Remarkable Pathologic Change in Advanced Prostate Cancer Patient Using Dendritic Cell–Cytokine-Induced Killer Combined Therapy: A Case Report

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Clinical Practice Points

- Dendritic cell–cytokine-induced killer immunotherapy is a novel method that is often used to treat castration-resistant prostate cancer.
- It is a safe and effective treatment for patients with malignant tumors.
- Here we describe what is to our knowledge the first case of a patient with advanced prostate cancer who was successfully treated with androgen deprivation combined immunotherapy.
- The patient underwent surgery after treatment, and the pathologic analysis revealed only prostatic intraepithelial neoplasia and no cancer tissue.

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Introduction

Although the mortality of prostate cancer has dropped by 40% in the past 20 years,[1] it remains the most frequently diagnosed cancer and the sixth leading cause of cancer-associated deaths in men worldwide.[2] Because of the development of imaging systems and examinations, most early stage prostate cancer cases can be effectively treated by surgery. Unfortunately, up to one third of patients with early stage prostate cancer and 4% of all newly diagnosed patients ultimately present with metastatic disease, with or without castration-resistant prostate cancer (CRPC).[3] In such cases, the United States Food and Drug Administration (FDA) approved the first therapeutic anticancer vaccine, sipuleucel-T, for the treatment of metastatic CRPC in April 2010, which introduced a novel era of immunotherapy for prostate cancer.[4] Currently, various forms of immunotherapy are being investigated in clinical trials for prostate cancer, including dendritic cell (DC)-based vaccines, immune checkpoint inhibitors, virus-based vectors, and cell-based polyvalent vaccines. To our knowledge, none of the patients in these trials has ultimately experienced pathologic remission. Here we report and discuss a case of advanced prostate cancer in a patient who was successfully treated with androgen deprivation therapy (ADT) combined immunotherapy and share our experience in treating such patients.

Case Report

A 54-year-old man presented with dysuria and excessive urination at night with no apparent cause in November 2012 at his local doctor. Computed tomographic (CT) scan and ultrasound of the abdomen revealed an enlarged prostate (50 × 59 × 71 mm), an inhomogeneous gland, and a significantly enhanced tissue mass next to the left iliac artery, which was thought to be lymphatic metastasis (Figure 1A). His prostate-specific antigen (PSA) level at diagnosis

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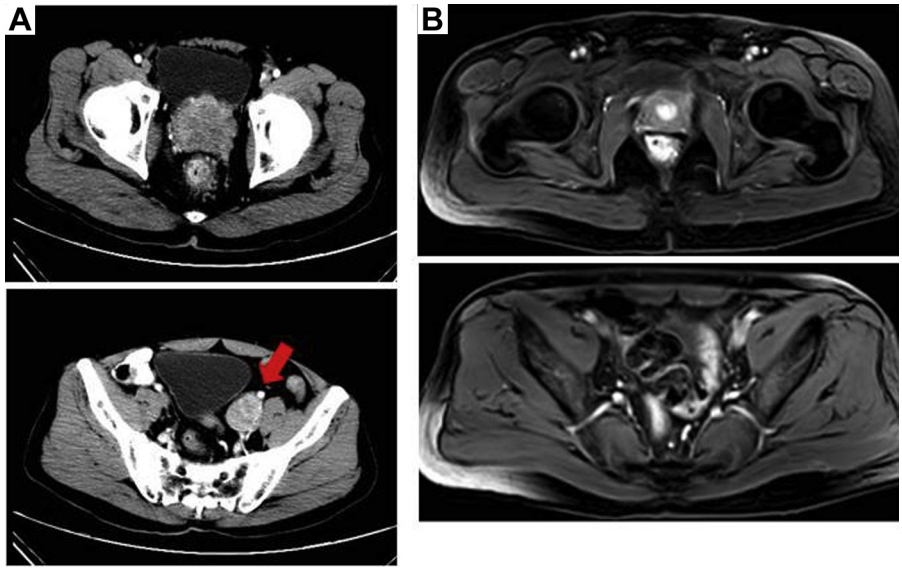
Figure 1 Patient Status Before and After DC-CIK Immunotherapy. Appraisal Included CT Scan at Initial Presentation and MRI Series During Reexamination. (A) An Enlarged Prostate (50 × 59 × 71 mm) With a Heterogeneous Gland and a Significantly Enhanced Tissue Mass (38 × 28 × 44 mm) Next to the Left Iliac Artery, Which Was Thought to Be Lymphatic Metastasis, Was Observed by CT Scan at Hospital Admission. (B) After 2 Series of DC-CIK (3 DC + 2 CIK) Therapy, MRI Revealed That the Volume of the Prostate Had Decreased Markedly, to 31 × 19 × 33 mm; the Invasion Foci in the Seminal Vesicle and the Left Iliac Lymph Nodes Had Also Disappeared. However, There Was a Suspicious Enlarged Lymph Node on the Right Side of the Inguinal Region



Abbreviations: CIK = cytokine-induced killer; CT = computed tomography; DC = dendritic cell; MRI = magnetic resonance imaging.

was 475.4 ng/mL (Figure 2). To confirm the diagnosis, we performed a systemic 15-needle biopsy, which confirmed that he had advanced prostate cancer; 14 of the 15 needles detected cancer cell infiltration and significant heterogeneity. Gleason score was 4 + 5 = 9 (Figure 3A). According to the tumor, node, metastasis classification system, the disease was labeled T3bN1M0; however, no consensus was reached by the medical team regarding further surgical intervention. Chemoradiotherapy was subsequently considered; however, the patient was treated with ADT because of his young age and because ADT has fewer associated complications.

In December 2012, the patient was administered ADT via goserelin (3.6 mg once a month) and bicalutamide (50 mg once a day). The patient's PSA levels were reduced to 65.4 ng/mL after 3 months of ADT; further, it did not decrease. The patient returned for review in January 2013, when a CT scan revealed a shrunken volume of both the prostate and the enhanced tissue mass near the iliac artery. However, the gland was heterogeneous and seminal vesicle invasion remained. Therefore, the tumor was classified as refractory to hormone therapy. Chemoradiotherapy was discussed again but was refused by the patient.

During this period, the patient usually experienced sudden pain in his femur without definite reason. After consultation and discussion with oncologists, we decided to administer DC—cytokine-induced killer (CIK) immunotherapy in addition to the ADT. The patient signed the informed consent for the treatment protocol, which was approved for tumor patients by the ethics committee of Zhujiang Hospital. Written informed consent was signed by the patient to authorize the publication of this case report and the images therein.

DC and CIK cells were generated as described previously.[5,6] To culture autologous DCs, peripheral blood mononuclear cells were purified from patients and cultured in X-VIVO 20 medium (Lonza) supplemented with 1000 U/mL interleukin 4 and 500 U/mL granulocyte and macrophage colony-stimulating factor to facilitate DC growth. After 7 days of culture, CIK cells were obtained as previously reported[7,8] and were cocultured with stimulated DCs for another 7 days. Safety tests were performed during the course of the cell culture. All products were free from bacterial and fungal contamination.

Between February and August 2013, the patient received 2 courses (3 DC + 2 CIK) of DC-CIK therapy. During the treatment, the patient experienced fever twice and fatigue once after injection, which are common immune-related adverse events.[9,10] However, he recovered well after proper treatment. By late February 2013, magnetic resonance imaging (MRI) demonstrated that the prostate volume had decreased to 33 × 27 × 41 mm, although the seminal vesicles and left external iliac lymph nodes were enlarged. Remarkably, his PSA levels had returned to 0 ng/mL (Figure 2). MRI indicated that the invasion foci on the seminal vesicle and the left external iliac lymph nodes had disappeared (Figure 1B). The patient's weight had also increased.

The patient was then appraised by a multidisciplinary team (including urologists, radiation oncologists, medical oncologists, and radiologists), and after balancing the benefits and adverse effects of