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Case Report

Androgen-secreting ovarian tumor complicated by secondary erythrocytosis in a postmenopausal women

Nataliia Pertseva [1]*, Tetiana Chursinova [2], Olexandr Bondarenko [2]

[1] Department of Endocrinology, Dnipro State Medical University, Dnipro, Ukraine

[2] Department of Pathological Anatomy, Forensic Medicine and Pathological Physiology, Dnipro State Medical University, Dnipro, Ukraine

* Correspondence to: Tetiana Chursinova, Department of Endocrinology, Dnipro State Medical University, 26 Pasteur str., Dnipro, Ukraine, 49038. Phone: +380501832389; E-mail: tvchursinova@gmail.com

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Abstract

Androgen-secreting ovarian tumors are a rare pathology that occurs both in a woman's reproductive period and in the postmenopausal period. We have described a rare clinical case of acute virilization growth in the postmenopausal woman. The diagnosis of the left ovary androgen-secreting tumor was made on the base of a significant increase in testosterone and 17-OH progesterone, suppression of gonadotropic hormones, and left ovary solid hypoechoic lesion obtained by ultrasound examination. The patient had concomitant pathologies: type 2 diabetes mellitus, arterial hypertension, and secondary erythrocytosis. After panhysterectomy with omentectomy, the patient experienced gradual regression of hirsutism and virilization. Laboratory examinations 6 months after the operation showed that testosterone and 17 OH progesterone levels were normalized, gonadotropin levels corresponded to the postmenopausal period and erythrocytosis was eliminated.

Keywords: testosterone, hirsutism, ovary, postmenopause.

Introduction

Non-epithelial ovarian tumors account for 10% of all ovarian cancers [1]. These tumors are classified as pure stromal tumors, pure-sex cord tumors, and mixed-sex cord-stromal tumors. Leydig cell tumors belong to pure stromal tumors and typically produce androgens. The clinical features of these tumors are manifested by rapid and progressive virilization symptoms of the female body [1–4]. Pure stromal tumors are mostly benign, have a favorable prognosis, and rarely metastasize [1, 4].

Case description

A 59-year-old woman with a history of diabetes mellitus and arterial hypertension was admitted to the clinic with symptoms of hirsutism. She developed excess hair growth on the face, chest, upper back, arms, and legs. The patient had cosmetic procedures for hair removal. The patient also complained of hair loss on the head crown.

Hirsutism was developed rapidly one year ago. Type 2 diabetes mellitus and arterial hypertension were also diagnosed two years ago. During the reproductive period, the menstrual cycle was regular. She has one child, natural birth. Menopause since 53 years old.

Clinical examination: BMI – 26.2 kg/m^2. Greasy skin, facial erythema, deep voice, male pattern baldness, and breast atrophy were found during the examination. There was hirsutism, Ferriman-Gallwey score was 26 (Figures 1 and 2). Blood pressure was 160/90 mmHg, heart rate was 96 beats per minute. Slight clitoral enlargement was found.

The patient's hormonal status was characterized by a significant increase in testosterone level, an increase of 17-OH progesterone, and gonadotropic hormone

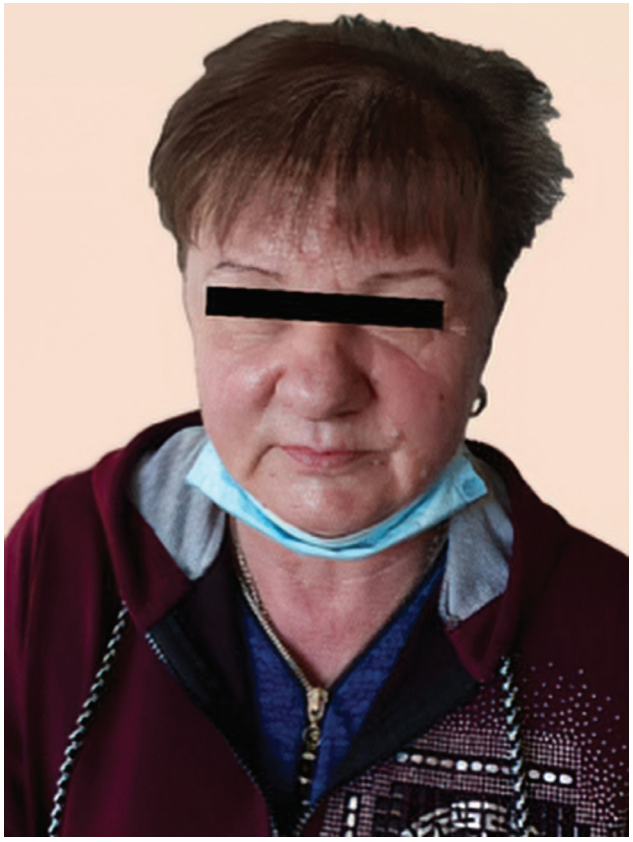

Figure 1: Patient's appearance in the midst of hyperandrogenism clinical symptoms, sparse hair growth on the head, greasy skin, facial erythema.

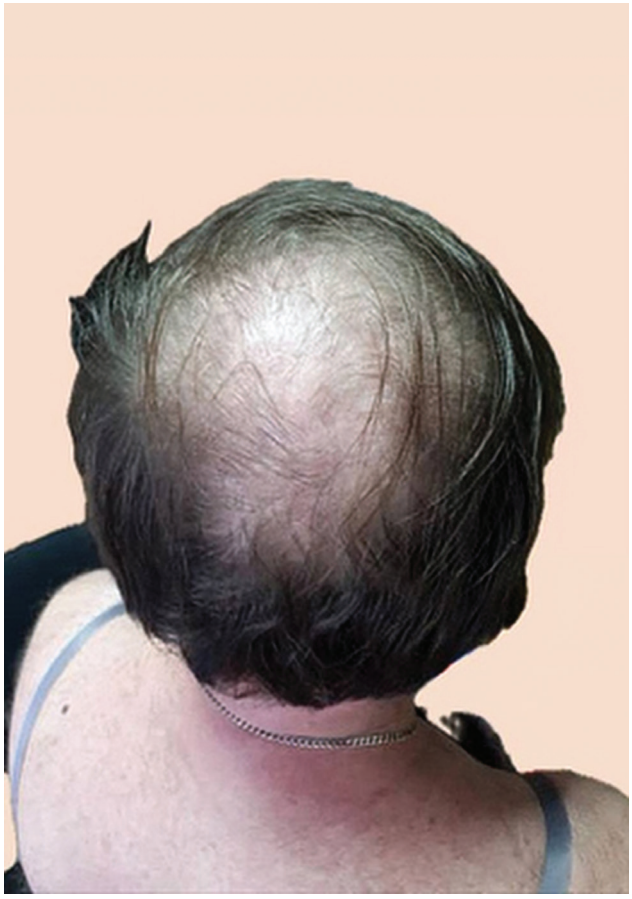

Figure 2: Male pattern baldness.

suppression. Erythrocytosis has been identified in the hematology sample, which is a consequence of the testosterone-stimulating effect on erythropoiesis [5, 6]. An increased level of 17-OH progesterone may occur with adrenal tumors, ovarian tumors, and congenital adrenal hyperplasia [7]. Ovarian cancer antigen CA-125 was negative.

Transvaginal ultrasound revealed: that the uterus is increased in size 90*70*88 mm due to multiple subserosal and intramural fibroids. The ovaries are asymmetrical, the right ovary is 18*10*12 mm, the left ovary is 32*20*24 mm, solid hypoechoic lesion of the left ovary is 25*33 mm with low vascularisation.

The diagnosis was suspected: Androgen-secreting tumor of the left ovary. Secondary erythrocytosis. Multinodular uterine leiomyoma.

Diabetes mellitus type 2, well controlled. Arterial hypertension.

During surgery, (panhysterectomy with omentectomy) the uterus along with both ovaries, fallopian tubes, and part of the greater omentum were removed.

The pathohistological examination revealed well-circumscribed nodular neoplasia with a solid cut surface of red-brown color located in the ovarian hilus. The cellular component was composed of polygonal cells with abundant eosinophilic granular cytoplasm, which were intermittent with some cells with clear cytoplasm. Neoplastic cells contained uniform round nuclei with vesicular chromatin and prominent single central nucleoli, although some nuclei were found with eosinophilic pseudo inclusions, and some larger nuclei were present. The tumor cell nuclei are rounded and medium-sized nucleoli. The clustering of nuclei with the formation of intervening eosinophilic nuclear-free zones was also noticed. Occasionally, the elongated eosinophilic inclusions were found in a few cells of the represented tumor.

These inclusions were interpreted as the Reinke crystals. Mitoses were absent; however, Ki67 immunolabelling demonstrated positive nuclei in 4% of the neoplastic cell population. The changes of blood vessel walls in the form of fibrinoid necrosis were commonly visible in tumor stroma. Immunohistochemically, tumor cells have strongly positive cytoplasmic staining for calretinin and moderately positive staining for EMA. Besides that, the regular membrane CD99 expression was found in all neoplastic cells, as well as the strong nuclear staining for AR (Figure 3).

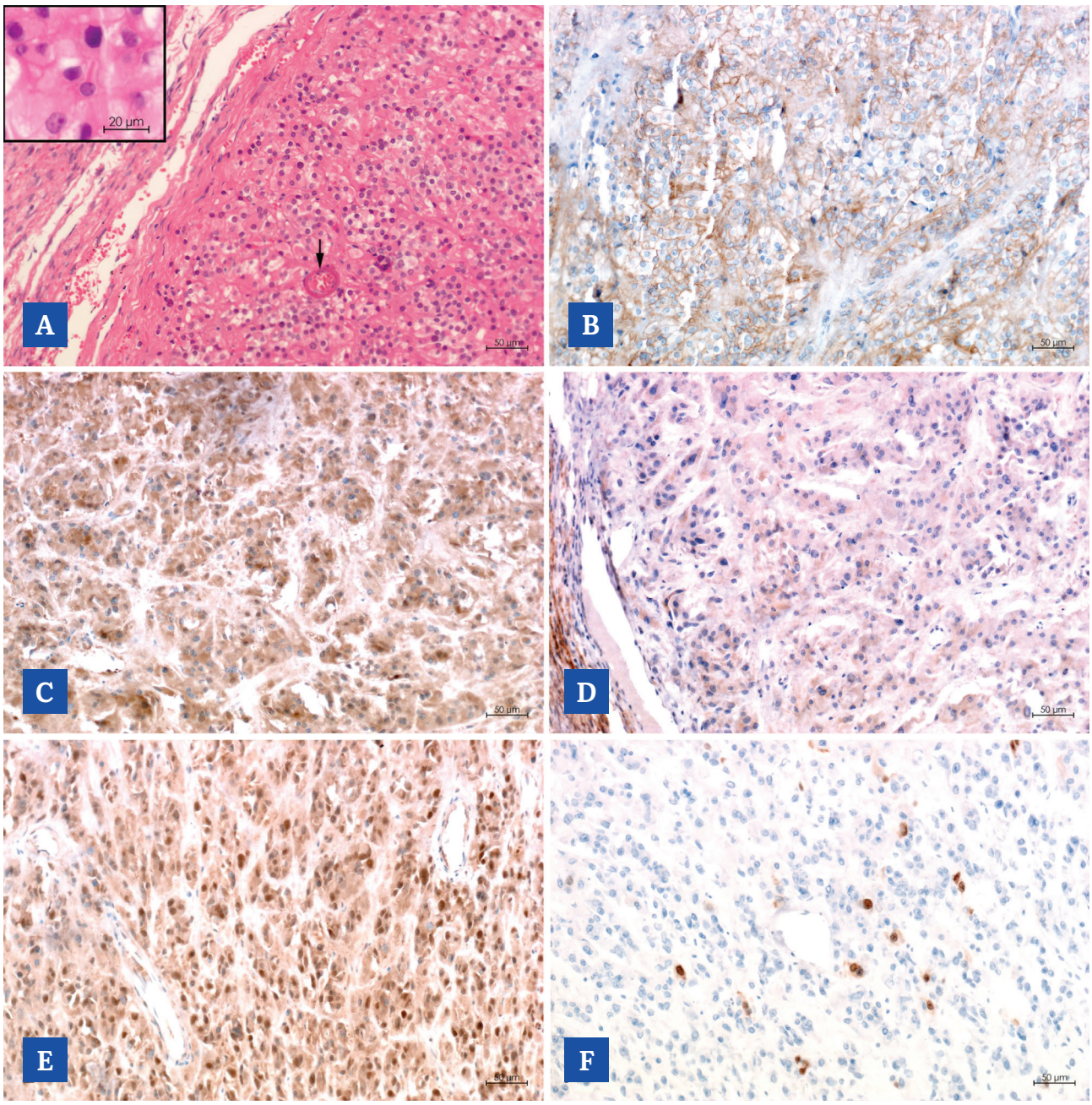

Figure 3: Histological and immunohistochemical features of the reporting ovarian tumor: A – this well-circumscribed tumor appeared as the growth of predominately uniform cells with abundant eosinophilic cytoplasm, the eosinophilic fibrinoid changes in the wall of the blood vessel are apparent (arrow); tumor fibrous capsule and ovarian stroma are visible on the left-upper side (H&E staining, ×200). Inset: Reinke crystal in neoplastic cell (H&E, ×400). B – CD99 membrane staining in tumor cells. C – calretinin, strong cytoplasmic staining in neoplastic cells. D – EMA, moderate cytoplasmic staining in neoplastic cells. E – AR, strong nuclear staining in all neoplastic cells. F – Sparsely distributed Ki67-positive nuclei represent the low-level proliferative activity of the tumor (B–F: immunoperoxidase method, ×200).

After the tumor excision, the patient's condition gradually improved, hair growth on the face, body, and limbs had been decreased, and scalp hair had been increased (Figures 4 and 5). Also 6 months after the surgery, the levels of testosterone and 17-OH progesterone decreased, the level of gonadotropins began to correspond to the postmenopausal period, and erythrocytosis was eliminated (Table 1).

Discussion

The article presents a clinical case of virilization that appeared in a postmenopausal woman. Virilization developed acutely and was accompanied by specific changes in appearance, a significant increase in testosterone level, gonadotropic hormone suppression, and secondary erythrocytosis.

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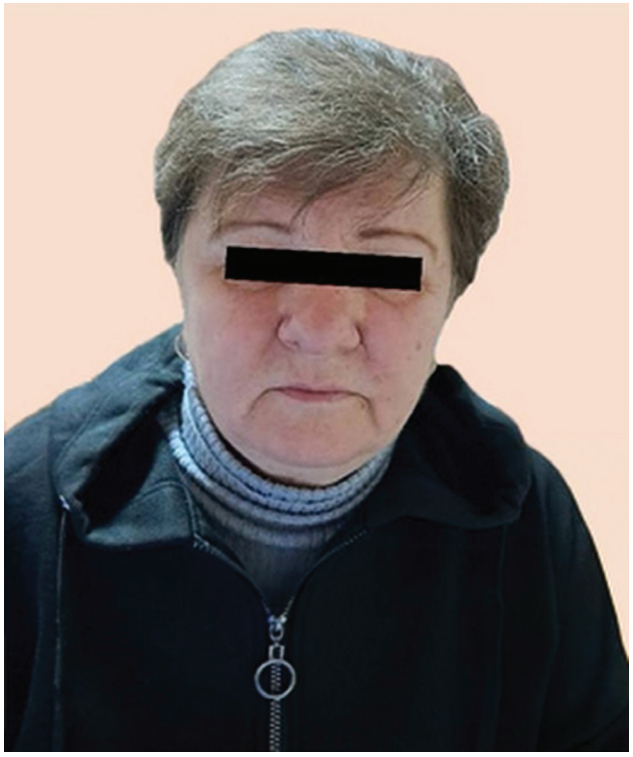

Figure 4: The patient's appearance 6 months after surgery.

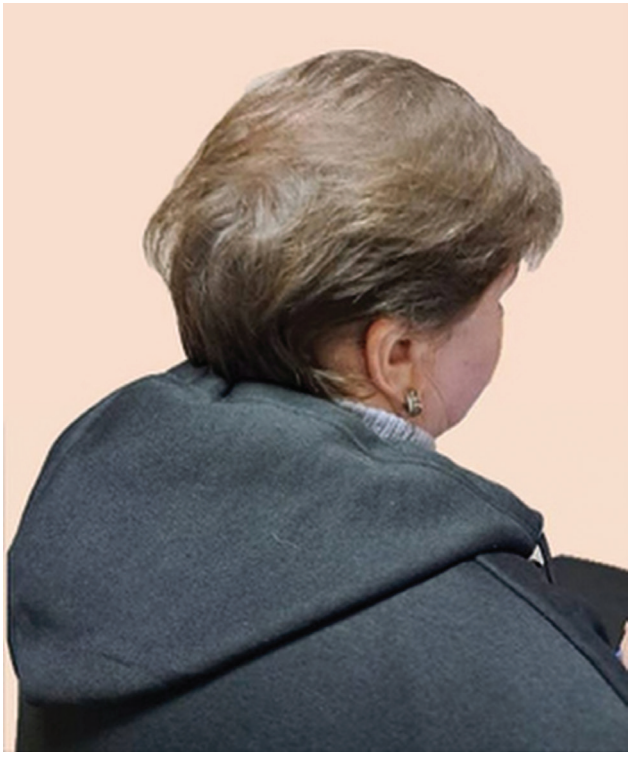

Figure 5: Increased hair growth on the scalp.

A differential diagnosis was made with Cushing's syndrome, polycystic ovary syndrome, congenital adrenal hyperplasia, and ovarian stromal hyperthecosis. The diagnosis of Cushing's syndrome was excluded based on the patient's lack of cushingoid appearance and a positive 1 mg-overnight dexamethasone suppression test. Polycystic ovary syndrome (POS) is the most common cause of hyperandrogenism, its clinical symptoms develop during the reproductive period of a woman's life [8]. Our patient during the reproductive period had no symptoms of ovarian dysfunction and did not have specific ultrasound symptoms of polycystic ovaries. The hormonal status of a postmenopausal patient with POS is characterized by gonadotropic hormones increased, unlike our patient. The nonclassic congenital adrenal hyperplasia also manifests as hirsutism and menstrual

Table 1: Laboratory parameters of the patient.

Laboratory test	Unit	Basal value	6 months after surgery value	Normal value
Hemoglobin	g/l	183	147	118–150
Red blood cells	1012/L	6.18	4.7	4.0–5.0
Hematocrit	%	52	40	36–42
Glycosylated hemoglobin	%	6.9	6.7	7
Total testosterone	nmol/l	57.2	1.63	<1.7
Dehydroepiandrosterone sulfate	µg/dl	107.9	ND	26–200
17-OH progesterone	ng/ml	3.13	0.5	0.13–0.51
FSH	IU/l	2.0	14.3	21.7–153
LH	IU/l	0.07	12.6	15.9–54
Cortisol (1 mg-overnight dexamethasone suppression test)	µg/dl	0.7	ND	<1.8
CA-125	U/ml	<20	ND	<30

Note: FSH – follicle stimulating hormone; LH – luteinizing hormone; CA-125 – cancer antigen 125; ND – not done.

dysfunction during puberty [5]. Ovarian stromal hyperthecosis is accompanied by hirsutism, virilization, obesity, and insulin resistance, which our patient has. As a rule, ovarian stromal hyperthecosis is characterized by symmetric bilateral ovarian enlargement with an increase in ovarian stroma; the diagnosis is confirmed by postoperative histological examination [9]. The patient had the asymmetrical left ovary enlargement with a solid hypoechoic lesion; pathohistological examination confirmed the Leydig cell ovarian tumor presence.

Mild clinical signs of hyperandrogenism may appear in women during menopause [10]. In case of acute virilization, it is necessary to check a source of androgen hypersecretion. Testosterone and dehydroepiandrosterone evaluation is principal for diagnostical tools between ovaries and adrenal glands pathology. Based on the obtained hormonal parameters, it is important to focus on the appropriate imaging methods – computed tomography, magnetic resonance imaging, and ultrasound of ovarian or adrenal glands. In patients with ovarian forms of postmenopausal hyperandrogenism differential diagnosis between androgen-producing tumors and ovarian stromal adenomatosis should be made. However, in both cases, the treatment method is bilateral oophorectomy [1, 11, 12]. Postoperative histological examination can be crucial in making a diagnosis [9]. The detection of histological features such as the clustering of cells with homogeneous morphology and the presence of Reinke crystals in their cytoplasm are decisive for the diagnosis of a Leidig cell tumor [13]. Moreover, immunohistochemical markers, such as positive staining for inhibin, calretinin, and steroidogenic factor-1, are also helpful in diagnosis [13].

Leydig cell tumors are rare neoplasias arising from ovarian stromal tissue with endocrine manifestations. This pathology, in combination with diabetes mellitus, arterial hypertension, and secondary erythrocytosis can lead to cardiovascular risks. Correct diagnosis and treatment require interaction between an endocrinologist, gynecologist, oncologist, and pathologist.

Conclusion

This case highlights the importance of thorough hormonal evaluation, appropriate imaging, and histological confirmation for accurate diagnosis. Leydig cell tumors, though rare, can have significant systemic implications, including increased cardiovascular risk. Effective management requires interdisciplinary collaboration and typically involves bilateral oophorectomy.

Conflict of interest

The authors declare no conflict of interest.

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