

# Dramatic prostate-specific antigen response with activated hemicellulose compound in metastatic castration-resistant prostate cancer

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**Castration-resistant prostate cancer (CRPC) is an incurable disease with limited treatment options. Herbal supplements are unconventional treatments for a variety of diseases. Active hemicellulose compound (AHCC) is a Japanese supplement discovered by hybridizing several mushrooms used in traditional healing for the purpose of maintaining 'super immunity'. We report on a 66-year-old gentleman with CRPC with an excellent serologic response to AHCC. This case hypothesizes that AHCC may have potential activity against CRPC. *Anti-Cancer Drugs* 20:215–216 © 2009 Wolters Kluwer Health | Lippincott Williams & Wilkins.**

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## Introduction

The median survival of patients with castration-resistant prostate cancer (CRPC) is approximately 18 months. After failure of hormonal therapy, secondary hormonal maneuvers, ketoconazole, and taxotere-based chemotherapy remain the mainstay of treatment. The use of unconventional herbal supplements in many malignancies has been increasing over the last several years. We report our experience with active hemicellulose compound (AHCC), a composition of mushroom mycelia extract, in a patient with CRPC.

## Case presentation and management

The patient was a 66-year-old Caucasian gentleman who initially presented in July 2006 with a 2 month history of left hip pain and 12 pound weight loss. MRI of the lumbar spine demonstrated osteoblastic metastases along with vertebral collapse at multiple levels consistent with metastatic disease. Subsequently, he was admitted to hospital and initial prostate-specific antigen (PSA) was greater than 2000 ng/ml. Digital rectal exam revealed a hard, multinodular prostate. Transrectal ultrasound-guided biopsy revealed high-grade prostate adenocarcinoma with Gleason score of 4 + 5 = 9. He was initiated on complete androgen blockade with leuprolide and bicalutamide. He also received palliative radiotherapy to the lumbar spine. At the time of discharge from the hospital, his PSA had declined to 993 ng/ml. Subsequent PSA levels continued to decline through November 2007 at which time it was 2.57 ng/ml (Fig. 1). In January 2007, he received one infusion of samarium-153 because of persistent bone pain.

Unfortunately, starting in February 2007 his PSA began to rise. By April 2007, his PSA had escalated to 29.3 ng/ml.

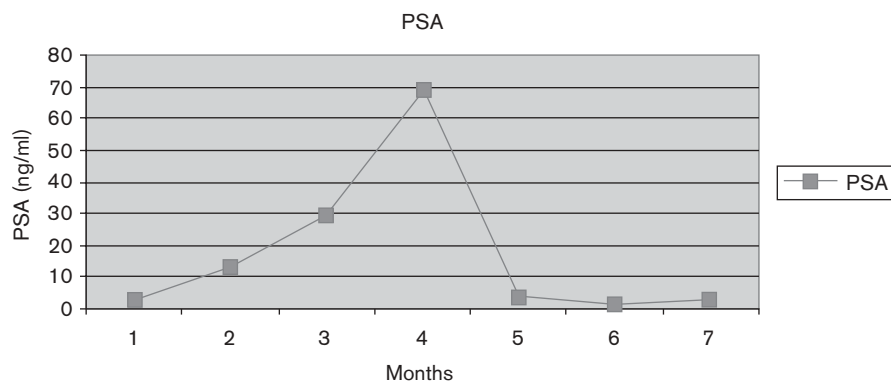
Casodex was then discontinued to assess for androgen withdrawal response; however, his subsequent PSA values continued to escalate to a level of 69.3 ng/ml by June 2007. Several therapeutic treatment options were discussed with him; however, it was at this time that he began self-administering ImmPower's AHCC mushroom supplement. By the end of June 2007 his PSA had declined to 3.35 ng/ml (95% reduction). Further follow-up demonstrated that his PSA dropped to a nadir of 1.5 ng/ml by August 2007. The most recent PSA level in November 2007 remained low at 2.57 ng/ml. Repeat imaging revealed stable bone disease and he continues to supplement with AHCC at this time. He has been doing well symptomatically with an improvement in his ambulation because of alleviated pain.

## Discussion

Prostate cancer is the sixth most common cancer in the world, but is the single most common noncutaneous malignancy in the United States representing approximately 29% of all cancers diagnosed in men each year. In the United States, approximately 218 890 cases are diagnosed annually, and approximately 27 050 deaths were estimated to occur in 2007.

The use of unconventional herbal supplements in malignancy has been increasing over the past few years. A review of complementary alternative medicine around the world estimates average prevalence of complementary alternative medicine at 31% [1]. Herbal remedies including plant and fungi extracts have been utilized in the treatment of prostate cancer for several years. AHCC is a compound consisting of mushroom mycelia, extract, candelilla wax, cyclodextrin, and microcrystalline

Fig. 1



At 4 months, the patient began self-administering activated hemicellulose compound. PSA, prostate-specific antigen.

cellulose. It has been demonstrated that AHCC has activity in prostate cancer, ovarian cancer, and multiple myeloma [2].

As detailed in our case, we report a case of a 66-year-old Caucasian gentleman with CRPC with high-risk features who benefited less than 6 months from initial complete androgen blockade.

Subsequently, androgen withdrawal demonstrated no benefit given a surge in his PSA and ultimately, the self-administration of AHCC resulted in a dramatic PSA decrease within 1 month, which continued to control his disease today, over 6 months from initial supplementation with AHCC.

Although the exact mechanism by which AHCC boosts natural killer (NK) activity remains under investigation, theoretically it seems that AHCC works by stimulating NK cells and by direct anticancer activity.

It has been hypothesized that AHCC activates NK cells by increasing their binding capacity to tumor cells by two-fold, and also by increasing natural cell granularity. In addition, we speculate that  $\beta$ -1,4-glucans are recognized by C-type lectins, such as lectin-1 on NK cells, thus initiating innate immunity. C-type lectins are also expressed on other cell types, including macrophages, dendritic cells, and  $\gamma\delta$ -T cells, which may further influence NK cells and the innate immune response through the production of cytokines. Earlier reports suggest that AHCC influences the production of a variety of cytokines [3], including enhanced IL-12 (NK

stimulatory factor) production by macrophages [4] and IFN- $\gamma$  production by antigen-specific CD8 + T cells [5].

In the study by Ghoneum *et al.* [6], it seems that two tumor cell lines were analyzed, K562 (an erythroleukemia cell line) and Raji (a Burkitt cell lymphoma) of human origin. Results demonstrated that AHCC inhibits tumor cell growth in a dose-dependent manner. Both tumor cell lines were sensitive toward AHCC toxicity, but Raji cells were more sensitive than K562. AHCC at a concentration of 1 mg/ml caused 21 and 43% reduction in growth of K562 and Raji cells, respectively.

In conclusion, based on limited studies to date, it seems that AHCC may have a role in the management of prostate cancer patients especially those who have failed hormonal therapy. Larger studies are required to analyze the impact on this new therapy in prostate cancer patients.

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