J Surg Med. 2018;2(3):374-376.
DOI: 10.28982/josam.424326

Journal of Surgery and Medicine
e-ISSN: 2602-2079

A case of postmenopausal ovarian hyperandrogenemia diagnosed only by selective catheterization of ovarian vein

Ovaryen venlerin selektif kateterizasyonu ile tanı alan bir postmenapozal ovaryen hiperandrojenemi vakası

Vedat Uğurel [1], Mehmet Musa Aslan [2], Koray Elter [1]

[1] Trakya University, Faculty of Medicine, Department of Gynecology and Obstetrics, Edirne, Turkey
[2] Muş State Hospital, Department of Gynecology and Obstetrics, Muş, Turkey

ORCID ID of the authors
VU: 0000-0002-1307-4688
MMA: 0000-0002-7830-5002
KE: 0000-0001-7143-6037

Corresponding author / Sorumlu yazar:
Mehmet Musa Aslan
Address / Adres: Muş Devlet Hastanesi, Kadın Hastalıkları ve Doğum Kliniği, Muş, Türkiye
e-Mail: jinopdrmma@gmail.com

Informed Consent: The author stated that the written consent was obtained from the patient presented in the study.
Hasta Onamı: Yazar çalışmada sunulan hastadan yazılı onam alındığını ifade etmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

06 – 09 Mart 2016 tarihleri arasında Grand Yazıcı Otel Uludağ'da gerçekleştirilen 1.Üreme Endokrinolojisi ve İntertilite Akedemisi 6. Jinekolojik Endoskopi Sempozyum ve Çalıştayında bildiriri olarak sunulmuştur

Received / Geliş tarihi: 17.05.2018
Accepted / Kabul tarihi: 25.06.2018
Published / Yayın tarihi: 25.06.2018

Abstract

Hyperandrogenemia in a postmenopausal woman is usually related to a tumor in either ovaries or adrenal glands. To differentiate between these two endocrine organs is a diagnostic challenge when the tumor size is too small to be detected with the aid of usual imaging modalities. 54 years-old postmenopausal woman with signs of virilization was referred to our institution with serum total testosterone levels of 294 ng/dl. Contrast-enhanced computed tomography (CT) revealed a lesion consistent with the tumor 1 cm in diameter in the adrenal gland and magnetic resonance imaging (MRI) could not confirm this finding. The location of androgen hypersecretion could only be determined after selective venous catheterization and hormonal sampling of both adrenal and ovarian veins. The right ovarian venous total testosterone level was found as > 1009.40 ng / dl. A right-sided ovarian Leydig cell tumor was diagnosed in the specimen of laparoscopic hysterectomy and bilateral salpingo-oopherectomy. This case report underlines the importance to carry on the search with the selective venous catheterization and hormonal sampling from both the ovarian and the adrenal veins when there is difficulty to demonstrate the true source of androgen hypersecretion in a postmenopausal woman.

Keywords: Postmenopause, Hyperandrogenism, Ovarian Neoplasms, Leydig cell tumor, Selective venous catheterization

Öz

Postmenapozal dönemde hiperandrojenemi genellikle over veya adrenal bezlerdeki tümörlerle ilişkilidir. Her iki endokrin organdaki tümörlerin çapları çok küçük olduğunda görüntüleme yöntemleri tanıda yetersiz kalmaktadır. 54 yaşında postmenapozal hasta, klitoromegali ve artış gösteren hirsutizm bulguları olan hasta serum total testosteron seviyesi 294 ng/dl ile bölümümüze başvurdu. Kontrastlı bilgisayarlı tomografide (BT) adrenal bezde 1 cm çapında tümör ile uyumlu lezyon saptandı ancak manyetik rezonans (MR) ile bu bulgu teyit edilemedi. Androjen hipersekresyonunun orijininin tespit edilememesi üzerine bilateral ovaryen ve adrenal venlerin selektif venöz kateterizasyonu ve hormonal örneklemesi yapıldı. Sağ ovaryan ven total testosteron düzeyi >1009,40 ng/dl olarak bulundu. Laparoskopik histerektomi ve bilateral salpingooferektomi yapılan hastanın patoloji sonucu sağ over kaynaklı Leydin Hücreli Tümör olarak geldi.

Bu olgu sunumunda, postmenopozal bir kadında androjen hipersekresyonu kaynağını bulunamadığında , hem ovaryen venden hem de adrenal venlerden selektif venöz kateterizasyon ve hormonal örnekleme yapmanın önemi vurgulanmaktadır.

Anahtar kelimeler: Postmenopoz, Hiperandrojenizm, Yumurtalık Neoplazmaları, Leydig hücreli tümör, Selektif venöz kateterizasyon

Introduction

Androgens in premenopausal women are synthesized in the ovaries, adrenal glands and from the peripheral conversion of dehydroepiandrosterone sulfate (DHEA-S), dehydroepiandrosterone (DHEA) and androstenedione (A). Serum concentrations of potent androgens, namely testosterone (T) and dihydrotestosterone (DHT) are low compared to the precursor hormones of DHEA-S, DHEA and A [1]. A half of serum T is produced from the peripheral conversion of A. The remaining 50% is split between the ovaries and the adrenal glands with equal contribution [2]. Although adrenal androgen production declines after the third decade of life to a nadir between 70 to 80 years of age, ovarian T production remains constant after natural menopause.

Hyperandrogenism is the most common endocrinopathy during the reproductive period with a prevalence of 5-10%. Polycystic ovary syndrome comprises 82% of cases as the most common cause whereas androgen-secreting neoplasms make up only 0.2% of cases [3].

How to cite / Atıf için: Uğurel V, Aslan MM, Elter K. A case of postmenopausal ovarian hyperandrogenemia diagnosed only by selective catheterization of ovarian vein. J Surg Med. 2018;2(3):374-376.

However in postmenopausal women, hyperandrogenism with recently developed and rapidly progressing clinical signs might indicate the presence of a tumor more than so in the reproductive age women.

After the exogenous causes of androgen excess are ruled out the attention is directed to find out the exact location of endogenous androgen hypersecretion to determine the type of surgical operation. Although transvaginal ultrasound, computed tomography or magnetic resonance imaging (MRI) might sometimes demonstrate a tumor, a small lesion of less than 2 cm is usually difficult to be detected [4]. Selective venous catheterization and hormonal sampling (SVCHS) of at least four venous vessels (bilateral ovarian-adrenal veins) might help to confirm the presence of an androgen producing tumor either in the ovary or adrenal gland and its laterality [5]. We report a case of postmenopausal virilizing 1.5 cm Leydig cell tumor on the right ovary which could only be diagnosed after the selective catheterization of the adrenal and ovarian veins.

Case presentation

A 54-year-old, postmenopausal woman (gravida:2) was referred to our department with symptoms of worsening hirsutism and clitoromegaly for 1 year. She was in menopause for 17 years. On admission, Ferriman–Gallwey score of hirsutism was 18 (Figure 1). She had a bitemporal alopecia and a cliteromegaly of 3.5 cm in length (Figure 2).

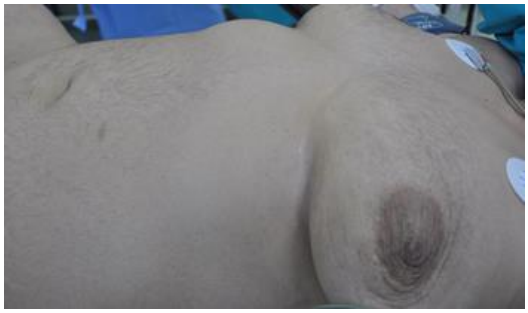

Figure 1: Ferriman–Gallwey score of hirsutism was 18

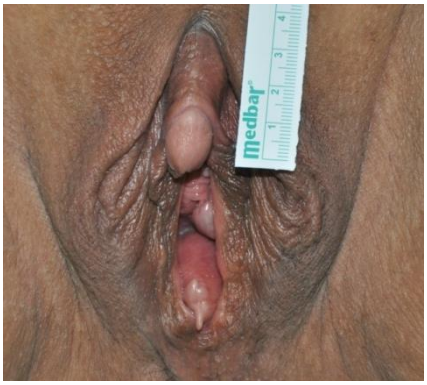

Figure 2: Cliteromegaly of 3.5 cm in length

She reported that she was aggressive and had mood swings but did not disclose her sexual history. The patient was class II obese (body mass index 37 kg/m2) and hypertensive (arterial blood pressure 140/90). She had a history of diabetes mellitus and hypothyroidism and was on metformin 1000 mg and levothyroxin 50 µg treatment for 3 years. Family history was negative for hirsutism or other hyperandrogenism signs.

Laboratory evaluation revealed substantially elevated levels of serum total testosterone (Total T 294 ng/dl [normal values 13-108 ng/dl]) and elevated postmenopausal-range follicle-stimulating hormone (FSH 85.1 mlU/ml) and luteinizing hormone (LH 31.9 mlU/ml) values. Serum estradiol level was undetectable. Androstenedion, Cortisol, Sex Hormone Binding Globulin, Adrenocorticotropic Hormone, DHEA-S, 17α-hydroxyprogesterone levels were in normal ranges. Serum cortisol was suppressed after the 1-mg overnight dexamethasone suppression test.

Because the transvaginal ultrasonography of both ovaries failed to demonstrate any tumor, we proceeded to other imaging modalities. The contrast-enhanced CT scan of the abdomen and pelvis demonstrated a nodule of low density approximately 1 cm in diameter with no distinct borders at the lateral crus of the left adrenal gland. The radiology department suggested ordering an MRI scan to further investigate the suspected adrenal tumor but the upper and lower abdominal MRI was negative for any lesion including both the ovaries and adrenal glands. PET/CT of the patient was reported to show no FDG uptake in any body parts but as expected, low FDG affinity malignant disorders could not be excluded.

A decision to perform SVCHS (Figure 3) was taken upon the inability to find the location of androgen hypersecretion and the rapid rise of total testosterone level up to 518 ng/dl until the aforementioned imaging studies were completed. The venous sampling results of five vessels are shown in Table 1. Total laparoscopic hysterectomy and bilateral salpingo-oophorectomy was performed and the uterus and ovaries were sent for pathologic diagnosis (Figure 4).

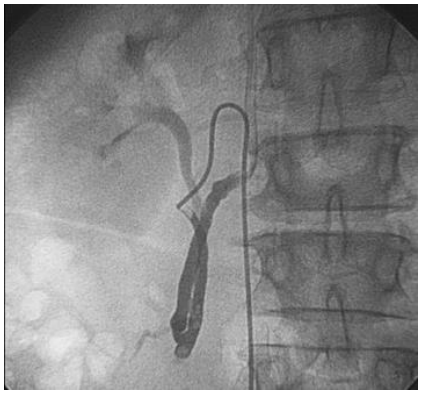

Figure 3: Selective venous catheterization and hormonal sampling

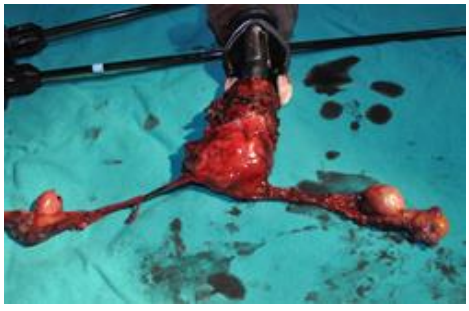

Figure 4: Total laparoscopic hysterectomy and bilateral salpingo-oophorectomy specimen

Table 1: Serum TT and DHEA-S levels of the samples 5 catheterized veins.

	ROV	LOV	IVC	RRV	LRV
TT (ng/dl)	>1009.40	334.39	390.31	284	402.57
DHEA-S (µg/dl)	40.2	38.1	41.2	39.9	41.2

TT: Total testosterone, DHEA-S: Dehydroepiandrosterone sulfate, ROV: Right ovarian vein, LOV: Left ovarian vein, IVC: Inferior vena cava, RRV: Right renal vein, LRV: Left renal vein

The dimension of the right ovary on pathologic examination was 3x2x2 cm and it was noted that there was a 1.5 cm brown-yellow solid tumor on cross-section. The left ovary was 2x1.5x1.5 cm with nonspecific findings.

Immunohistochemical evaluation of the right ovarian tumor was positive for inhibin, calretinin, vimentin and 1-3 % positive for Kİ-67 but negative for CK7, CEA and AFP.

Microscopic examination revealed the eosinophilic cytoplasm and the low mitotic index of 1-2% of the tumor. The final diagnosis was an ovarian Leydig cell tumor less than 1 mm close but not reaching to the ovarian cortex.

Discussion

Virilization in a postmenopausal woman almost always indicates a serious endocrinopathy related to a tumor. The diagnostic work-up is directed to discern the source of hypersecretion between two paired endocrine organs, the ovaries and the adrenal glands.

Ovarian sex cord-stromal tumors are a rare group of neoplasms comprising only 1.2 % of all primary ovarian cancers [6]. They arise from the cells surrounding oocytes. They may secrete ovarian hormones and lead to signs of estrogen or androgen excess [7,8]. These neoplasms are classified as malignant but they generally demonstrate low-grade cytological abnormalities. Sertoli-Leydig cell type of sex cord-stromal tumors constitutes only 0.5 % of all ovarian tumors [9]. There is a predilection to be found in younger patients (the average age at diagnosis 25 years) than their epithelial counterparts which are the most common histologic type of ovarian cancer [10].

Tubular structures that produce androgens are the main histologic figures; hence they may lead to rapidly progressing virilization [11]. Because sex cord-stromal tumors are diagnosed at an early stage and rarely metastasize to lymph nodes, total abdominal hysterectomy and bilateral salpingo-oopherectomy is the preferred surgical intervention in postmenopausal patients. The diameter of these tumors range from 1 to 50 cm with an average size of 13 cm. Small sized tumors may escape detection with transvaginal ultrasound. As in our case, CT or MRI findings may indicate the suspected presence of an adrenal lesion which is not the source of androgen hypersecretion and may fail to demonstrate the ovarian tumor. In this case the final management may differ and the patient might even be operated for a ghost adrenal tumor. Due to the low grade nature of these neoplasms, PET/CT may not demonstrate the presence of an active FDG (Floro 2 Deoksi Glukoz) uptake by the tumor [10,11].

More sophisticated diagnostic methods are required to sample the venous blood to differentiate the origin. Some researchers favor the use of SVCHS, but also point out its low feasibility, the need for expertise and the high failure rate of catheterization as drawbacks. SVCHS is not recommended to be performed routinely for the investigation of hyperandrogenic women but in the presence of a small ovarian tumor when all endocrinologic studies and imaging results fail, it should be kept in mind as a last resort for definitive diagnosis [4].

Hyperandrogenemia with signs of virilization in a postmenopausal woman might be due to an androgen secreting ovarian tumor which might be too small to be detected by imaging techniques including high resolution transvaginal ultrasound, contrast-enhanced CT or MRI. Moreover, the presence of an adrenal tumor might be over-reported by the radiologist under the pressure to find a focus [8-11].

This case report underlines the importance to carry on the search with selective venous catheterization and hormonal sampling from both the ovarian and the adrenal veins to demonstrate the true source of androgen hypersecretion.

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