MATHEWS JOURNAL OF CASE REPORTS

MATHEWS Open Access Journals

Case Report

ISSN: 2474-3666

Vol No: 4, Issue: 1

Received Date: Mar 20, 2019

Published Date: May 8, 2019

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A Novel Patient Case Report to Show the Successful Termination of Untreatable Androgen-independent Prostate Cancer: Treatment with Cabergoline (Dopamine agonist).

ABSTRACT:

Introduction: Testosterone promotes the initial development of androgen-dependent prostate cancer. This is the basis for androgen ablation treatment, which attenuates, but does not terminate, the malignancy. Instead, it leads to prolactin-dependent malignancy; in which patient death generally occurs within 5 years. This report describes the novel treatment of a patient; which terminated androgen-independent prostate cancer.

Results: Patient "XY" was diagnosed with prostate malignancy and metastases. He received hormonal androgen ablation treatment, chemotherapy, and radiation treatment. He developed androgen-independent prostate cancer; with expected death in 2-3 years. He was treated with cabergoline (dopamine agonist) treatment, which decreased the plasma prolactin 88%; by inhibiting the pituitary production of prolactin. The subsequent PET scan (positron emission tomography) revealed the absence of malignancy; and the CTC (circulating tumor cells) decreased from count=5.4 to count=0.

Discussion: The cause of androgen-independent malignancy has been unknown, and an effective chemotherapy did not exist. The activities of normal and malignant prostate cells are regulated primarily by testosterone. When testosterone availability diminishes; prolactin regulation is manifested. This is represented when androgen ablation results in the development of prolactin-dependent malignancy. An effective chemotherapy would be targeted to eliminate the plasma prolactin-manifestation of the androgen-independent malignancy.

Conclusions: This report of a novel chemotherapy for androgen-independent malignancy corroborates our understanding of the implications of prolactin in its development and treatment. There are about 165,000 cases/year with 25,000 deaths/year in the U.S.; and 1.0 million cases/year with 260,000 deaths/year worldwide. Those patients with androgen-independent prostate cancer can now employ this cabergoline treatment to prevent or terminate this deadly type of prostate cancer.

Keywords: Androgen-Independent Malignancy; Advanced Prostate Cancer; Cabergoline Treatment; Case Report

INTRODUCTION

Advanced prostate cancer accounts for about 25,000 deaths/year in the U.S. and 260,000 deaths/year worldwide [1] Its treatment generally includes hormonal androgen ablation; which leads to androgen-independent malignancy, followed by death generally within 2-5 years. An efficacious treatment does not exist, mainly due to the poor understanding of the factors that are implicated in the development and progression of androgen-independent malignancy. Especially relevant is the issue of the hormonal regulation of normal and malignant prostate acinar epithelial cells. Costello and Franklin [2,3] have provided extensive reviews of these issues.

Testosterone and prolactin regulation of normal and malignant acinar epithelial cells: androgen ablation and the development of prolactin-dependent malignancy

The activities of the normal prostate acinar epithelial cells and their malignant cells are achieved by the dual hormonal regulation of testosterone and prolactin [4]. Generally, testosterone provides the "primary" regulation; and prolactin regulation is manifested when testosterone regulation declines. This relationship exists when testosterone ablation for the treatment of androgen-dependent prostate cancer leads to the development of androgen-independent malignancy; with a life expectancy of up to 5 years.

The cause of androgen-independent malignancy had not been established, which has deterred progress in the development of an effective treatment. This report provides corroborating evidence for our concept [2,3] that androgen-independent prostate cancer is "prolactin-dependent malignancy". Cabergoline (dopamine agonist) has been employed to suppress the pituitary lactotropic production of prolactin in cases of hyperprolactinemia [5,6]. These relationships provided the basis for our initiation of cabergoline treatment to decrease plasma prolactin, and abort untreatable androgen-independent prostate cancer.

This is the first case report to describe an efficacious treatment of a patient that successfully aborted terminal androgen-independent prostate cancer. Notably, there were no consequential adverse side effects of the treatment. Other patients can now employ cabergoline treatment to terminate this deadly cancer.

Case history of patient "XY", who presented with terminal androgen-independent prostate cancer

On 8/14/2017 and 9/11/2017, "XY" exhibited a prostate specific antigen (PSA)=21 and PSA= 33, respectively. Prostate biopsy on 10/1/2017 revealed Gleason grade 8 prostate cancer. This was followed by focal laser ablation of the left side of the prostate gland. The subsequent Axumin PET (positron emission tomography) showed the spread of malignancy to the right side of the prostate gland and lymph node metastasis. The oncology diagnosis was the presence of incurable malignancy; and an expected 3-year survival with hormonal androgen ablation and chemotherapy. From about 11/1/2017 - 4/1/2018; "XY" treatment included hormonal androgen ablation, chemotherapy, and radiation therapy. Beginning around 11/01/2017, androgen ablation along with chemotherapy was initiated; which included lupron, casodex, zytiga, prednisone, neulista, and Lu177-PSMA (prostate specific membrane antigen). Prior to androgen ablation, PSAs were ~20-40; and the post-androgen ablation +chemotherapy PSAs<1.0. However, the 4/18/2018 PET revealed prostate gland malignancy and extensive metastases, which represented the development of untreatable androgen-independent malignancy.

On 6/20/2018, "XY" enlisted Dr. Yu as the oncologist and Dr. Costello as the collaborating consultant to manage and treat his androgen-independent malignancy. 3% Clioquinol Cream plus 50mg zinc supplement/day along with Lu177-PSMA radiation therapy was added to the treatment of "XY". After 8 weeks, a PET scan revealed an arrest of the androgen-dependent malignancy.

However, the persistence of untreatable terminal androgen-independent malignancy presented the major problem. We expected that the development of this malignancy was likely due to the manifestation of prolactin-dependent malignancy; as had been described by Costello and Franklin [2,3]. On 12/8/2018, cabergoline treatment (Dostinex; 0.5mg 2x week) was initiated to inhibit the pituitary production of prolactin; decrease the plasma concentration of prolactin; and terminate the prolactin manifestation of androgen-independent malignancy. After 7 weeks, the plasma prolactin concentration decreased from 11.3 ug/ml (normal prolactin level) to 1.3 ug/ml (extremely low prolactin). The 1/31/2019 MRI and PET revealed the absence of detectable malignancy. A CTCPC (circulating tumor prostate cells count) count = 5.4 on 8/27/2018, which is indicative of ~21 months of survival; and on 2/22/2019, the count=0. This

reveals that the imminent death from androgen-independent metastases had been terminated. These collective results following the initiation of cabergoline treatment corroborate our concept that prolactin manifests the development and progression of androgen-independent prostate cancer. This novel case report presents a successful treatment of a patient that successfully aborted terminal androgen-independent prostate cancer.

ADDITIONAL IMPLICATIONS

The terminal androgen-independent malignancy was not aborted by the treatment with Lu177-PSMA, which is consistent with another report [7]. In contrast, the cabergoline treatment did terminate the malignancy. This suggests that the terminal androgen-independent malignant cells might not express detectable levels of PSMA, or the PSMA is mutated and not detectable.

It is also notable that the post-androgen ablation subsequent development of androgen-independent malignancy was not associated with an increase in PSA; thereby indicating that these malignant cells might not express PSA.

Those relationships are consistent with our understanding that the androgen-dependent cells and the androgen-independent cells are different populations of malignant cells.

Disclosures: Clioquinol (3% Clioquinol Cream) and cabergoline (Dostinex) treatments were in conformity with the FDA policy for the "off label use" of a clinical trial safe drug; and in conformity with the "right to try" policy for the use of the safe drug for the treatment of patients with terminal medical conditions.

Patient "XY" was presented with the manuscript for his input into the content and the publication of the manuscript.

In accordance with HIPAA policy, the authors removed identifiers (including unique patient characteristics) from the data prior to submission and publication of the article; so that a signed privacy authorization is not needed.

ACKNOWLEDGEMENTS:

Studies of LCC and RBF cited in this report were supported in part by NIH grants CA79903 and DK42839.

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