



THE UNIVERSITY OF
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MEDICINE &
BIOLOGICAL
SCIENCES

40-Year-Old Female with Elevated Testosterone Levels

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Endorama 4/10/2025

Patient Presentation

40-year female with history of PCOS, hirsutism and secondary amenorrhea

Patient established care with OBGYN on 12/2024 for routine GYN care found to have total testosterone of 750 ng/dL

TVUS showed no ovarian abnormality and an endometrial stripe of 7.5 mm.

Referred to Endocrinology for further work up for elevated testosterone levels

What are key questions would like to know about this patient?



History

- **Menstrual History:**

- Menarche: Age 9
- PCOS diagnosed at age 16
- -Regular menses until 15–16, then irregular (every 21 days → 2–4 months apart)
- Last period: Sept 18, 2024
- Prior to that: 3–5 year gap

- **Androgen-Related Symptoms:**

- Acne: None
- Skin Tags: Increased
- Hair Loss: Since May 2021
- Hirsutism: Started ~5 years ago (face, chest, torso, back)
- Voice Deepening: Present
- Clitoromegaly: Present
- Increased Muscle Mass: Denied (but sister notes back changes)
- Increased Libido: Present

- **Other Clinical Features:**

- No purple striae
- Hand grip weaker (has carpal tunnel)
- No easy bruising
- No history of hypertension
- Has prediabetes
- No history of increasing hat, ring, or shoe size



History

Medications

- Oral minoxidil: Never taken (used topical 1–2 years ago)
- No use of danazol, antiepileptics, anabolic steroids, or exogenous androgens
- No family members using topical androgens
- OCPs: Used from age 17 to mid-20s
- Spironolactone: Started within the past week

• Reproductive History:

- Never been pregnant
- Not interested in pregnancy

• Family History:

- Sister with PCOS
- Family history of breast cancer



Physical Exam

BP: BP 115/75 | Pulse 76 | Temp 36.3 °C (97.4 °F) Ht 165.1 cm (5' 5") | Wt (!) 145 kg (319 lb 9.6 oz) |
LMP 09/18/2024 | SpO2 97% | BMI 53.18 kg/m²

General: No apparent distress. Appears stated age.

HEENT: PERRL, EOMI.

Neck: No neck tenderness. No thyromegaly. No thyroid nodules appreciated.

Cardiovascular: Regular rate and rhythm. No peripheral edema.

Pulmonary/Chest: Clear to auscultation bilaterally.

Gastrointestinal: Soft, non-tender, non-distended. No rebound or guarding.

GU exam performed with chaperone present: **clitoromegaly present**

Musculoskeletal: normal range of motion of joints without deformities.

Neurological: Alert & oriented, no focal deficits, no proximal muscle weakness

Lymph: No cervical or supraclavicular lymphadenopathy.

Skin: **Male-pattern hair loss. Severe acanthosis nigricans present. Ferriman Galleway score of 34. No purpuric striae present. No ecchymosis. Oily skin.**

Psychiatric: Normal mood, thought content appropriate



Physical Exam



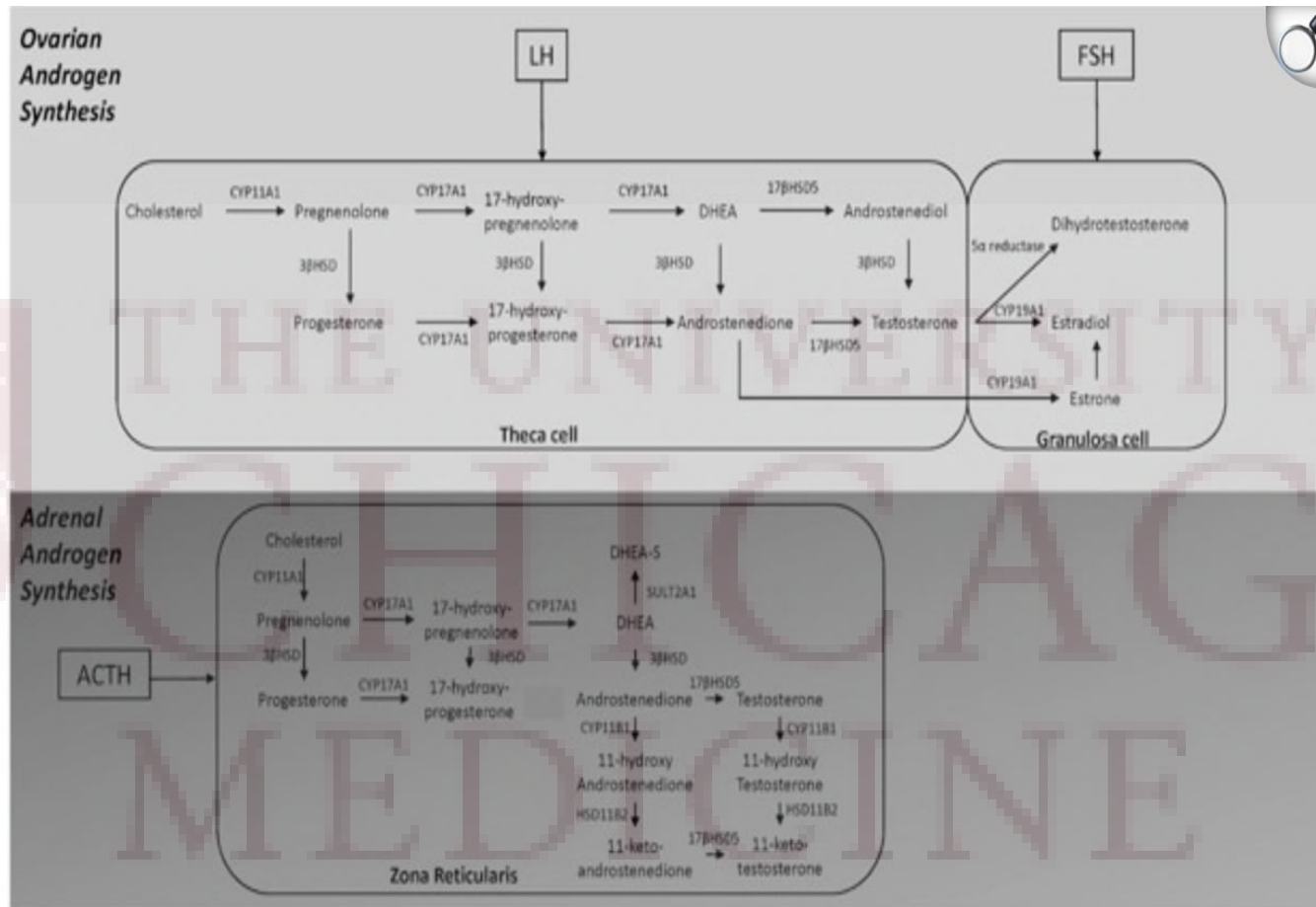
Physical Exam



Work up for Hyperandrogenism Labs and Imaging?

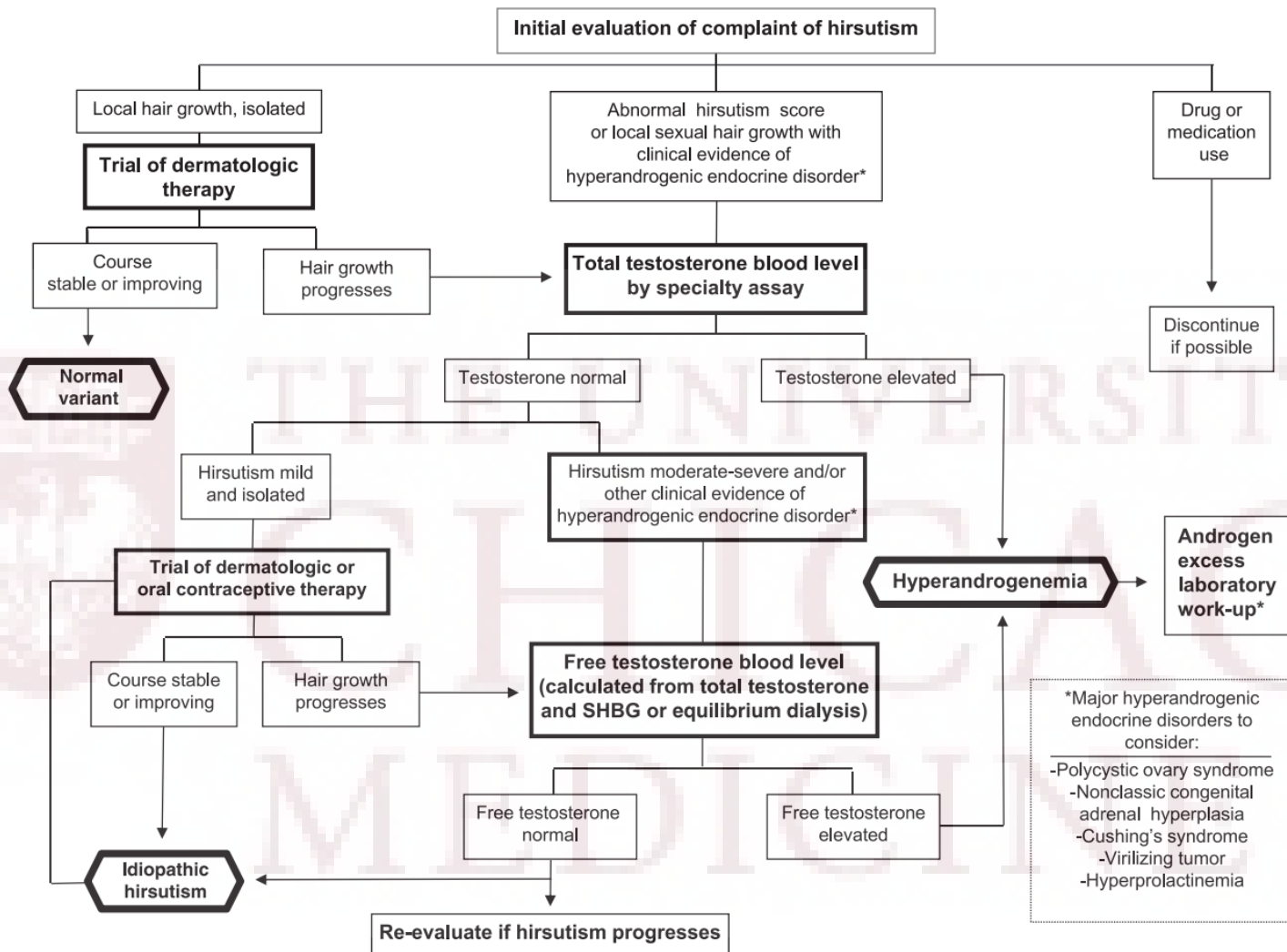


Androgen Synthesis in Women



A DHEA-S level above 700 mcg/dL suggestive an androgen-secreting adrenal tumor
Normal DHEA-S: helps localize the source to the ovary, not adrenal





Kathryn A Martin et al. Evaluation and Treatment of Hirsutism in Premenopausal Women: An Endocrine Society Clinical Practice Guideline, *The Journal of Clinical Endocrinology & Metabolism*, Volume 103, Issue 4, April 2018, Pages 1233–1257,



Patients Labs: Interpretation

	Latest Reference Range & Units
Estradiol, Serum	55
FSH	<0.3
LH	<0.3
Prolactin	4.80 - 23.30
Te Binding Globulin	17.00
Calculated Free Testosterone	30
Total Testosterone	277 (H)
DHEA-S	750 (H)
	130.0

	Latest Reference Range & Units
Thyroid Stimulating Hormone (TSH)	0.30 - 4.00 uIU/mL
	1.79

Salivary Cortisol, MS	0.022
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TVUS

Uterus is anteverted, enlarged in size, globular in contour and the myometrium is heterogenous in appearance. This may be suggestive of adenomyosis.

Endometrium measures 7.5 mm in thickness.

Cervix is normal in appearance.

Ovaries are normal in size and appearance. A simple, right para-ovarian cyst is seen as noted above - O-RADS2.

No free fluid is visualized in the cul de sac.

No prior ultrasound for comparison.



Imaging

CT Abdomen and Pelvis

- ADRENAL GLANDS: **No significant abnormality noted**
- RETROPERITONEUM, LYMPH NODES: Small shotty no pathologic size nodes. Retroperitoneal nodes nonpathological in size.

MRI Pelvis

- UTERUS, ADNEXA

Uterus is measuring 12.5 x 7.5 x 8.8 cm. The uterus is anteverted and anteflex. The junctional zone is preserved and there is no endometrial thickening, measuring up to 0.8 cm. There is normal preservation of the cervical low signal stroma with no discrete cervical mass. There are no fibroids identified. Following contrast, there is normal enhancement of the myometrium and cervix. The parametrium is normal.

Small nabothian cysts are noted.

Bilateral cystic lesions are noted in ovaries in the right side measuring 2.6 x 2.5 cm and in left side measuring 3 x 2.2 cm (7, 7), suggesting follicles. No solid suspicious lesion is noted.

PET Skull Base To Mid Thigh

- **A solid right adnexal lesion is markedly avid but nonspecific and may represent a corpus luteum cyst, however neoplasm cannot be excluded. Recommend follow-up ultrasound in 2 months.**
- An avid cutaneous focus in the proximal lateral right arm is favored to be inflammatory. Recommend further evaluation with direct inspection.
- Asymmetrically prominent soft tissue density deep to the right nipple is nonspecific.



Clinical Course

- PET scan 2/2025 consistent with hypermetabolic activity in the right ovary (patient without menses)
- Hypermetabolic activity localized to the right ovary
- No evidence of metastatic disease
- No bilateral ovarian involvement
- Seen by Dr. Yamada in Gyn Onc
- Recommended **conservative surgical management** based on clinical findings and patient's lack of desire for future childbearing
- Underwent right Salpingo-oophorectomy and left salpingectomy on 4/3/25



Pathology: Benign Leydig Cell Tumor

Final Diagnosis

A. Left ovarian adhesions; excision:

- Adhesions.

B. Left fallopian tube; left salpingectomy:

- Fallopian tube with cystic Walthard rests and focal thermal artifact.

C. Right fallopian tube and ovary; right salpingo-oophorectomy:

- Ovary with Leydig cell tumor (3.0 cm); see comment.
- Fallopian tube with paratubal cystadenoma (3.0 cm)

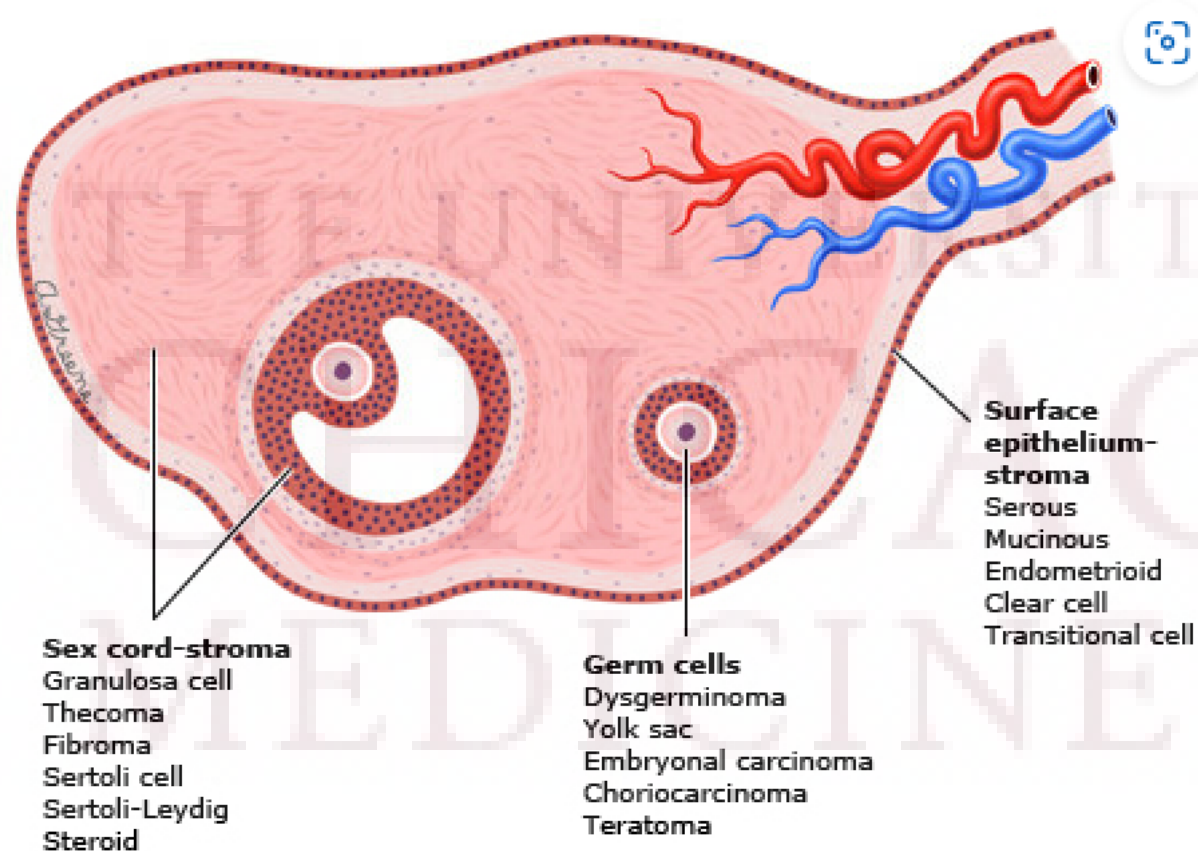
Comment

The right ovary contains a well-circumscribed, hilar-based mass composed of mildly to moderately atypical epithelioid cells with abundant eosinophilic cytoplasm. Occasional mitoses and multinucleated cells are seen. Nuclear clustering with eosinophilic nuclear-free zones and fibrinoid material within the vessel walls is present. No unequivocal Reinke crystals are identified. The morphology is consistent with a Leydig cell tumor, which are nearly always benign. The tumor is focally present at the inked surface.

Clinical Information



Origin of the various ovarian cancer subtypes and their sub-classifications



Sex Cord Stromal Tumors

Sex cord-stromal tumors
Pure stromal tumors
▪ Ovarian fibroma ▪ Thecoma ▪ Luteinized thecoma associated with sclerosing peritonitis ▪ Sclerosing stromal tumor ▪ Microcystic stromal tumor ▪ Signet-ring stromal tumor ▪ Leydig cell tumor ▪ Steroid cell tumor ▪ Ovarian fibrosarcoma
Pure sex cord tumors
▪ Adult granulosa cell tumor ▪ Juvenile granulosa cell tumor ▪ Sertoli cell tumor ▪ Sex cord tumor with annular tubules
Mixed sex cord-stromal tumors
▪ Sertoli-Leydig cell tumor ▪ Sex cord-stromal tumors NOS ▪ Gynandroblastoma

Incidence of SCSTs
0.2 per 100,000
females



Leydig Cell Tumor

- Rare sex cord-gonadal stromal tumor (<0.1% of ovarian tumors)
- 70–85% associated with androgen secretion → virilization, hirsutism
- Imaging:
 - Pelvic US/MRI: small, solid ovarian mass (<5 cm)
 - May be difficult to detect — biochemical clues are key
- Histology: Reinke crystals may be seen (not always present)
- Management:
 - Surgical removal (typically unilateral salpingo-oophorectomy)
 - Fertility-sparing surgery possible in younger patients
 - Hormonal symptoms resolve rapidly after removal
- Prognosis:
 - Excellent for benign tumors
 - Rare malignant transformation (<20% become malignant)



Role of Imaging of Adnexal Mass

High-Resolution TVUS:

- First-line imaging for **adnexal lesion evaluation**
- **High sensitivity and specificity**
- Limited in detecting fat or calcium within masses

CT Scan:

- **Poor** contrast resolution for adnexal structures
- **Excellent** at identifying **calcium- and fat-containing masses**
- Preferred for evaluating **adrenal tumors**

MRI:

- Superior **soft tissue characterization**
- Enhanced contrast resolution
- **Contrast-enhanced MRI** has higher **PPV & NPV** than TVUS for **androgen-secreting ovarian tumors**



Role of Imaging: Utility of PET/CT scans in detecting small LCTs

- It can be challenging to confirm the presence of a small ovarian tumor with conventional imaging modalities
- PET/CT scan can be a useful tool to detect it when the lesion is small.

The Hidden Source of Testosterone Hypersecretion in a Female—A 30-Year Journey

Almira J Yang , Iqbal Munir

JCEM Case Reports, Volume 2, Issue 3, March

<https://doi.org/10.1210/jcemcr/luae025>

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Case Report



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Science

Diagnosis of an indistinct Leydig cell tumor by positron emission tomography-computed tomography

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Follow Up & Next Steps

- Plan for repeat testosterone levels
- Schedule for follow up tomorrow 4/11/25 with Dr. Yamada



Summary: Learning points

- Virilizing ovarian tumors are rare but a clinically important diagnosis in a patient presenting with hyperandrogenism.
- Workup of hyperandrogenism is challenging with a broad range of differentials, including adrenal and ovarian pathology
- Small SLCT tumors could be challenging to localize by conventional imaging
- When conventional imaging modalities cannot localize the source of androgen hypersecretion, **PET should be considered.**



References

- Almira J Yang, Iqbal Munir, The Hidden Source of Testosterone Hypersecretion in a Female—A 30-Year Journey, *JCEM Case Reports*, Volume 2, Issue 3, March 2024, luae025,
- Kathryn A Martin, R Rox Anderson, R Jeffrey Chang, David A Ehrmann, Rogerio A Lobo, M Hassan Murad, Michel M Pugeat, Robert L Rosenfield, Evaluation and Treatment of Hirsutism in Premenopausal Women: An Endocrine Society Clinical Practice Guideline, *The Journal of Clinical Endocrinology & Metabolism*, Volume 103, Issue 4, April 2018, Pages 1233–1257
- Kong, Jinkyong, et al. "Diagnosis of an indistinct Leydig cell tumor by positron emission tomography-computed tomography." *Obstetrics & Gynecology Science* 62.3 (2019): 194.
- Sharma A, Welt CK. Practical Approach to Hyperandrogenism in Women. *Med Clin North Am*. 2021 Nov;105(6):1099-1116. doi: 10.1016/j.mcna.2021.06.008. Epub 2021 Sep 8. PMID: 34688417; PMCID: PMC8548673.



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