New-onset hirsutism

This postmenopausal patient developed hirsutism following a surgical procedure. Thorough lab work directed us to the unusual cause.

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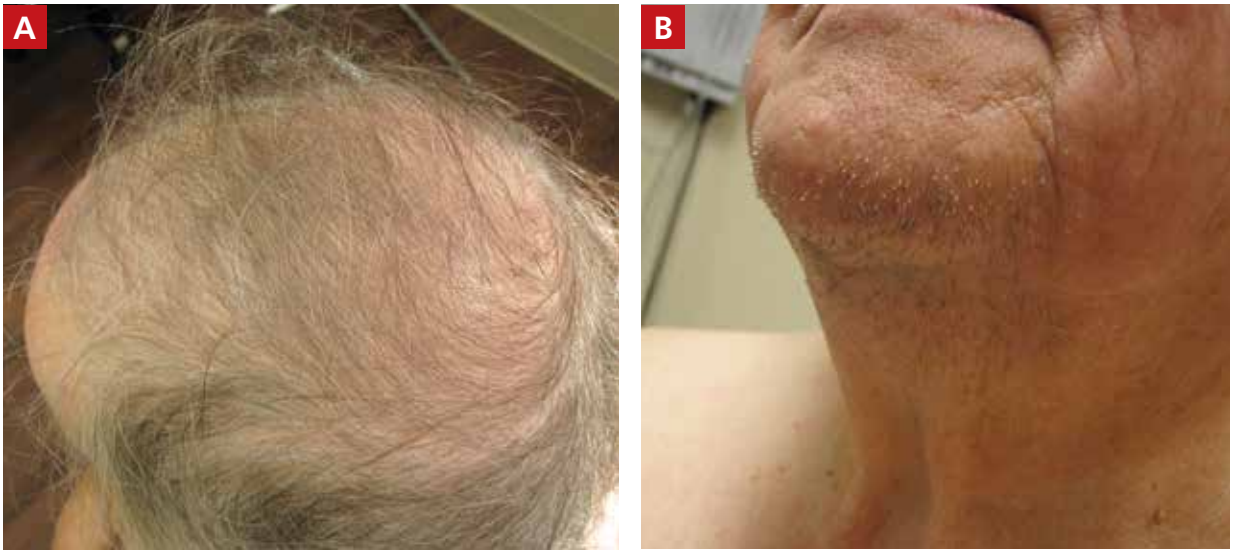
A 74-YEAR-OLD WOMAN presented to the dermatology clinic for follow-up 3 months after the surgical excision of a basal cell carcinoma on her left jawline. During this postop period, the patient developed new-onset hirsutism. She appeared to be in otherwise good health.

Family and personal medical history were unremarkable. Her medication regimen included aspirin 81 mg/d and a daily multivitamin. The patient was postmenopausal and had a body mass index of 28 and a history of acid reflux and osteoarthritis.

Physical examination of the patient's scalp showed male-pattern alopecia (**FIGURE 1A**). She also had coarse terminal hairs on her forearms and back, as well as on her chin (**FIGURE 1B**).

- WHAT IS YOUR DIAGNOSIS?
- HOW WOULD YOU TREAT THIS PATIENT?

FIGURE 1
Virilization with male-pattern balding (**A**) and coarse terminal hairs of the chin (**B**)



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Hirsutism is more often associated with adrenal or ovarian tumors in postmenopausal patients.

Dx: Androgen-secreting ovarian tumor

Based on the distribution of terminal hairs and marked change over 3 months, as well as the male-pattern alopecia, a diagnosis of androgen excess was suspected. Laboratory work-up, including thyroid-stimulating hormone, dehydroepiandrosterone sulfate (DHEAS), follicle-stimulating hormone, luteinizing hormone, prolactin, complete blood count, and complete metabolic panel, was within normal limits. Pelvic ultrasound of the ovaries and abdominal computed tomography (CT) of the adrenal glands were also normal.

Further testing showed an elevated testosterone level of 464 ng/dL (reference range: 2-45 ng/dL) and an elevated free testosterone level of 66.8 ng/dL (reference range: 0.2-3.7 ng/dL). These levels pointed to an androgen-secreting ovarian tumor; the androgen excess was likely the cause of her hirsutism.

Hirsutism or hypertrichosis?

Hirsutism, a common disorder affecting up to 8% of women, is defined by excess terminal hairs that appear in a male pattern in women due to production of excess androgens.[1] This should be distinguished from hypertrichosis, which is generalized excessive hair growth not caused by androgen excess.

Testosterone and DHEAS—produced in the ovaries and adrenal glands, respectively—contribute to the development of hirsutism.[1] Hirsutism is more often associated with adrenal or ovarian tumors in postmenopausal patients.[2] Generalized hypertrichosis can be associated with porphyria cutanea tarda, severe anorexia nervosa, and rarely, malignancies; it also can be secondary to certain agents, such as cyclosporin, phenytoin, and minoxidil.

While hirsutism is associated with hyperandrogenemia, its degree correlates poorly with serum levels. Notably, about half of women with hirsutism have been found to have normal levels of circulating androgens.[1] Severe signs of hyperandrogenemia include rapid onset of symptoms, signs of virilization, and a palpable abdominal or pelvic mass.[3]

Is the patient pre- or postmenopausal? Polycystic ovary syndrome (PCOS) accounts for up to three-fourths of premenopausal hirsutism.[3] The likelihood of hirsutism is actually decreased in postmenopausal women because estrogen levels can drop abruptly after menopause. That said, conditions linked to hirsutism in postmenopausal women include adrenal hyperplasia, thyroid dysfunction, Cushing syndrome, and least frequently, androgen-secreting tumors (seen in this patient). (Hirsutism can also be idiopathic or iatrogenic [medications].)

Methods for detection

Research suggests that when a female patient is given a diagnosis of hirsutism, it's important to explore possible underlying ovarian and/or adrenal tumors and adult-onset adrenal hyperplasia.[1] The following tests and procedure can be helpful:

Serum testosterone and DHEAS. Levels of total testosterone > 200 ng/dL and/or DHEAS > 700 ng/dL are strongly indicative of androgen-secreting tumors.[1]

Imaging—including ultrasound, CT, or magnetic resonance imaging—can be used for evaluation of the adrenal glands and ovaries. However, imaging is often unable to identify these small tumors.[4]

Selective venous catheterization can be useful in the localization and lateralization of an androgen-secreting tumor, although a nondiagnostic result with this technique is not uncommon.[4]

Dynamic hormonal testing may assist in determining the pathology of disease but not laterality.[2] For example, testing for gonadotropin-releasing hormone agonists can be helpful because the constant administration of such agonists can lead to ovarian suppression without affecting adrenal androgen secretion.[5]

Testing with oral dexamethasone may induce adrenal hormonal depression of androgens and subsequent estradiol through aromatase conversion, which can help rule out an ovarian source.[6] Exogenous administration of follicle-stimulating hormone or luteinizing hormone can further differentiate the source from ovarian theca or granulosa cell production.[4]

Treatment varies

The specific etiology of a patient's hirsutism dictates the most appropriate treatment. For example, medication-induced hirsutism of-

ten requires discontinuation of the offending agent, whereas PCOS would necessitate appropriate nonpharmacologic and pharmacologic interventions.

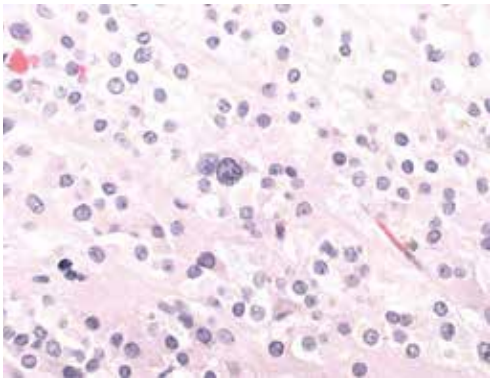
For our patient, the elevated testosterone and free testosterone levels with normal DHEAS strongly suggested the presence of an androgen-secreting ovarian tumor. These findings led to a referral for bilateral salpingo-oophorectomy. The surgical gross appearance of the patient's ovaries was unremarkable, but gross dissection and pathology of the ovaries (which were not postoperatively identified to determine laterality) showed one was larger (2.7 × 1.5 × 0.8 cm vs 3.2 × 1.4 × 1.2 cm).

The larger ovary contained an area of brown induration measuring 2.3 × 1.1 × 1.1 cm. This area corresponded to abundant eosinophilic cytoplasm with nuclear, rich, round-cell proliferation, consistent with the diagnosis of a benign ovarian Leydig cell tumor (**FIGURE 2**). Thus, the bilateral salpingo-oophorectomy was both diagnostic and therapeutic.

Six weeks after the surgery, blood work showed normalization of testosterone and free testosterone levels. The patient's hirsutism completely resolved over the course of the next several months. **JFP**

FIGURE 2

Pathology of the patient's ovarian Leydig cell tumor



Shown here is a high-power field view of the stromal tumor with abundant eosinophilic cytoplasm and nuclear, rich, round-cell proliferation.

References

1. Hunter M, Carek PJ. Evaluation and treatment of women with hirsutism. *Am Fam Physician*. 2003;67:2565-2572.
2. Alpañés M, González-Casbas JM, Sánchez J, et al. Management of postmenopausal virilization. *J Clin Endocrinol Metab*. 2012;97:2584-2588.
3. Bode D, Seehusen DA, Baird D. Hirsutism in women. *Am Fam Physician*. 2012;85:373-380.
4. Cohen I, Nabriski D, Fishman A. Noninvasive test for the diagnosis of ovarian hormone-secreting-neopolasm in postmenopausal women. *Gynecol Oncol Rep*. 2016;15:12-15.
5. Gandrapu B, Sundar P, Phillips B. Hyperandrogenism in a postmenaupsal woman secondary to testosterone secreting ovarian stromal tumor with acoustic schwannoma. *Case Rep Endocrinol*. 2018;2018:8154513.
6. Curran DR, Moore C, Huber T. What is the best approach to the evaluation of hirsutism? *J Fam Pract*. 2005;54:458-473.

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8. Pombo F, Rodríguez E, Mato J, et al. Patterns of contrast enhancement of tuberculous lymph nodes demonstrated by computed tomography. *Clin Radiol*. 1992;46:13-17. https://doi.org/10.1016/s0009-9260(05)80026-1
9. Chatha N, Fortin D, Bosma KJ. Management of necrotizing pneumonia and pulmonary gangrene: a case series and review of the literature. *Can Respir J*. 2014;21:239-245. https://doi.org/10.1155/2014/864159
10. Dursunoğlu N, Başer S, Evyapan F, et al. A squamous cell lung carcinoma with abscess-like distant metastasis. *Tuberk Toraks*. 2007;55:99-102.
11. Bartlett JG. The role of anaerobic bacteria in lung abscess. *Clin Infect Dis*. 2005;40:923-925. https://doi.org/10.1086/428586
12. Gudiol F, Manresa F, Pallares R, et al. Clindamycin vs penicillin for anaerobic lung infections. High rate of penicillin failures associated with penicillin-resistant Bacteroides melaninogenicus. *Arch Intern Med*. 1990;150:2525-2529.
13. Levison ME, Mangura CT, Lorber B, et al. Clindamycin compared with penicillin for the treatment of anaerobic lung abscess. *Ann Intern Med*. 1983;98:466-471. https://doi.org/10.7326/0003-4819-98-4-466
14. Fernández-Sabé N, Carratalà J, Dorca J, et al. Efficacy and safety of sequential amoxicillin-clavulanate in the treatment of anaerobic lung infections. *Eur J Clin Microbiol Infect Dis*. 2003;22:185-187. https://doi.org/10.1007/s10096-003-0898-2
15. Hammond JM, Potgieter PD, Hanslo D, et al. The etiology and antimicrobial susceptibility patterns of microorganisms in acute community-acquired lung abscess. *Chest*. 1995;108:937-941. https://doi.org/10.1378/chest.108.4.937
16. Marina M, Strong CA, Civen R, et al. Bacteriology of anaerobic pleuropulmonary infections: preliminary report. *Clin Infect Dis*. 1993;16(suppl4):S256-S262.https://doi.org/10.1093/clinids/16.supplement_4.s256