

Case Report

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Efficacy of Traditional Chinese Medicine Treatment alone for Recurrent and Refractory Castration-Resistant Prostate Cancer: A Case Report and Literature Review

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Abstract

Introduction: Prostate Cancer (PCa) is a malignant tumor that occurs in the epithelial gland of prostate, and it ranks 6th in the incidence rate of malignant tumors among men in China, while the death rate ranks 2nd. The probability of distant metastasis can be as high as 70%, with bone metastasis being the most common. Currently, the treatment of metastatic Prostate Cancer (mPCa) is mainly endocrine therapy, but hormone resistance occurs in almost all patients, which makes the disease recurring and the difficulty of treatment dramatically increased. This paper aims to provide a new therapeutic idea and a turnaround for the treatment of androgen-resistant recurrent refractory prostate cancer through the treatment of a case of recurrent refractory prostate cancer by simple traditional Chinese medicine.

Patient concerns: Most of the literature reports that Traditional Chinese Medicine (TCM) has produced satisfactory results in the treatment of cancer patients as an adjuvant treatment for various malignancies in an 83-year-old male patient who developed advanced Prostate Cancer (PCa) with multiple bone metastases throughout his body. Due to the failure of multiple lines of endocrine therapy and the development of multiple bone metastases throughout the body and a persistent rise in PSA, the patient chose to receive TCM treatment alone in the hope of prolonging his life and improving his quality of life.

Diagnosis: An 83-year-old male patient with mPCa who failed treatments such as medical castration, and administration of bicalutamide, abiraterone, and enzalutamide, developed multiple new bone metastases throughout the body, pain in both legs and even inability to walk, and his PSA continued to rise.

Interventions: The patient requested that the final therapeutic strategy be Chinese medicine as monotherapy for long-term treatment. The patient took 30-50 mL of the decoction 1 h after a meal, three times a day.

Outcomes: After undergoing TCM treatment for four weeks, the patient's pain, and symptoms such as fatigue and anorexia were remarkably relieved, and the serum PSA dropped to 69 ng/ml. After 4 months of continuous medication, the patient was able to walk on his own, and the serum PSA dropped to 49.7 ng/ml.

Conclusion: This case is the first one in the world where TCM treatment alone has achieved remarkable efficacy for the treatment of recurrent and refractory castration-resistant PCa.

Keywords: Traditional Chinese medicine; Alternative therapy; Castration resistance.

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Introduction

PCa is one of the most common malignant tumors in elderly men. Approximately 30% of men are at risk of prostate cancer, and the vast majority of patients have already developed distant metastasis at the time of detection, with up to 66.3% developing bone metastasis [1] and 3% of patients dying from mPCa [2]. Although the mortality rate is relatively low, symptoms such as bone pain, spinal cord compression, pathological fractures and other symptoms caused by bone metastases can greatly affect patients' quality of life.

Currently, Androgen Deprivation Therapy (ADT) is still the basic treatment of mPCa. The main ADT methods include orchiectomy or castration with administration of Gonadotropin Releasing Hormone (GnRH) agonist, and the first-line use of ADT with combined androgen blockade, such as with androgen receptor antagonists (apalutamide, enzalutamide, bicalutamide, etc. [3,4]) which is supported by several experiments. 90% of newly-treated patients with mPCa may respond to ADT, but more than half of patients with distant metastasis will develop hormone resistance in less than 2 years and progress to metastatic castration-resistant prostate cancer. Thereafter, in addition to continuing ADT, abiraterone, enzalutamide, Sipuleucel-T, and docetaxel can be administered. For example, abiraterone inhibits androgen synthesis by inhibiting CYP17, a key enzyme in androgen synthesis. However, the median Overall Survival (OS) can only be extended for about 4 months [5,6] with the use of abiraterone. Patients will also be resistant to abiraterone, thus resulting in limited clinical benefits. Although hormone therapy, targeted therapy, immunotherapy or chemotherapy can be conducted if more extensive bone metastases or even visceral metastases occur after second-line treatment, the therapeutic effect is limited as suggested in existing studies. For example, the median Progress Free Survival (PFS) of chemotherapy as a subsequent treatment after disease progression is only 3 months [7]. In addition, the severe toxicity caused by chemotherapy can also affect the metabolism and proliferation of normal cells, especially of some elderly patients, which severely reduces their quality of life. Eventually, chemotherapy resistance will develop, affecting the subsequent treatment. According to guidelines of the National Comprehensive Cancer Network (NCCN) for prostate cancer, there are no effective drugs to treat this type of recurrent and refractory castration-resistant prostate cancer.

In our recent clinical practice, a patient with mPCa who failed treatments such as medical castration, and administration of bicalutamide, abiraterone, and enzalutamide, developed multiple new bone metastases throughout the body, pain in both legs and even inability to walk, and his PSA continued to rise. Then TCM treatment was conducted alone according to patient's willingness. The TCM treatment has achieved desired results. Bone related pain was improved significantly in a short period of time, and the corresponding serum PSA decreased rapidly. In the long-term follow-up, the patient's quality of life was greatly improved. Most surprisingly, it was suggested from the patient's recent bone scan results that there were significantly fewer bone metastases than before. This case is reported here. Permission was obtained, and a written informed consent from the patient was presented in this case.

Case report

Liao, an 85-year-old male, presented with dysuria, pain in both lower limbs with no obvious causes in July 2016, was diagnosed with prostate cancer (T3, with a Gleason score of 5+3) by clinical examination and prostate biopsy, with PSA>100 ng/ml at onset, and bone scan suggesting signs of bone metastasis signs (Figure 1). After initiation of CAB with bicalutamide plus goserelin acetate in August 2016, his PSA continued to decrease until June 2018. However, the patient experienced worsening bone related pain, and multiplying PSA. There was no relief in bone related pain after sequential treatment with abiraterone acetate plus prednisone, enzalutamide, and others. Patient's PSA remained high, and bone scan suggested new bone metastases in multiple ribs, multiple segments of the spine and pelvis with signs of extensive bone metastases (Figure 2). According to the NCCN guidelines, there is no reliable treatment for prostate cancer, and the patient expected to receive treatment with TCM. So, he went to Affiliated Hospital of Chengdu University of TCM for TCM treatment in July 2018. Before the initiation of TCM, the patient was unable to move voluntarily due to bone pain, with serum PSA of 128.91 ng/ml, NRS score of 7, and bone scan suggesting signs of extensive bone metastases. Regarding the patient's symptoms, such as pain and discomfort, inability to walk, insomnia, and poor appetite, he was diagnosed as impediment syndrome according to TCM syndrome differentiation and treatment. Dangguiuliuhuang decoction was used as the main prescription with modification. The main components were as follows: Radix angelicae sinensis 15 g, Rehmannia glutinosa 15 g, Stragalus membranaceus 60 g, Scutellaria baicalensis georgi 15 g, Coptidis rhizoma 6 g, Phellodendron amurense 15 g, Radix rehmanniae preparata 15 g. The administration was as follows: Put herbs above into the pot for decocting. Then pour 2 liters of water. After the decoction is boiled by the high fire, then turn to low fire and boil for about half an hour. Each prescription is decocted twice and then mixed, and is divided into two portions for administering for 2 days. Take it 3 times a day, 30-50 ml of it each time 1 hour after meal.

After undergoing TCM treatment for four weeks, the patient's pain, and symptoms such as fatigue, anorexia and insomnia were remarkably relieved, and he could stand and walk briefly with the help of tools, with a pain NRS score of 4, and his serum PSA was reduced to 69 ng/ml. After 4 months of continuous medication, the patient was able to walk on his own without relying on tools, with a pain NRS score of 2, significant improvement in quality of life, and a decrease in serum PSA to 79.7 ng/ml. In the subsequent follow-up visits every three months, the patient's general symptoms and quality of life gradually improved, and the serum PSA also reduced (shown in Figure 4). The latest bone scan showed a significant reduction in bone metastases (shown in Figure 3), and no adverse events such as hepatic or renal impairment were found during the follow-up.

Data availability statement: Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

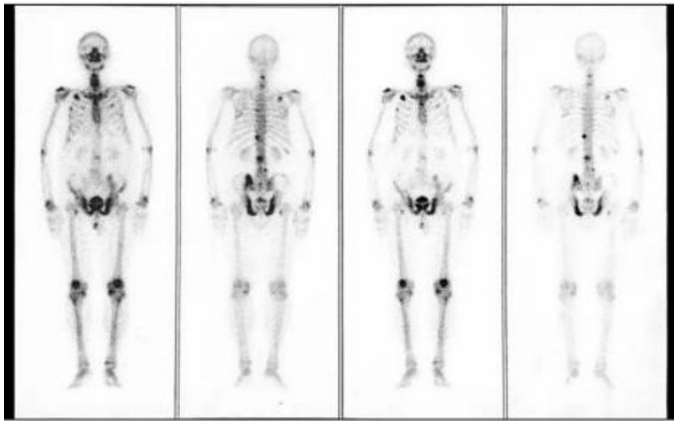


Figure 1: July 2016, bone scan suggested signs of bone metastasis.

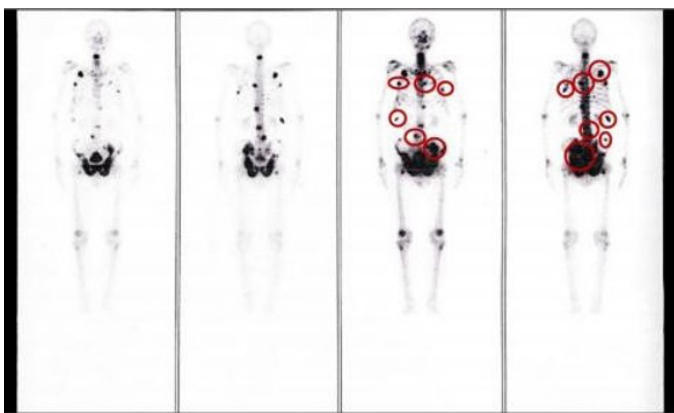


Figure 2: June 2018, bone scan suggested new bone metastases in multiple ribs, multiple segments of the spine and pelvis; (Note: major bone metastases indicated by red circles).

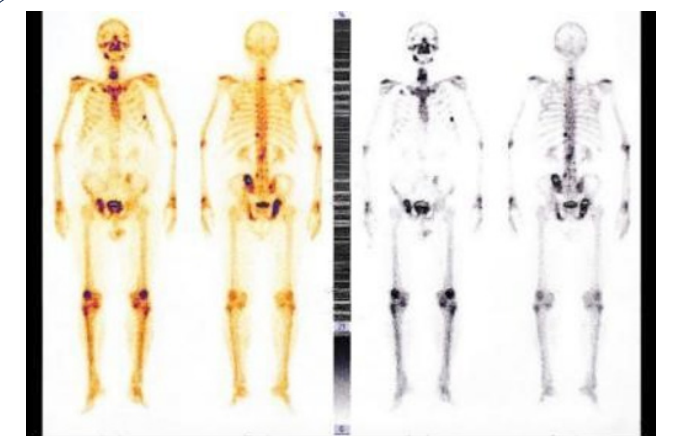


Figure 3: July 2021, bone scan suggested that the number of foci was significantly reduced compared with the previous bone scan (June 2018).

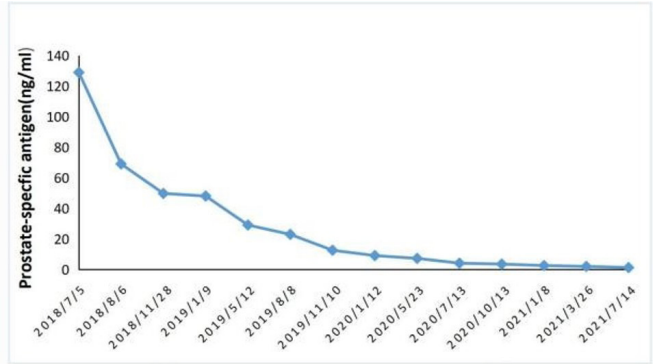


Figure 4: PSA response to TCM.

Discussion

Prostate cancer is the second most common malignant tumor in men. In China, the incidence rate of prostate cancer is increasing year by year due to the aging of population and the changes in diet [8]. Two thirds of patients have detected distant metastases at the time of initial diagnosis [9], and the 5-year OS of prostate cancer. It is suggested by experts that the first-line use of ADT combined with androgen deprivation of mPCa is 30% [10]. At present, ADT remains as the basic treatment of metastatic prostate cancer, such as enzalutamide, can reduce the risk of death by 33% [11,12]. The oncological results of ADT achieved by surgical or medical castration are similar. At present, medical castration has basically replaced surgical castration [13], but long-term ADT treatment will lead to hypogonadism, causing a series of adverse events such as osteoporosis, sexual dysfunction and cardiovascular disease, seriously affecting the quality of life and even resulting in death [14,15]. More than 50% of patients with mPCa will develop metastatic Castration-Resistant Prostate Cancer (mCRPC) within 2 years after endocrine therapy, with a median OS of only 14 months [16].

The first-line treatment for patients with mCRPC is abiraterone, enzalutamide, Sipuleucel-L, or docetaxel. Abiraterone is a CYP17 inhibitor. Although it has been reported that abiraterone can prolong the median OS and PFS of patients with mCRPC and delay the time of pain progression [17], the effects are not ideal, especially for patients who have received chemotherapy before. In a clinical study of abiraterone acetate for mCRPC after chemotherapy, the median OS of patients administered with abiraterone acetate plus prednisone was only 14.8 months, and the median time to PSA progression was only 5.6 months [18]. If the disease progresses again, the clinical efficacy still remains limited although chemotherapy, immunotherapy, and targeted therapy, such as pembrolizumab, can be performed for subsequent treatment, the median rPFS is only 3.7 months [19]. Therefore hormone resistance, chemotherapy resistance, disease progression and many other factors have driven us to find better treatment methods.

Fortunately, in this clinical practice, the patient with mPCa who failed multiple lines of endocrine therapy chose TCM according to his willingness. After treatment, the patient's bone-related pain improved significantly within a short period of time, and the corresponding serum PSA decreased rapidly, and the quality of life improved greatly. It is especially worth noting that the latest bone scans suggested a significant decrease in bone metastatic lesions. And in the long-term follow-up, no adverse events occurred, and

a very small economic cost was paid. Traditional Chinese medicine has been used for thousands of years. The efficacy of TCM as an adjuvant therapy in preoperative control of tumor progression, postoperative recovery and prevention of recurrence [20], and mitigation of toxicity and side effects during radiotherapy [21] has been confirmed, but there are few reports on using TCM alone to control tumors. TCM has been successfully practiced as a monotherapy to treat advanced Hepatocellular Carcinoma (HCC), which has shown significant efficacy and high safety [22]. However, regarding TCM for treating recurrent and refractory castration-resistant prostate cancer, we reviewed relevant literatures on the treatment of prostate cancer with TCM at home and abroad. We found that all these treatments are based on single Chinese herbal medicine, Chinese herbal medicine extract, Chinese patent medicine, acupuncture, patch and enema and other TCM treatment combined with endocrine therapy, chemotherapy or radiotherapy to treat prostate cancer, with the main purpose to reduce the side effects of related treatments. This is the first case in the world in which recurrent and refractory castration-resistant prostate cancer is treated with TCM alone.

The anti-tumor effect of traditional Chinese medicine has been confirmed in many studies: 1) The direct anti-tumor effect of TCM, such as *Curcuma longa*, *Andrographis paniculata* and other Chinese herbal medicine extract can inhibit cell viability, induce apoptosis and inhibit tumor growth [23,24]. 2) the role of TCM in improving the tumor microenvironment. For example, studies have shown that artemisinin derivatives [25], astragalus extracts [26] can inhibit TGF- β in the tumor microenvironment because the overexpression of Transforming Growth Factor- β (TGF- β) can lead to tumor microenvironment imbalance and tumor progression [27]. 3) TCM improving the body immunity. Studies have reported that *Panax ginseng* has a wide range of anti-cancer activity, because ginsenosides, the ginseng extract, can inhibit the proliferation of tumor cells without affecting the vitality of normal gastric epithelial cells. It shows anti-tumor effect while supporting the healthy qi [28]. 4) the synergistic effect of the compound prescription. Each herb in the compound prescription has a variety of anti-tumor active ingredients. And in the process of decoction, every herb or several herbs can interact with and promote each other. The mechanism of effect of TCM needs further research in order to obtain greater benefits in clinical practice.

It is the first case in the world where TCM treatment alone has achieved remarkable efficacy for the treatment of recurrent and refractory castration-resistant prostate cancer, which provides a new way for the treatment of it, as well as various treatments for all stages of prostate cancer and other types of malignant tumors.

Abbreviations: MPCa: Metastatic Prostate Cancer; TCM: Traditional Chinese Medicine; PCa: Prostate Cancer; PSA: Prostate Specific Antigen; Pca: Prostate Cancer; ADT: Androgen Deprivation Therapy; GnRH: Gonadotropin-Releasing Hormone; OS: Overall Survival; PFS: Progress Free Survival; NCCN: National Comprehensive Cancer Network; MCRPC: Metastatic Castration-Resistant Prostate Cancer; HCC: Hepatocellular Carcinoma; TGF- β : Transforming Growth Factor- β .

Declarations

Ethical approval: This study involving human participants was reviewed and approved by the Medical Ethics Committee of the Hospital of Chengdu University of Traditional Chinese Medicine (No. 2015BL-003). And this study was performed in accordance with the Declaration of Helsinki. The patient provided his written informed consent to participate in this study.

Author contributions: Sq X: The patient was diagnosed and treated in Traditional Chinese Medicine. Q Y, she contributed by examining the patient, following up the patient, writing up the manuscript, and reviewing the literature. J S, Jq Q, H M, P D, Li H, Di W, all contributed by examining the patient, following up the patient. Sq X guided writing and revised the manuscript. All authors read and approved the final manuscript.

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