

## What's common is common ... What's rare might happen still!

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### **Day1. 10: 00 hours. Ain-Shams University (ASU)-Out-patient Gynecology clinic**

An 18 years old virgin presented complaining of cessation of menstruation for the last 6 months, associated with progressive hair growth in abnormal sites, preceded by 2 years of light infrequent periods. She gave a history of menarche at the age of 11 and a regular normal menstrual pattern till the age of 15.

*What is the definition of hair growth in abnormal sites?*

*What is the relation between the abnormal hair growth and her menstrual complaint?*

*What is the differential diagnosis of this case?*

*How does her menstrual history direct the differential diagnosis?*

### **Day1. 10: 00 hours. ASU- Out-patient Gynecology clinic**

On examination, the patient was tall (178 cm), skinny (52 kg) with loss of female contour and excessive muscular built. She had a deep voice, a shaved beard and moustache, facial acne, and poorly developed breasts with inter-mammary hair growth and no galactorrhea. Her blood pressure was 110/70 mmhg, her pulse was 78 bpm.

*What are the signs of defeminization and of masculinization?*

*Based on the examination results, what differential diagnoses did you exclude so far, and why?*

*What other data would you like to look for on examining such case?*

### **Day1. 12: 00 hours. ASU-The ward**

The patient was admitted to the ward, abdominal examination had shown a male pattern of pubic hair and no palpable masses. Genital inspection had shown striking clitoromegaly and no labial fusion or abnormal site of the urethral meatus. Per Rectum examination was unremarkable. A hormone profile was requested and pelvic ultrasonography showed a heterogonous left ovarian mass (4x5 cm). Pelvi-abdominal CT scanning confirmed the U/S findings and did not show any evidence of adrenal masses, ascites or other focal lesions.

*What are the levels that you would expect in this case for the following hormones?*

- a) s. Testosterone
- b) s. DHEA-S
- c) s. FSH & LH
- d) s. 17 (OH) Progesterone

*What would be your next step in management?*

## Case Studies

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### Day2. 09: 00 hours. ASU-The Operating theatre

The patient underwent an exploratory laparotomy with systematic examination of the abdominal and pelvic regions. Unilateral adnexectomy was done and frozen section examination showed a sex cord-stromal tumor. Paraffin section histopathologic examination later on confirmed this to be a Leydig Cell tumor.

*What are the steps of a staging laparotomy for this case?*

*Based on the management, what was the stage of this tumor?*

*What is the long-term prognosis of this tumor?*

*What further surgical management is required?*

### Day2. 12: 00 hours. ASU-The ward

The patient had a smooth postoperative recovery and was discharged for follow up in the OPC.

*How would you follow up the case?*

*Would you prescribe any antiandrogens on discharge, and why?*

*How would the patient's obstetric future be affected by such diagnosis?*

### Comment by the editors:

Hirsutism, excessive facial and body hair caused by excess androgen production, is usually associated with anovulatory ovaries and loss of cyclic menstrual function. The more severe states of virilism (clitoromegaly, deepening of the voice, balding and changes in body habitus) are rarely seen and usually are secondary to adrenal hyperplasia or androgen-producing tumors of adrenal or ovarian origin. Although these are rare, diagnostic evaluation is required.

Most cases of hirsutism caused by hyperandrogenemia are associated with oligohypomenorrhea or amenorrhea, either which can be a cause or a result of the other. Chronic hyperandrogenemia of whatever source causes an androgenic milieu that leads to anovulation.

Polycystic ovaries syndrome should be the first possible diagnosis to consider. After excluding PCOS, other possibilities to consider include: androgen-producing tumors (the most serious) whether ovarian or adrenal, late-onset (non-classic) adrenal hyperplasia, Cushing's syndrome, androgenic drugs and some pituitary or thyroid disorders. However, the diagnostic workup of each individual case should be directed by its clinical presentation. In this particular case, the rapidly progressing virilization has strongly pointed to the possibility of an androgen-producing tumor. The fact that the patient had a past history of normal menstrual pattern excludes the possibility of causes of intersex or heterosexual puberty as congenital adrenal hyperplasia or 5 $\alpha$ -reductase deficiency.

In this case, general examination findings (defeminization, virilization, low weight and normal blood

pressure) generally excluded causes as PCOS and Cushing syndrome. Signs of defeminization include amenorrhea, breast atrophy and loss of female body contour while signs of virilization include hirsutism, balding, deep voice, muscular built, and clitoromegaly. Looking for clinical evidence of ovarian and adrenal masses in such case is mandatory. Genital examination was very important to determine the severity of clitoromegaly and hence, the need for its surgical correction.

Based on the imaging results, the probable diagnosis then was an androgen-producing ovarian tumor which would be associated with a high ( $>200$  ng/dl) Testosterone level which was actually 1000 ng/dl in this case. As a result of feedback mechanism, a hypogonadotrophic state is expected (levels  $<0.5$ ), they were 0.1 u/L in this case.. 17-(OH)-Progesterone and DHEAS levels would be within normal ranges ( $<200$  ng/dl and  $<350$  µg/dl, respectively).

The next step of management was to properly diagnose and stage this tumor by performing an exploratory staging laparotomy with frozen section biopsy of the tumor and assessment of the contralateral ovary for enlargement which would indicate biopsing it as well. A stage **Ia** sex cord-stromal tumor, as was this case, is a low grade malignant tumor that can be managed by adnexectomy (NOT ovarian cystectomy) to preserve the patient's potential fertility and regular vigilant follow up by clinical and radiological examination and by following up the serum testosterone level as a tumor marker, for fear of recurrence or metastasis.

Clitoromegaly is indicated in this particular case in view of the striking size of the clitoris and its potential side effect on the patient's psychosexual health later on in her life. The timing of such intervention is a matter of controversy.

On discharge there is no need to prescribe anti-androgens as the level of testosterone would be expected to drop on its own, there may be a point in cosmetic advice for managing residual hirsutism although this too is expected to fade off to a major extent. The patient should understand the steps of management that were done and the need for regular follow up. She needs to understand that her fertility was preserved to a major extent but that there are always chances for tubal adhesions as well as decreased fertility after such operations.

*"Everything should be made as simple as possible, but not simpler."*

Albert Einstein