CASE REPORT

Prostate cancer: endogenous chemical castration

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SUMMARY

We report treatment of intermediate risk prostate cancer in a patient with a brief period of androgen deprivation secondary to a pituitary adenoma. This was a patient with intermediate risk prostate cancer diagnosed in the setting of an elevated prostate-specific antigen (PSA). The patient subsequently demonstrated a decline in PSA along with symptoms of hypogonadism and visual disturbance, and was consequently found to have a pituitary tumour. Trans-sphenoidal resection of the sellar mass was performed with normalisation of hormone profiles. The patient subsequently completed a course of radiation therapy for prostate cancer with PSA nadir to undetectable levels without evidence of biochemical recurrence at 7 months follow-up.

BACKGROUND

Prostate cancer is the second most common cancer globally in men. Within the USA alone, there were projected to be over 200 000 cases and nearly 30 000 deaths in 2014 as a result of prostate cancer.¹

With regard to pituitary malignancy, the incidence of pituitary adenomas between 1992 and 2007 was reported to be 4 per 100 000.² Pituitary lesions usually are detected incidentally on cross-sectional imaging or on further evaluation of symptoms such as headache, visual disturbance, hot flashes and low energy. Adenomas of the pituitary are classified based on size (lesions <1 cm classified as microadenomas and >1 cm termed macroadenomas), cell of origin, functioning versus non-functioning and malignant potential. Clinically silent or non-functioning adenomas involve no hormonal up or downregulation unless, by mass effect, they compromise function by compression and interruption of blood flow.

Patients diagnosed with prostatic adenocarcinoma are generally stratified into low, intermediate or high-risk groups to establish prognosis and guide treatment decisions. Depending on staging and risk stratification, treatments for those who are candidates for neither active surveillance nor watchful waiting include: radiation therapy with or without androgen deprivation therapy (ADT), brachytherapy, proton therapy, cryoablation, radical prostatectomy and chemotherapeutic treatment. Per the American Urological Association (AUA) and the National Comprehensive Cancer Network (NCCN) guidelines, primary ADT is not deemed a 'standard' treatment option for localised prostate cancer.³ For intermediate risk prostatic adenocarcinoma, options for management include: radical prostatectomy with pelvic lymph node dissection if the predicted probability of lymph node metastasis is

greater than or equal to 2%, external beam radiation therapy with or without ADT for 4–8 months, with or without brachytherapy or brachytherapy alone.

In this paper, we discuss an interesting case involving endogenous androgen deprivation and subsequent decline in PSA levels secondary to a pituitary adenoma in a patient with known intermediate risk disease.

CASE PRESENTATION

We present a case of a 69-year-old African-American with a rising PSA. His PSA had risen from 1.46 ng/mL in 2008 to 5.1 ng/mL in 2012. He elected to undergo transrectal ultrasound-guided prostate biopsy. Prior to biopsy, a repeat PSA was performed and found to be 0.1 ng/mL. The low PSA value was thought to be spurious and the patient proceeded with prostate biopsy. Pathology revealed Gleason 4 + 3 disease in two cores at the left apex and one core at the right apex, and low glandular volume (11 cm³). A repeat PSA value was obtained and found to be undetectable.

The patient denied undergoing any hormonal treatments or other intervention. He denied a history of previous testosterone replacement, human chorionic gonadotropin injections, ADT, radiation or chemotherapy. He had fathered five children and denied prior history of fertility issues. On further questioning, the patient endorsed occasional hot flashes, headaches, changes in vision, decreased libido and worsening erectile dysfunction. On examination, he was found to have bilateral testicular atrophy in addition to a small prostate.

A paper by Grotas and Nagler⁴ in 2006 described a case in which a patient with prostate cancer experienced a dramatic decline in PSA and was discovered to have a pituitary macroadenoma (prolactin secreting).

INVESTIGATIONS

Owing to concern for hypogonadism, serum testosterone, luteinising hormone and prolactin were measured. These studies revealed low testosterone of 13 ng/dL (normal 240–870 ng/dL) and low luteinising hormone of 0.2 mIU/L (normal 1.8–12.0 mIU/L) with normal prolactin levels.

Cross-sectional imaging of the brain with MRI confirmed our suspicion, demonstrating a 1.9×1.5×1.6 cm enhancing mass within the sella turcica with minimal superior extension contacting the undersurface of the optic chiasm (see figures 1 and 2). The enhancing sellar mass abutted both cavernous portions of the carotid arteries and

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Figure 1 Coronal cross-section of pituitary adenoma on T1-weighted MRI of the brain with contrast.

surrounded approximately 50% of both internal carotid arteries.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis included primary versus secondary hypogonadotropic hypogonadism. Initially, our attention was turned to the possibility of an exogenous hormone source, which the patient denied. This would result in low LH levels as a result of feedback of testosterone to the hypothalamus, which we did not see. Other agents that may have been causative, such as ketoconazole, cimetidine, flutamide, chemotherapy or aromatising agents, were ruled out during the history-taking. Primary testicular atrophy or trauma was considered as well, given the physical examination findings of decreased bilateral testicular size; however, the patient denied a recent physical change and

Figure 2 Sagittal cross-section of pituitary adenoma on T1-weighted MRI of the brain with contrast.

had not sustained an injury to account for this particular diagnosis. In attempts to evaluate for secondary hypogonadotropic hypogonadism such as Kallmann's or Klinefelter's syndrome, we concluded that this was unlikely, given the time course and age at presentation, and lack of pathognomonic physical and laboratory findings. Also, this did not fully explain the sudden onset of active visual disturbances and headaches, which led us to evaluate a pituitary source in the hypothalamic–pituitary–gonadal endocrine axis. In order to investigate this further, cross-sectional imaging of the brain was acquired.

TREATMENT

The patient subsequently underwent a successful trans-sphenoidal resection of the pituitary macroadenoma.

With regard to prostate cancer management, after review of treatment options available per NCCN guidelines, the patient opted for and was treated with external beam radiation, completing a 79.2 Gy/44Fx protocol a few months following pituitary mass resection. PSA and testosterone measured following radiation treatment were 0.82 ng/mL and 349 ng/dL, respectively.

OUTCOME AND FOLLOW-UP

On follow-up with endocrinology and neurosurgery, the patient had recovered well with no evidence of disease recurrence. He continues to follow-up for prostate cancer monitoring since diagnosis in January 2014.

DISCUSSION

Studies have demonstrated that the postoperative management of patients with pituitary adenoma from an endocrine standpoint involves following hormone levels (growth hormone, thyroid hormone, cortisol, antidiuretic hormone) up to 18 months postoperatively,⁵ with an approximately 84% remission rate in microadenomas and 70% remission rate in macroadenomas.⁵

One question is whether the presence of endogenous chemical castration suggests a good prognosis indicating the presence of hormone-sensitive and well-differentiated prostatic adenocarcinoma cells. Additionally, the course of this patient mimics the normal timeline of therapy involving combined radiation therapy with ADT in which ADT is initiated 2 months prior to initiation of radiation.

Also of importance is being aware of the risk of pituitary apoplexy following gonadotropin-releasing hormone agonist administration for prostate cancer in patients with pituitary adenomas. This has been reported in the setting of functional and non-functional pituitary adenomas.^{6,7} For this reason, though there are limited cases reported regarding this, it is imperative to make the patient aware of these risks, have a heightened sensitivity to the initial signs and symptoms and to adopt a multidisciplinary approach in treatment of these rare cases.

Ultimately, our case sheds light on the importance of obtaining a thorough and comprehensive genitourinary history and physical. Having encountered undetectable or low repeat PSA values may have misled many physicians and resulted in the decision to cancel the biopsy of the prostate. This furthermore would have delayed subsequent investigation, resulting in a missed opportunity for appropriate treatment of intermediate risk prostate cancer and pituitary lesion.

With collection of more case-controlled studies, we can begin to address and develop a framework for approaching rare cases of prostate cancer in the setting of endogenous androgen deprivation.

Learning points

- ▶ It is imperative to obtain a thorough genitourinary history including focused endocrine review in patients with presumed prostate cancer.
- ▶ This case stresses the importance of continued multidisciplinary collaboration in follow-up and management of synchronous tumours.
- ▶ Counselling your patient regarding cancer treatment guidelines despite rare unusual cases allows for educating and empowering the patient to take an active role in their care.

Contributors OOM drafted the manuscript and performed a review of the literature. NS provided guidance on formulating the important points of care of patients with prostate cancer with emphasis on endocrine-related symptoms. She also served as the attending physician for the patient. NS and MMP revised the original draft, and provided critical editing of technical and clinical details for intellectual content. All the authors gave approval for the final version of the submission.

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