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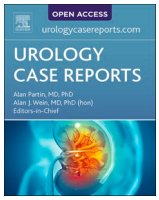

Oncology

Tislelizumab: An effective anti-PD-1 antibody for the treatment of advanced basal cell carcinoma of the prostate

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ABSTRCAT

Basal cell carcinoma (BCC) of the prostate is a rare and enigmatic tumor with uncertain biological behavior and treatment modalities. Some studies suggest that BCC exhibits invasive characteristics and a high degree of malignancy, necessitating proactive management and vigilant monitoring. Notably, there is a lack of reported effective treatment utilizing programmed cell death protein-1 (PD-1) inhibitors for advanced BCC of the prostate. This study explores the efficacy of tislelizumab, as a single-agent therapy, in the successful treatment of advanced prostate BCC.

1. Introduction

BCC, a profoundly uncommon histopathological subtype of prostate cancer, constitutes less than 0.01 % of all malignant prostate gland neoplasms.[1] This distinctive variant was initially characterized by Frankel et al. in their seminal work from 1974,[2] and to date, fewer than a hundred cases have been documented globally. Due to its exceptional rarity, BCC lacks standardized treatment protocols, particularly for advanced stages of the disease within the prostate gland. For localized BCC, radical prostatectomy is often considered the optimal therapeutic approach.[3] However, BCC does not exhibit androgen dependence, rendering the conventional androgen deprivation therapy ineffective.[4] Moreover, genomic and transcriptomic analyses have demonstrated that prostate BCC displays inherent resistance to chemotherapy regimens.[3] It has been reported that chemotherapeutic agents such as docetaxel and cisplatin fail to diminish either the number or size of primary tumors or metastases. Although radiotherapy can effectively manage primary lesions, it is often accompanied by the development of distant metastatic oligoprogressions during the course of treatment.[4] Recently, advancements in single-cell RNA-Seq technology have revealed a substantial presence of immune cells infiltrating the tumor microenvironment in BCC.[5] Notably, PD-1 inhibitors have shown promise with successful clinical outcomes in treating both BCC and associated metastatic lesions.[6] In our current study, we present a case of an advanced basal cell carcinoma of the prostate, which was successfully managed with tislelizumab, a novel anti-PD-1 antibody. This case underscores the potential for immunotherapy to pave the way for innovative treatment strategies for BCC, offering new hope in managing this rare and challenging condition.

2. Case report

A 68-year-old male patient was referred to our institution presenting with the primary complaints of recurrent urinary retention and dysuria. The patient underwent a comprehensive evaluation, which included routine blood biochemical tests, color ultrasonography, and physical examination. His serum prostate specific antigen (PSA) level was measured at 3.2 ng/mL, while prostatic acid phosphatase (PAP) concentration stood at 0.6 ng/ml. Upon digital rectal examination, an enlarged prostate gland with a seemingly regular capsule was detected.

Based on these initial findings, the patient was initially diagnosed with benign prostatic hyperplasia and consequently underwent transurethral resection of the prostate (TURP). Histopathological assessment of the surgical specimens under hematoxylin-eosin (HE) staining at × 100 magnification revealed nodular tumor cell clusters displaying peripheral palisading patterns, with common central necrosis within the cancer nests (Fig. 1A). A notably high mitotic count of up to 25 mitoses per 10 high-power fields (HPFs) was observed. Furthermore, approximately 65 % of the tumor cells were positively stained for nuclear antigen Ki-67 (Fig. 1B). Immunohistochemical analysis demonstrated positive reactions against basal cell markers 34βE12 and p63 (Fig. 1C and D), leading to a postoperative pathological diagnosis of BCC.

Despite this diagnosis, the patient declined radical prostatectomy and chemotherapy, and was discharged upon symptom resolution. However, just one month later, during an outpatient follow-up, there was evidence of significant enlargement in the primary lesion and newly

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detected liver metastasis. Magnetic resonance imaging (MRI) showed a well-defined mass with inhomogeneous hyperintensity on fat-suppression T2-weighted sequences (Fig. 2A), corresponding to a lesion in the right peripheral zone of the prostate that exhibited marked diffusion weighted imaging (DWI) hyperintensity, ADC hypointensity, and a mean ADC value of 0.527×10^{-3} mm^2/s. Additionally, MRI scans revealed multiple round lesions with bright signals on fat-suppressed T2 sequences in the liver parenchyma (Fig. 2B), indicative of metastatic infiltration. Given these findings of aggressive tumor progression and metastasis, the patient was promptly readmitted for further and more intensive cancer treatment.

Through extensive review of relevant literature, the author discovered that BCC of the prostate is a non-secretory neoplasm with no response to chemical castration therapy. To establish a theoretical foundation for subsequent treatment strategies, we conducted immunohistochemical analysis of critical markers including prostate-specific antigen (PSA), androgen receptor (AR), and PD-1. Notably, expression of both PSA and AR was absent in the tumor tissue samples (Fig. 3A and B).

For the detection of PD-1 expression, we utilized a rabbit recombinant monoclonal PD-L1 antibody [28-8] from Abcam as the detector antibody, which specifically recognizes PD-L1. The results indicated that PD-L1 was predominantly expressed in the membrane and cytoplasm of cancer cells (Fig. 3C).

A multidisciplinary team comprising urologists, radiologists, and oncologists collaborated to devise and administer the treatment plan. Upon obtaining the patient's written informed consent, tislelizumab at a dose of 200 mg was administered intravenously every three weeks. Remarkably, during the course of immunotherapy, the patient did not experience any immune-related adverse events (irAEs). After just three cycles of treatment, the patient achieved a remarkable durable response and full remission.

The efficacy of tislelizumab was evident on CT enhanced scans after 3 months of treatment, where both the primary prostate lesion and liver metastases had completely vanished (Fig. 4A and B). Following this significant response, the patient underwent radical prostatectomy and received two additional cycles of immunotherapy post-surgery. However, due to financial constraints, the patient declined further treatment after completing a total of five cycles of immunotherapy.

As of now, the patient has survived for a period of 10 months without any evidence of tumor progression or recurrence, underscoring the potential of tislelizumab in treating advanced BCC of the prostate.

3. Discussion

To date, there is a lack of large-scale clinical research on BCC of the prostate, leading to controversies regarding its biological behavior and treatment approaches. While some scholars view BCC of the prostate as a potentially malignant tumor with a favorable prognosis.[7] An increasing number of researchers consider it a rare tumor characterized by strong invasiveness, high aggressiveness, and a propensity for metastasis, necessitating proactive management and close monitoring.[8,9] In the early stages of prostate BCC, urologists advocate for prompt radical prostatectomy. However, for advanced BCC cases, there remains a notable absence of systematic and efficacious treatment options. Distinct from prostate adenocarcinoma, BCC lacks secretory cells and androgen receptor expression, making endocrine therapy less effective in this context. Notably, some patients have experienced disease progression following endocrine therapy.[9]

Monoclonal antibodies targeting PD-1/PD-L1 have demonstrated significant antitumor activity in various advanced malignancies.[10,11] Clinical trials have shown impressive antitumor responses, with objective response rates ranging from 6 % to 17 %, across malignancies such as malignant melanoma, non-small cell lung cancer, and renal cell carcinoma..[12,13] The study found that there was a certain trend towards efficacy and prognosis in patients with expression of PD-1/PD-L1 in several tumors.[13,14] However, a clinical study has shown that the patients with advanced prostate cancer failed to respond to anti-PD-1/PD-L1 treatment, the researchers speculated that the reason is rare PD-L1 expression in prostate cancer.[15] In a recent 3 phase randomized clinical trial, the researchers found that tislelizumab plus chemotherapy improved progression-free survival in patients with advanced squamous non-small-cell lung cancer, even regardless of PD-L1 expression.[16,17] In evaluating the expression of PD-L1 in BCC of the prostate, the recombinant anti-PD-L1 antibody [28-8] was utilized as a detector antibody, revealing high PD-L1 expression in prostate BCC.[18] Tislelizumab, an anti-PD-1 antibody, administered as monotherapy, demonstrated durable responses in patients with solid tumors and hematological malignancies.[19] In our case, multidisciplinary team (MDT) recommended tislelizumab treatment, resulting in the complete disappearance of liver metastasis and the primary prostate lesion on CT imaging after three treatment cycles. Subsequent laparoscopic radical prostatectomy was performed, leading to a favorable outcome with no evidence of recurrence or metastasis during the 10-month follow-up period.

While this report is based on a single case, it underscores the promising potential of immunotherapy in advancing the treatment of advanced basal cell carcinoma (BCC) of the prostate. Despite the patient undergoing only five treatment cycles, the long-term efficacy necessitates diligent monitoring. Our future endeavors will focus on conducting relevant basic research to elucidate the mechanism of tislelizumab in treating BCC of the prostate.

In conclusion, our findings highlight that BCC of the prostate exhibits a notable propensity for invasion and malignancy. Unlike conventional prostate adenocarcinoma, BCC of the prostate appears to exhibit enhanced responsiveness to immunotherapy. This study represents the first documented case of advanced BCC of the prostate benefiting from immunotherapy with tislelizumab, potentially paving the way for a novel therapeutic approach in managing BCC of the prostate.

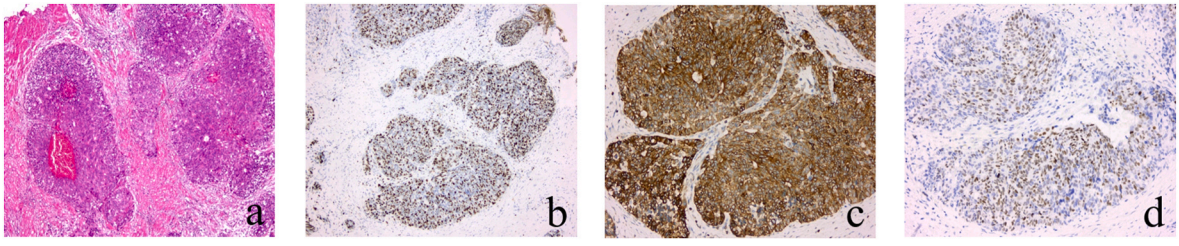

Fig. 1. Pathological findings and immunohistochemistry. (A) HE staining revealed that tumor cells were closely arranged and disordered in nodular nests of peripheral palisading, necrosis was commonly seen in the center of the cancer nest. Tumor cells are uniform in size (original magnification, × 100); (B) By immunostaining, the tumor cells were 65 % for ki-67 (magnification × 100); (C) On immunohistochemistry, the result of basal cell marker 34βE12 was strong positive (magnification × 200); (D) By immunostaining, the result of basal cell marker p63 was positive (magnification × 200).

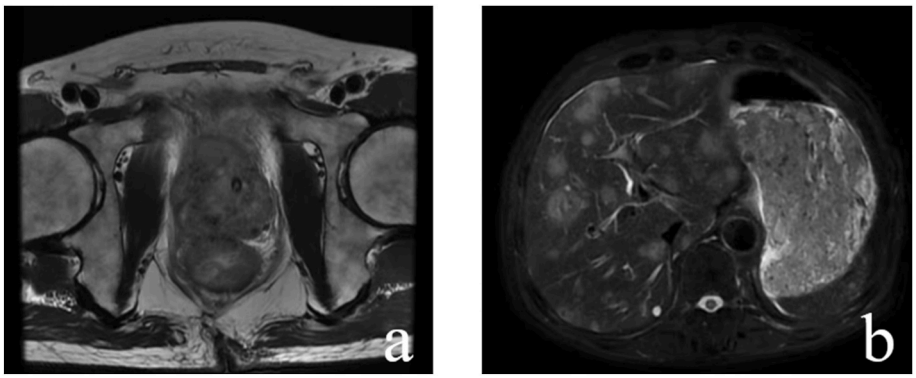

Fig. 2. The imaging findings of the patient before treatment. (A) A well-circumscribed mass displaying inhomogeneous hyperintensity on fat-suppression T2-weighted sequences in the prostate; (B) The metastatic lesions in the liver at diagnosis.

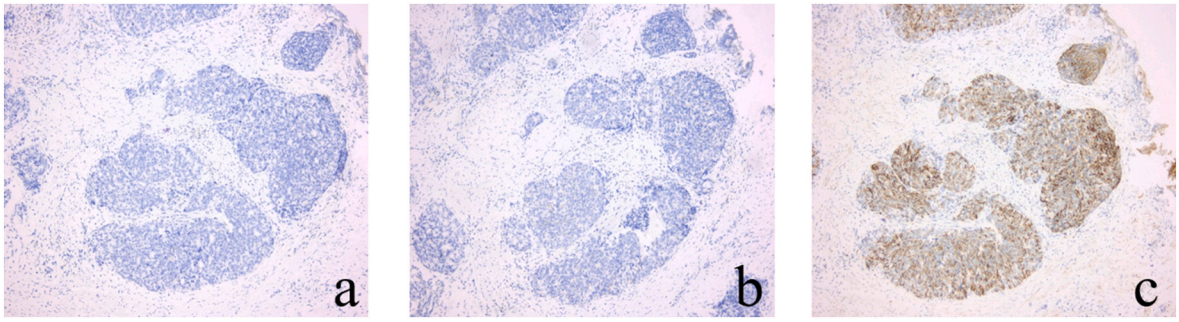

Fig. 3. Pathological findings and immunohistochemistry. (A, B) By immunostaining, expression of PSA and AR was negative in tumor tissues (magnification × 100); (C) Positive for PD-L1 (≥70 %, magnification × 100).

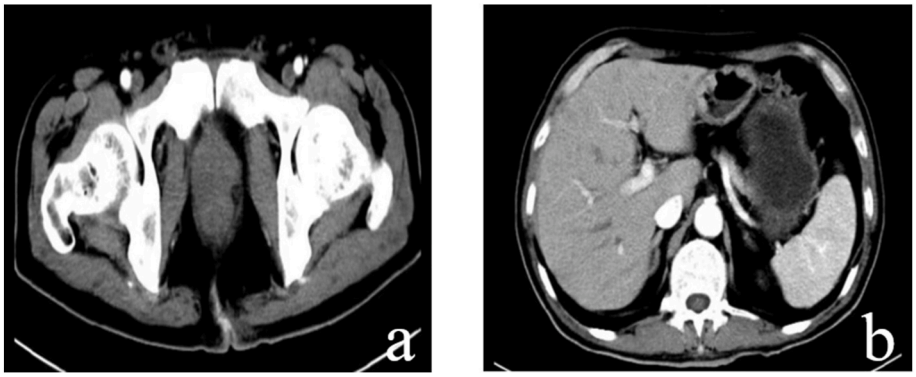

Fig. 4. Post-treatment imaging manifestations of the patient. (A, B) After three cycles immunotherapy showed the tumor response and remission of the primary and metastatic lesions with enhanced CT scan.

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CRediT authorship contribution statement

Hua Jiang: Writing – review & editing, Writing – original draft, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization.

Declaration of Competing interest

There are no conflicts of interest.

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