Rare case of testosterone producing serous cystadenoma

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Abstract

Postmenopausal virilization and symptoms of hyperandrogenism can be attributed to tumorous or nontumorous causes. Androgen secreting tumors can arise from either the ovarian sex cord/stromal cells or from the adrenal glands. Cystadenomas are relatively benign ovarian epithelial tumors that have rarely been implicated as the cause of hyperandrogenism. Histologically these tumors are classified as mucinous or serous. We present here a case of a 60-year-old postmenopausal female with symptoms of hyperandrogenism including hirsutism and virilization for one year. Labs were significant for high total testosterone levels persistently. On imaging, our patient was found to have a left adnexal cyst, which was subsequently removed and found to be of serous histology. Upon removal of the cyst, patients’ total testosterone levels normalized. Our case highlights the importance of including cystadenomas in the differentials when evaluating for tumorous causes of hyperandrogenism.

INTRODUCTION

Hyperandrogenism in postmenopausal women is difficult to diagnose due to the normal hormonal changes associated with aging. Rapid onset and progression of hyperandrogenism symptoms should raise concern for a possible tumorous source. Androgen secreting tumors can arise from either the adrenal glands or ovaries. Clinical manifestations include hirsutism, acne, anabolic appearance, androgenic alopecia, deepening of the voice and virilization [1]. The predominant androgens found in women are testosterone, dihydrotestosterone, dehydroepiandrosterone (DHEA) and dehydroepiandrosterone sulfate (DHEAS). High testosterone levels but normal DHEA and DHEAS levels indicate an ovarian origin for the increased androgens [2]. Most androgen secreting tumors of the ovaries arise from sex cord cells (thecal/granulosa) that surround the oocyte or from stromal cells. Androgen secreting adrenal tumors are commonly carcinomas, that secrete cortisol, resulting in women presenting with Cushingoid symptoms as well. Cystadenomas, tumors arising from the ovarian epithelium, account for 60% of ovarian tumors. They are usually benign adnexal masses further classified into serous or mucinous types [1]. Cystadenomas can secrete beta-human chorionic gonadotropin (beta-hCG), which can possibly stimulate androgen secretion resulting in virilization [3]. Very few reports have been published over time citing these benign adenomas as the cause of virilization in postmenopausal women. We present a rare case of a testosterone producing serous cystadenoma in a postmenopausal female.

CASE REPORT

A 60-year-old postmenopausal female, with only a past medical history of total abdominal hysterectomy 20 years ago due to uterine fibroids, presented to the gynecology clinic for clitoral enlargement, hirsutism, deepening of voice, decreased sexual drive and increasing abdominal circumference for 1 year. Chemistry showed Creatinine 0.90, Blood urea Nitrogen (BUN) 15, Glomerular filtration rate 70. Hepatic function panel revealed alkaline phosphatase 99, Alanine Transaminase (ALT) 19, Aspartate Transaminase (AST) 21. All unchanged from baseline labs 1 year ago. Lipid panel revealed normal cholesterol levels but an elevated LDL of 108. TSH was within normal limits. Pelvic ultrasound revealed an anechoic, nonvascular, cystic lesion measuring 10.5 × 5.9 × 6.2 cm in the left adnexa (Fig. 1).

A computed tomography (CT) scan of the abdomen and pelvis was subsequently ordered and confirmed the ultrasound findings of a cystic left adnexal mass and of importance, no adrenal mass was noted (Fig. 2). No abnormality was noted in the gastrointestinal tract. The stomach, liver, spleen and colon were unremarkable with no evidence of obstruction or abnormal growth.

Initial workup for hyperandrogenism revealed a normal free testosterone level of 4.2 pg/ml but an elevated total testosterone 264.3 ng/dl level. Further workup...
showed DHEA-S 29.2 ug/dl, CA-125 5 U/ml, Inhibin-A 1 pg/ml; all within the normal limits. The patient was scheduled for a repeat transvaginal ultrasound (TVUS) in 3 months for monitoring of the left adnexal cyst. Repeat TVUS showed no change in adnexal cyst size or characteristics but persistence of the hyperandrogenism symptoms. The patient was then referred to endocrinology clinic for further evaluation. Patient endorsed similar symptoms as before in the endocrinology clinic. Baseline labs were repeated again. Chemistry revealed unchanged with normal Creatinine, BUN, Glomerular Filtration Rate—indicating kidney function (GFR) and electrolytes. CBC also remained unremarkable, with no changed in baseline hemoglobin, hematocrit or white blood cells. Hemoglobin a1c was obtained, found to be 5.8. Hepatic functional panel also remained unchanged from before, with no elevation in bilirubin, alkaline phosphatase or ALT/AST. HIV and Hepatitis B workup was negative for the patient. Repeat lipid panel showed elevation in LDL (116) and triglycerides (178). The initial workup for hyperandrogenism was repeated. Repeat labs showed a slight elevation of free testosterone 4.7 pg/ml with continued elevated total testosterone of 276 ng/dl. Follicle Stimulating Hormone (FSH) (41.7 IU/L) and Leutinizing Hormone (LH) (26.6 IU/L) levels were within the normal limits for postmenopausal women. Fasting 8 am cortisol level was suppressed (1.0 ug/dl). DHEA, Estradiol and DHEA-S were within normal limits again. The patient had another TVUS that showed a slight increase in the adnexal mass, now measuring 11.7 x 5.5 x 8.3 cm. After a multidisciplinary meeting, including endocrinology, gynecology and gynecology-oncology, the patient was scheduled for a laparoscopic bilateral salpingo-oophorectomy. Surgical pathology report showed a serous cystadenoma of the left ovary. Repeat total testosterone levels, post-operative, returned to normal levels with gradual resolution of symptoms.

DISCUSSION

Hyperandrogenism in postmenopausal women is usually attributed to tumorous causes. Androgen secretion normally declines gradually with aging, with levels rarely higher than premenopausal women. These levels can usually cause mild hyperandrogenism symptoms, including decrease in scalp hair and presence of facial hair. Development of severe hirsutism along with symptoms of virilization (clitoromegaly, deepening of voice and male pattern baldness) usually indicate a tumorous origin of such symptoms. These tumors can arise from the adrenal gland or the ovaries. Elevation of the specific type of androgen, whether testosterone, DHEA or DHEAS helps to delineate the source. Androgen secreting adrenal tumors usually secrete cortisol and androgens simultaneously. These tumors are rare and usually carcinomatous in origin. Testosterone production from an adrenal origin is extremely rare. Zhou et al. published a case report of a purely testosterone-secreting adrenal tumor with no concomitant rise in DHEA or DHEAS. Such tumors are hypothesized to arise from translocation of gonadal cells or differentiation of adrenal cells into Leydig cells. Ovarian epithelial tumors are predominantly benign tumors, with very few cases citing cystadenomas as the cause of hyperandrogenism in postmenopausal women. Most cases of hyperandrogenism are reported in pregnant or women of reproductive age. Goudas et al. published a case in 1996 of an ovarian cyst as the cause of high testosterone levels in a postpartum female. Nizam et al. published a case report in 2021 attributing a mucinous cystadenoma as the source of postmenopausal virilization. In our report, postmenopausal virilization due to elevated testosterone is attributed to a cystadenoma of serous histology. Transformation of nonfunctional cystadenomas into androgen secreting tumors is not clear. High LH levels causing excessive stromal stimulation is a possible...
cause of such transformation, though in our case, LH levels were within normal limits. Another proposed mechanism is the stimulation of ovarian stromal cells by increased blood flow due to the large size of these tumors. Production of antibodies that mimic the effect of LH is another hypothesis. Secretion of hormones including beta-hCG is another possible mechanism that may cause these nonfunctional tumors to start producing testosterone [3, 4]. Evaluation of a patient with signs and symptoms of excess androgen requires thorough history taking, physical examination and diagnostic workup. In our case, initial imaging showed a relatively benign appearing cystic lesion which was later found to be the source of the excess testosterone. Adrenal causes were ruled out by CT imaging and normal DHEA/DHEA-S levels. Serial monitoring and a multidisciplinary approach are critical to efficient management of such cases. As shown in our case, prophylactic bilateral salpingo-oopherectomy proved to be beneficial and curative for our patient.

CONCLUSION
We presented a rare case of serous cystadenoma producing testosterone in an elderly female. Prior cases reported such clinical scenario in women of reproductive age, whereas this is a rare case reported in an elderly woman. Clinicians should keep it as a differential in elderly women presenting with rapid onset hirsutism and virilization.

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CONFLICT OF INTEREST STATEMENT
No conflicts of interest.

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ETHICAL APPROVAL
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CONSENT
Written consent was obtained from patient to publish the case.

GUARANTOR
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