CASE REPORT

Androgen deprivation therapy for patients with prostate carcinoma and Parkinson's disease: case report and review of literature

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ELSHAIKH MA, UNDERWOOD W, SOTO DE. Androgen deprivation therapy for patients with prostate carcinoma and Parkinson's disease: case report and review of literature. The Canadian Journal of Urology. 2009;16(1):4495-4497.

We report a case history of a patient with Parkinson's disease (PD) treated with androgen deprivation therapy (ADT) and external beam radiation for prostate cancer, who developed severe deterioration of his PD during ADT.

Key Words: prostate carcinoma, androgen deprivation, Parkinson disease

Introduction

Data from many prospective randomized studies has established the role of androgen deprivation therapy (ADT) in the definitive management of prostate adenocarcinoma[1-4] as well as in the palliative management of patients with metastatic disease. For patients with coexistent prostate carcinoma and Parkinson's disease (PD), no data exists examining the effects of ADT on PD symptoms.

To our knowledge, we are unaware of any published report describing the effect of ADT on patients with PD and prostate carcinoma. This report describes a patient diagnosed with PD and prostate carcinoma who received ADT as part of his management of prostate cancer that adversely impacted his PD symptoms. We also reviewed the available clinical research data, paying attention to the effect of different androgens on the features of PD.

Accepted for publication October 2008

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Case

A 64-year-old white male was referred to our institution with a new diagnosis of prostate carcinoma. His previous history was significant for mild to moderate PD diagnosed in May 2000. His baseline PD medications included carbidopa/levodopa 50 mg/200 mg (Sinemet CR) and pergolide 0.05 mg. Both medicines were taken orally three times a day (600 mg of levodopa/day) as a maintenance dose for the last several years. Other medical problems included well controlled peripheral vascular disease and chronic obstructive pulmonary disease. For these conditions, he received clopidogrel 75 mg orally once a day and albuterol inhaler as needed.

His prostate carcinoma was diagnosed in March 2005 with an initial PSA of 15 ng/ml, a biopsy Gleason score of 8, and a clinical tumor stage of T2. Staging workup was negative for metastatic disease. At presentation in March 2005, he was experiencing bilateral asymmetric resting hand tremors with rigidity, masked facies, and slow gait. He denied any freezing episodes, marked bradykinesia, dystonia movements, constipation, motor fluctuations or sleeping disturbance. He was able to walk with the occasional use of a cane. His baseline total testosterone level was 389 ng/dl. He received neoadjuvant and adjuvant injections of goserelin (Zoladex, 10.8 mg) in May and August of 2005, 12 weeks prior to as well as during definitive radiation treatment (RT) to the prostate. When he was seen 10 weeks after his goserelin injection, he was complaining of a significant worsening of his motor and cognitive symptoms. His complaints were also confirmed by some of his immediate family members. Specifically, he described an increase in his resting tremors, increased muscle rigidity, and extreme fatigue to the degree that he required a wheel chair for at least 2 months. In addition, he noted significant loss of appetite and worsening insomnia. There had been no changes in his medications and there was no other new development in his medical condition. His testosterone and PSA levels in July 2005 dropped to 30 ng/dl and 2.9 ng/ml, respectively. He was evaluated by his managing neurologist who gradually increased the dose of carbidopa/levodopa to 1000 mg per day. However, he did not experience any improvement in his symptoms. The patient was able to complete the course of RT, but with significant difficulty due to his extreme weakness and depression. Despite the increased dose of carbi/levodopa, his deteriorated PD symptoms remained with him until March 2006. On a routine follow up in May 2006, his testosterone and PSA levels were 190 ng/dl and 0.2 ng/ml, respectively. During this visit, he stated that he is "new born" and he was gradually returning to his baseline PD symptoms without any medical intervention. He was no longer requiring the use of a wheel chair. In August 2006, because of his continuous improvement in his PD symptoms, his carbi/levodopa doses were reduced. In February 2007, he was prescribed a maintenance dose of 600 mg/day of carbi/levodopa.

Discussion

Prostate carcinoma is the most common cancer in men in the United States. It is not rare to simultaneously diagnose PD in a prostate cancer patient or vice versa. One study found a trend towards an increased incidence of prostate cancer in PD patients.[5] Since the role of ADT is well established in the management of prostate cancer, a better understanding of its effect on PD features is potentially useful. PD often has devastating motor and cognitive symptoms. Interventions that succeed in delaying its rate of progression are likely to have a major health impact.

Testosterone seems to influence various aspects of behavior including memory. Recent studies have suggested a link between testosterone deficiency and Parkinson disease progression.[6,7] In fact, testosterone deficiency as a result of ADT might act as a "second hit" and exacerbate features of PD.

Although it had been previously thought that testosterone replacement could only improve non-motor symptoms of PD such as apathy, depression and memory loss,[7-9] testosterone therapy has recently been shown to also improve certain motor symptoms of PD such as resting tremor and fine motor control.[10]

To define the effects of testosterone therapy on motor and non-motor symptoms in men with PD, a small prospective, placebo controlled study was conducted. Although the study did not show significant differences in outcome, patients who received longer duration of testosterone experienced significant improvements.[11]

We acknowledge the limitation of our single patient observation. Although, the patient reported here had an obvious deterioration in his PD symptoms, there was no formal neuropsychological testing prospectively performed. Patients with PD may suffer from fluctuations in their symptoms. However, we can still suggest, based on our observation, that the patient's cognitive and motor deficits were exacerbated by ADT and this is consistent with the hypothesis that testosterone modulates certain aspects of cognitive and motor function. Our observation warrants further prospective investigations to further examine this possible correlation.

Conclusion

In summary, this case report adds to the increasing evidence that androgens play a role in modulating the expression of PD features. Based on our observation, which is supported to some degree by published literature, we can only draw a tentative conclusion that ADT can adversely impact PD and this potential interaction must be clearly explained and conveyed to patients, family and their managing physicians. As a result they will be able to make informed decisions when faced with the prospect of ADT as part of their prostate cancer treatment regimen. □

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