

GONADOTROPIN RELEASING HORMONE ANALOGUE ANTIANDROGEN FAILURE SECONDARY TO A PITUITARY ADENOMA

KENNETH OGAN, MYRON BERGER AND ROBERT BALL

From the Department of Urology, George Washington University, Fairfax Hospital, Fairfax, Virginia

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Antiandrogen therapy before radiotherapy for definitive treatment of localized prostate adenocarcinoma has become an acceptable neoadjuvant treatment alternative. Huggins first discovered the relationship between androgen deprivation and regression of advanced prostate cancer.¹ The lack of androgen stimulation on prostatic carcinoma cells initiates the process leading to apoptosis. This process is thought to be synergistic with the effects of ionizing radiation.²

Studies have clearly demonstrated that physiological doses of luteinizing hormone (LH)-releasing hormone (RH) analogues mimic LH-RH action, whereas, paradoxically, long-term administration of supraphysiological, pharmacological doses elicits antigonadal effects and regression of hormone dependent prostate tumors.³ We report on a man with prostate cancer whose testosterone did not decrease following treatment with an LH-RH analogue due to the concomitant presence of an asymptomatic functional pituitary adenoma.

CASE REPORT

A 65-year-old white man was initially evaluated for an elevated prostate specific antigen (PSA) of 8.0 ng./ml. (normal 0 to 4) approximately 3 to 4 years previously. Three transrectal ultrasound guided biopsies consisting of 6 to 8 cores each were performed during this 3-year period because of a continuously rising PSA. All biopsies were negative for carcinoma. Finally a PSA elevation to 45 ng./ml. prompted another set of biopsies, which revealed a focus of adenocarcinoma in 1 biopsy core from the transition zone. Gleason score was 4+4 with tetraploid deoxyribonucleic acid studies. Subsequent bone scan and magnetic resonance imaging (MRI) of the pelvis were negative for evidence of metastatic disease.

The patient elected to pursue external beam radiation with pretreatment androgen suppression. He received an oral antiandrogen for 10 days before a 3-month depot injection of leuprolide

acetate, and then 7,200 cGy. external beam radiation using a 3-dimensional conformal technique in 40 sessions. There were only minor radiation related complications, and leuprolide acetate was continued for 3 months after radiation treatment.

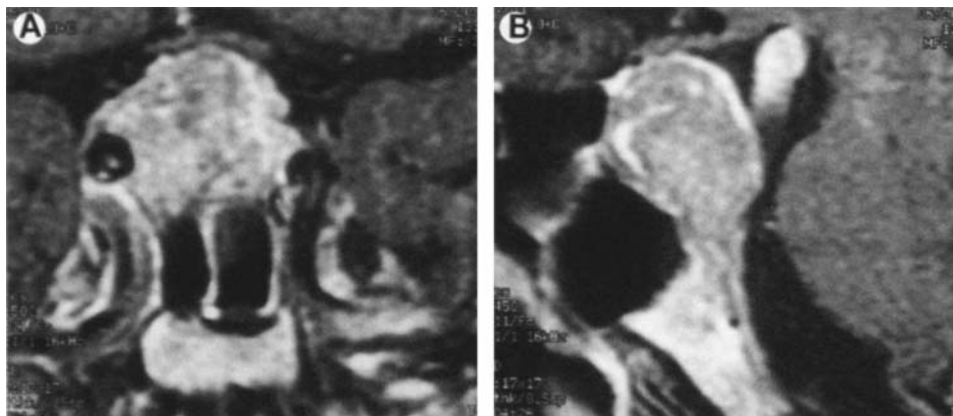
One month following radiation treatment PSA had decreased to only 25 ng./ml. Repeat bone scan was negative for metastatic disease. Serum hormone studies demonstrated normal testosterone (251 ng./dl), free testosterone (11.5 pg./ml.) and luteinizing hormone (3.8 IU/l.) levels. Abdominal computerized tomography showed no evidence of adrenal masses. MRI of the brain revealed a 2 cm. heterogeneously enhancing pituitary tumor filling the sella turcica with suprasellar and right cavernous sinus extension (see figure).

Transsphenoidal hypophysectomy was then performed. Pathological examination revealed a pituitary adenoma, and that the tumor cells were strongly positive on immunohistochemical stain for follicle-stimulating hormone (FSH) and focally positive for LH. Postoperative testosterone and PSA levels initially declined but subsequently rebounded into the normal range. Repeat MRI demonstrated residual adenoma, and the patient subsequently underwent bilateral orchiectomy.

DISCUSSION

Since the discovery of prostate cancer androgen sensitivity, hormonal ablation for treatment of metastatic prostate cancer has been the standard of care. Recently, LH-RH analogues have proved to be an effective method of pituitary suppression of LH and FSH, which under normal circumstances results in anorchid serum testosterone levels. Our patient had a functional pituitary adenoma secreting FSH and LH, which was resistant to the expected effects of LH-RH analogues and resulted in persistent production of testosterone from the testicles. Our case demonstrates that when the testosterone levels do not decrease to anorchid levels following treatment with LH-RH analogues, other sources of testosterone production must be sought. These sites could include active primary tumors of the testis and adrenal gland, as well as exogenous neuroendocrine tumors.

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A, gadolinium enhanced T1-weighted MRI of brain demonstrates pituitary mass enveloping right cavernous sinus with impingement of optic chiasm. B, sagittal view shows pituitary mass filling sella turcica.

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