy was performed in the present patient, as the appropriate therapeutic modality to resolve hyperandrogenism in Leydig cell neoplasm.

Conclusions

The differentiation of the causes of alopecia in postmenopausal women should be considered for hormone-producing ovarian and adrenal tumours. Androgen-secreting ovarian tumours, like Leydig cell neoplasms are extremely uncommon. The appropriate therapeutic modality to resolve hyperandrogenism in such case is bilateral salpingo-oophorectomy.

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