Unusual differential diagnosis of Hyperandrogenism in Adolescent female treated for Polycystic Ovarian Syndrome

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Background

Polycystic Ovarian Syndrome (PCOS) is the most common cause of oligomenorrhea and hyperandrogenism. Diagnostic criteria for PCOS includes ovarian dysfunction and clinical and/or biochemical evidence of hyperandrogenism. The differential diagnosis includes congenital adrenal hyperplasia as well as steroid producing tumors.

Clinical Case

18 year old female presented to the endocrine clinic for continuation of medical care for a prior diagnosis of PCOS after relocating from a different part of the country.

She initiated thelarche at 9, adrenarche at 10 and menarche at 11 years. She had oligomenorrhea, reporting only one menstrual period after menarche. Other clinical features she reported included hirsutism (hair on face, chest and back) and acne (chest, shoulders and back) and occasional right lower quadrant pain.

She was diagnosed with PCOS and was started on oral contraceptive pills (E2 + P), Spironolactone and Metformin since the age of 11 to 17 years. During the medical treatment, she reported monthly vaginal bleeding. She was off medications for 1 year before the clinic visit, without spontaneous resumption of menses and worsening hirsutism and acne.

She was born at term, uncomplicated pregnancy, normal birth weight and length. No family history of hyperandrogenism.

Physical Exam

Vital signs: BP 136/78, HR 64. Obese and Tall. Masculine features. Weight: 110.2 kg (99%), Height 174.5 cm (96%), BMI 36.19 kg/m2 (98%). Skin: acne with papules. Hair across upper lip, chin, abdomen. Dark chin pigmentation. Acanthosis nigricans, no striae. Normal neck exam. Abdomen obese, soft, non-tender, no organomegaly, no masses. Breast: Tanner stage V. Pubic hair Tanner stage V, clitoris was 4 cm in length by 1 cm in width, small vaginal introitus. No posterior fusion of the labia majora.

Investigation

Progesterone challenge: after receiving Medroxyprogesterone 10 mg daily for 10 days, patient did not bleed.

LABS	
Hemoglobin A1C	5.8%
Urine bHCG	Negative
Glucose	91 mg/dL
AST	31 IU/L
ALT	**51 IU/L**
TSH	0.89 mcIU/mL
17OH-Progesterone (morning)	**1261 ng/dL (36-200)**
DHEAS	202 mcg/dL
Testosterone Total LC/MS	**359 ng/dL (10-60)**
Testosterone Free LC/MS	**14 ng/dL (0.3-1.9)**
FSH	2 mIU/mL
Prolactin	12 ng/mL

LABS	
Glucose	89 mg/dL
Estradiol	16 pg/mL (Tanner V: 22-370)
Insulin level (fasting)	**25.5 mcIU/mL (<17)**
IGF1	589 ng/mL (147-842)
IGFBP3	5.7 ug/mL (2.7-8.9)
Karyotype	46,XX

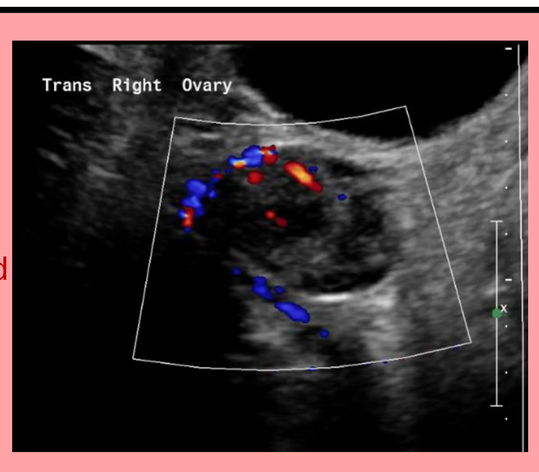
LABS	
ACTH (pg/mL)	14
Midnight Salivary Cortisol (ng/dL)	<50 (<100)

Cosyntropin stimulation Test		
	Baseline	**Post stimulated**
Cortisol (mcg/dL)	25	13
11-Deoxycortisol Specific (ng/dL)	54	27
Deoxycorticosterone (ng/dL)	14	9.7
17OHProgestone (ng/dL)	**877**	**1270**
17OHPregnenolone (ng/dL)	**970 (53-357)**	447
DHEA (ng/dL)	**1220 (160-800)**	848
Testosterone Total (ng/dL)	**349 (10-60)**	427
Androstenedione (ng/dL)	**535 (50-224)**	566
Progesterone ng/dL	118	130

Laboratory evaluation demonstrated elevated levels of androgens: Testosterone, Androstenedione, 17OHProgesterone and DHEA. Normal midnight salivary cortisol. The ACTH stimulation test demonstrated elevated androgens at baseline without elevation post stimulation.
Genetic Testing: Negative for common mutations of CYP21A2, the 21-Hydroxylase gene

Images

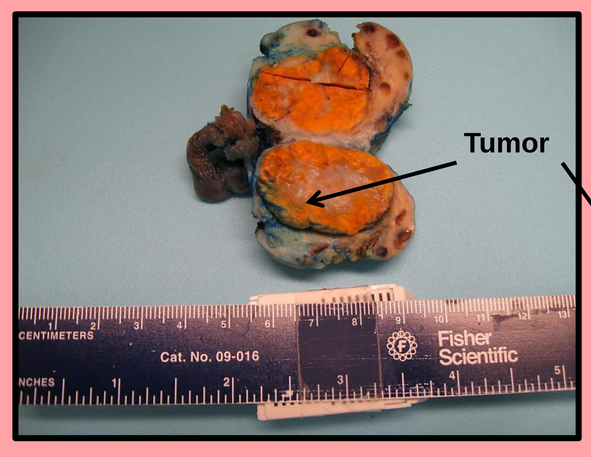
Pelvic Ultrasound Baseline
Right Ovary: 4.8 x 3.0 x 3.3 cm, volume 24.4 mL.
Right ovarian cyst: 3.6 x 2.5 x 2.1 cm, volume 9.6 mL, complex cyst, with sonographic characteristics of a corpus luteum cyst with hyperechoic periphery and hypoechoic central region
Left Ovary: 3.9 x 2.3 x 2.3 cm, volume of 10.5 mL, normal morphology. Normal doppler.
Uterus 6.2 x 4.3 x 2.5 cm, volume 34 mL
Adrenal glands appeared normal

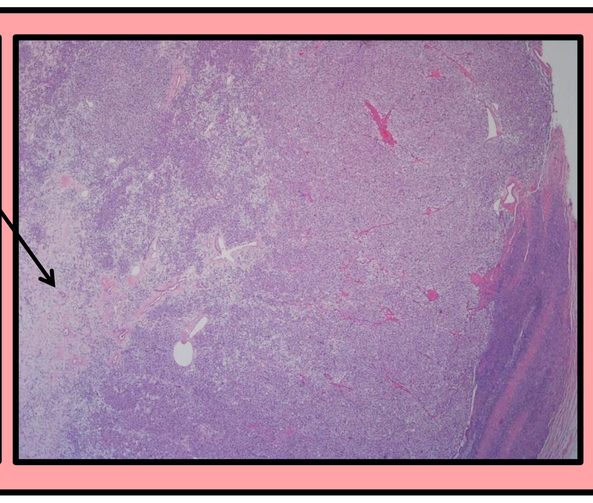


Repeat Ultrasound 3 weeks later
Right Ovary: 4.4 x 4.3 x 2.5, volume 24.8 mL
Right ovarian cyst: 2.9 x 3.4 x 1.9 cm, volume 10 mL. **No Changes**
Left Ovary 2.5 x 3.6 x 1.6 cm, 7.5 mL volume

CT pelvis and abdomen: No adrenal tumors.
The right ovary showed a 3.2 x 2 x 2.8 cm hyper-enhancing lesion with central hypodensity.

Given lack of regression after 10-14 days in a non-gravid patient, ovarian cyst was present for 8 weeks, stromal or sex cord tumor was considered. Patient had undergone laparoscopic right salpingo-oophorectomy.





Pathology report was consistent with **steroid cell tumor, not otherwise specified.** Hormonal levels normalized after resection.

	2 weeks after surgery	4 months after surgery
17OH-Progesterone (ng/dL)	<15 (before ~1200)	
DHEA (ng/dL)	352 (before 1220)	
DHEAS (mcg/dL)		211
Testosterone (ng/dL)	40 (before >300)	28
Free Testosterone (ng/dL)		1.0
Androstenedione (ng/dL)	145	
Estradiol (pg/mL)	23	
Inhibin A (pg/mL)	4.5 (<97.5 premenopausal)	6.3
Inhibin B (pg/mL)	49 (<139 premenopausal follicular, <92 premenopausal Luteal)	64

Discussion

Virilizing tumors are a very rare cause of hyperandrogenism in adolescents. Appropriate initial assessment of hyperandrogenism and irregular menstrual cycles can lead to early diagnosis and appropriate intervention.

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Gonads & DSD

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