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The Suppression of Prolactin is required for the Treatment of Advanced Prostate Cancer

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Abstract

Androgen-independent advanced prostate cancer is a terminal malignancy that generally results in death within five years. Its cause has been unknown, and a treatment did not exist. Prevailing views have mistakenly implicated impaired androgen receptor activity in the development of androgen-independent malignancy; which has deterred the existence of an effective treatment. Instead, recent reports have provided evidence that prolactin promotes the development and progression of androgen-independent malignancy; which follows androgen ablation treatment for androgen-dependent prostate cancer. That relationship dictates that a treatment for advanced prostate cancer should suppress the concentration plasma prolactin. This has been achieved with cabergoline (dopamine agonist; Dostinex) treatment of a patient that resulted in 88% decreased plasma prolactin, and terminated the malignancy. That likely represents the first effective treatment for advanced prostate cancer. It remains to establish if this treatment will be successful for other patients with advanced prostate cancer.

Keywords

Prolactin; Prostate Cancer; Malignancy; Metastasis

INTRODUCTION

Androgen-independent advanced prostate cancer continues to account for most of the ~30,000 prostate cancer deaths/year in the U.S. and ~1.2 million prostate cancer deaths/year worldwide. Despite decades of research and extensive funding, an effective treatment still does not exist.

A major reason has been the confusion regarding the development and progression of advanced prostate cancer. It must first be recognized that the normal prostate acinar epithelial cells and the malignant cells are regulated by testosterone and prolactin [1,2]. Testosterone provides the “primary” hormone regulation and promotes the initiation and progression of malignancy; i.e., “androgen-dependent” prostate cancer. Androgen ablation

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(castrate or hormonal) treatment is employed to limit the availability of testosterone and its manifestation of malignancy. This leads to the development of “androgen-independent” malignancy; which is the status of advanced prostate cancer (castration resistant prostate cancer; CRPC). Androgen-independent advanced prostate cancer results in patient death generally in 2–5 years.

DISCUSSION

An important unresolved issue is the cause of the development of androgen-independent malignancy. A prevailing view has focused on dysfunctional androgen receptor (inhibition of expression; mutation; impaired activity) as being implicated for the transformation of androgen-dependent malignancy to androgen-independent malignancy; and its potential as a target for an efficacious treatment. That is a mistaken understanding, which has contributed to the continued absence of an effective treatment for advanced prostate cancer.

The ***alternative*** is the recognition of the implications of prolactin in promoting the development and progression of androgen-independent advanced prostate cancer. However this relationship has been largely unrecognized and ignored by contemporary clinicians and biomedical investigators; including urologists and oncologists. This is apparent from a PubMed search of “prolactin and androgen-independent prostate cancer” that reveals only 12 citations; of which 5 were published within the recent 10 years (including Costello and Franklin [2]). The PubMed search with “prolactin and castration resistant prostate cancer” produced only 6 citations; 3 being published in the recent 10 years. Also notable is that the 2016 extensive review of prostate cancer with over 300 references makes no mention of prolactin [3].

Nevertheless, the ***implications*** of prolactin in the development of androgen-independent advanced prostate cancer has been clinically corroborated by our recent case report [4]. The patient was initially diagnosed with androgen-dependent prostate gland malignancy and lymph node metastasis. The patient had received androgen ablation treatment that included hormone therapy, chemotherapy, and radiation therapy. The androgen-dependent malignancy was terminated.

Summary of Evidence

However, androgen-independent malignancy developed; which likely is due to prolactin. Based on that expectation, cabergoline treatment (dopamine agonist; Casodex) was employed to inhibit the pituitary production of prolactin. Prior to treatment, the patient’s CTC (circulating tumor cell) count=5.4; which is indicative of survival for ~21 months. After 7 weeks treatment with cabergoline, the circulating tumor cell count=0. Correspondingly, the plasma prolactin concentration decreased 88% (11.3 to 1.3 ug/ml). This corroborates that prolactin, not impaired androgen receptor, is the required target for treating advanced prostate cancer.

CONCLUSION

The important conclusions are: 1. The targeting for treatment of terminal advanced prostate cancer has mistakenly focused on androgen receptor as the cause of the development of advanced prostate cancer. Consequently, targeting androgen receptor has failed to result in an effective treatment. 2. Advanced prostate cancer is a prolactin-dependent malignancy. 3. An efficacious treatment should be targeted at inhibiting the pituitary lactotropic production of prolactin to suppress the plasma prolactin concentration. This has been achieved with cabergoline (dopamine agonist; Dostinex). 4. These relationships and treatment were successfully applied to a patient who presented with advanced prostate cancer; which is possibly the first reported case of an effective treatment that terminated advanced prostate cancer.

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