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COMMUNICATIONS IN BRIEF

Detection of an estrogen-suppressible lipoid cell ovarian neoplasm by bilateral ovarian venous sampling

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HIRSUTISM is a common problem seen by the gynecologist. Most of the women have normal androgen levels and constitute idiopathic or constitutional hirsutism. However, a sizable minority does have increased androgen levels that could be of either an adrenal or an ovarian source or both. The most common disorder in the androgen excess group is the polycystic ovarian disease syndrome (PCOD). These patients typically have a history of ovulatory disorders, acne, oily skin, and hirsutism.

Except in rare circumstances an ovarian rather than an adrenal source for the hyperandrogenic state can be determined by increased serum testosterone levels with normal or slightly increased[1] 17-ketosteroids (predominantly of adrenal origin). At this point the patient with suspected PCOD is given a nonandrogenic oral contraceptive; if the serum testosterone is reduced to a normal level, then treatment for a prolonged period is usually sufficient since significant clinical improvement in the hirsutism may take well over a year.

However, an ovarian neoplasm cannot be excluded on the basis of testosterone suppression with oral contraceptives.[2] Therefore, the physician must be on guard for certain clinical clues precipitating further investigation. These include rapidity of symptoms, associated virilization (deep voice, clitoromegaly, male musculature, and high serum testosterone levels), and an estrogen deficiency on the vaginal smear.

In this report a 15-year-old girl who developed rapid, severe hirsutism associated with mild virilization is described. Though the baseline serum testosterone values were greatly elevated, they were suppressed to normal values during administration of 2.5 mg. of conjugated estrogens for two months. Nevertheless, because of clinical suspicion, further studies were performed and led to the discovery of a virilizing lipoid cell tumor of the ovary.

Table I. Testosterone levels during estrogen suppression

Sample site	*Testosterone (ng./100 ml.)*
Left ovarian vein	175
Right ovarian vein	430
Left adrenal	125
Right adrenal	185
Inferior vena cava	140

The patient (medical record No. 403739) presented at age 15 with a history of progressive hirsutism for one year and deepening of the voice. She had mild acne but no alopecia. Menarche was at age 12 and she had regular monthly menstrual periods up to six months prior to her visit when they became slightly irregular (every three to six weeks).

On physical examination the girl was 60 inches tall and weighed 101 pounds, with a tendency toward male musculature. There abundant coarse hair on the lips, chin, sternum, abdomen, and buttocks and there was a male-pattern escutcheon. The breasts were small but physiologically normal, and the clitoris was slightly enlarged. Because of a virginal introitus bimanual pelvic examination could not be performed adequately but rectal examination did not appear to show any mass lesions. Vaginal hormonal cytology showed significant atrophic changes with 87 per cent parabasal cells. This was somewhat surprising in view of her mentrual history.

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Baseline laboratory data revealed a serum testosterone level of 296 ng. per 100 ml. (normal = 50 to 100 ng. per 100 ml.) with slightly low luteinizing and follicle-stimulating hormone values (6.6 and 3.3 mI.U. per milliliter, respectively). The 8 A.M. serum cortisol level was 14 μg per 100 ml. while the 4 P.M. value was 5.3. Urinary 17-ketosteroids were increased, at 20.3 mg. per 24 hour collection.

After three weeks of prednisone administration, 2.5 mg. three times per day, the ketosteroid value remained increased (24 mg. per 24 hours) as did the serum testosterone level (316 ng. per 100 ml.). During 0.5 mg. of dexamethasone four times per day for four days, with 3,000 I.U. of human chorionic gonadotropin given on days 3 and 4, the 17-ketosteroid value rose to 64 mg. per 24 hours, the hydroxycorticosteroid level remained low, at 2.2 mg. per 24 hours, the pregnanetriol increased from 2.2 to 20.4 mg. per 24 hours, and the serum testosterone rose to 466 ng. per 100 ml. However, after six weeks of 2.5 mg. of conjugated estrogens per day the testosterone level was suppressed to 65 and 75 ng. per 100 ml.

Bilateral adrenal and ovarian vein samplings were obtained during estrogen suppression and the testosterone levels are seen in Table I.

Because of the high unilateral ovarian vein levels of testosterone, a laparotomy was performed. The right ovary measured 6 by 4 by 1 cm. in diameter while the left ovary measured 3 by 2.5 by 1.5 cm. Exploration of the right ovary revealed yellow lobular soft tissue which on frozen section revealed "lipoid cell" tumor. The right ovary and tube were resected and a final pathologic diagnosis of a lipoid cell tumor without Reinke's crystals of the ovary was made by Drs. Lang, Strimel, and Sculley.

The rapidity of onset of the hirsutism and the development of virilization over such a short period of time made us clinically suspicious that the girl might have a testosterone-secreting neoplasm. This diagnosis was supported further by the high baseline serum testosterone level.

However, during estrogen suppression the serum testosterone values returned to well within normal limits. In most cases of hirsutism suppression of the testosterone levels to normal limits with medication justifies continuing medical therapy. But if the suspicion of a neoplasm exists it is necessary to persist with further studies despite good testosterone suppression since even neoplasms can be suppressed.[2]

Frequently, a unilateral androgen-secreting lesion causes the contralateral ovary to hypersecrete androgens and thus localization can be difficult even after ovarian venous sampling. Therefore, we performed the ovarian and adrenal venography during estrogen suppression and the data indicated a right ovarian source.

Twenty per cent of lipoid cell tumors are malignant, thus illustrating the importance of not overlooking the diagnosis of an androgen-secreting tumor even if the androgen levels are suppressed to normal with medical therapy.

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