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A Testosterone-Secreting Adrenal Adenoma

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A third case of a testosterone-secreting adrenal adenoma is presented. It differs from the other 2 cases in additionally having glucocorticoid abnormalities. Clinically, the patient had been considered as having polycystic ovaries and did show some improvement with estrogen therapy. In fact, were it not for enlarging uterine leiomyomata on this therapy which prompted a more in depth investigation to look for alternative therapy, this potentially malignant adrenal lesion may never have been discovered.

THE ADRENAL ADENOMA usually presents with glucocorticoid and mineralocorticoid signs and symptoms. Frequently 17-ketosteroids are suppressed, and especially in women, clinical manifestations of androgen deficiency may be present. However, some of these tumors secrete increased androgens and are associated with very high levels of 17-ketosteroids.¹ There have been two case reports of testosterone-secreting adrenal adenomas with normal or slightly elevated ketosteroids with normal 17-hydroxycorticosteroids (17-OHC) and cortisols.^{2,3} This report describes a woman with an adrenal adenoma with only slightly elevated ketosteroids but with high serum testosterone levels and non-suppressible OHC and serum cortisol.

CASE REPORT

The patient was a 41-year-old female who came to us for a second opinion regarding management of acne, hirsutism, edema, weight gain, and leiomyomata. She had been advised by an endocrinologist that she probably had polycystic ovaries and, in fact, she did demonstrate improvement of her acne on therapy with Enovid E. However, this therapy caused her leiomyomata to enlarge and the patient wanted a second opinion whether a hysterectomy should be performed to allow Enovid therapy to continue.

The patient lacked the classic glucocorticoid manifestations of adrenal hyperfunction such as trunkal obesity, moon face, striae, or nuchal fat pad. There was abundant facial hair,

especially on the upper lip and chin, and moderate abdominal hair with a male escutcheon. This had been progressive over the last 3 years despite treatment with Enovid E for the last 2 years. There was mild acne on the face and back which the patient stated had significantly improved with the use of Enovid. Her blood pressure when sitting was 170/98 mmHg; height, 66 inches; weight 150 pounds. She had moderate bilateral fibrocystic disease of the breasts. Pelvic examination was normal with the exception of an irregularly shaped uterus enlarged one and a half times normal size consistent with uterine leiomyomata. There was a brawny edema of the lower extremities and the patient stated that she had swelling of the face, feet, and fingers which worsened at the end of the day.

Because of the edema and hypertension, we felt that an adrenal as well as an ovarian source needed to be excluded. The Enovid was stopped; 3 weeks later the serum testosterone levels were very high at 377 and 284 ng/100 ml (normal 20-70). Her 8 AM cortisol level was 18 µg/100 ml. Following ingestion of 1 mg dexamethasone at midnight her 8 AM cortisol level showed inadequate suppression to 9 µg/100 ml. Baseline 17-OHC levels were increased at 8 mg/g of urinary creatinine, while the 17-ketosteroid levels were just slightly increased. After administration of 2 mg dexamethasone on 2 consecutive days, repeat urinary 17-OHC did not suppress (8.3 mg/g of creatinine) while the ketosteroids suppressed slightly (10.7 mg/g of creatinine). On 8 mg of dexamethasone for 2 days, the 17-OHC levels remained elevated (8.7) while the ketosteroid levels remained at 10.7. The plasma cortisol failed to suppress also (17.5 µg/100 ml).

Intravenous pyelography showed a possible mass causing an impression on the superior surface of the right kidney. Arteriography demonstrated a 5-cm hypervascular neoplasm involving the right adrenal gland. Bilateral venography was attempted but was not successful.

At surgery a well-encapsulated 4 × 3 × 5 cm adenoma of the right adrenal was removed, leaving some adrenal tissue behind. Pathologic evaluation revealed an atypical cortical adenoma with nuclear pleomorphism and occasional mitosis. However, because of its small size and lack of necrosis, hemorrhage, or invasion, it appeared benign.

Within 6 months after surgery the patient's acne had cleared, her hirsutism was significantly diminished, her facial plethora disappeared, she lost 12 pounds, her edema problem disappeared, and she became normotensive. Her 8 AM cortisol level was 12.3 µg/100 ml and serum testosterone dropped to a normal level of 50 ng/100 ml. Her urinary hydroxycorticosteroids decreased to a normal 4 mg/g of creatinine. Her 17-ketosteroids were now normal.

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ADRENAL ADENOMA

DISCUSSION

This case is unique in that in contrast to the two previously described testosterone-secreting adrenal adenomas without marked elevation of the 17-ketosteroids, the glucocorticoids in this case were mildly elevated and were nonsuppressable by dexamethasone. Associated polycystic ovaries responsible for the elevated testosterone is unlikely in view of the degree of elevation of the testosterone and the rapidity of improvement following extirpation of the tumor. Therefore, glucocorticoids should always be evaluated simultaneously with ketosteroids in a hirsute female even if the degree of testosterone elevation suggests a primary ovarian source. In this case the slight elevation in ketosteroids was more consistent with polycystic ovaries than an adrenal neoplasm.

By determining an adrenal rather than an ovarian source for the elevated testosterone levels, an unnecessary hysterectomy was avoided and the patient was spared potentially dangerous high-dose estrogen therapy. In 1 year off all medications, the patient's acne, hirsutism, edema, and hypertension have completely

cleared; she has lost 15 pounds; and her serum cortisol and testosterone and urinary hydroxycorticosteroids and 17-ketosteroids have remained at normal levels.

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