

# A Case of Locally Advanced Castration-resistant Prostate Cancer With Remarkable Response to Nivolumab

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## Clinical Practice Points

- We present a unique case of castration-resistant prostate cancer with primarily local failure in the pelvis.
- The patient had a remarkable response to single-agent nivolumab after failures of many lines of therapy.
- This case report illustrates immunotherapy showing its promise in the treatment of castration-resistant cases of prostate cancer.

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## Introduction

High-risk prostate cancer and regional disease with nodal metastasis require local treatment with androgen deprivation therapy (ADT) and/or radiation therapy.<sup>1,2</sup> Adjuvant treatment for pathologic nodal metastasis in prostate cancer favors immediate ADT.<sup>3,4</sup> Retrospective data have supported the use of radiation therapy in an adjuvant setting.<sup>5</sup> Until about a decade ago, there were not many options available when prostate cancer progressed on ADT. At present, there are several options, including docetaxel, cabazitaxel, abiraterone, enzalutamide, radium-223, and sipuleucel-T. As in other cancers, checkpoint blockade therapies are also being explored in the treatment of prostate cancer.

## Case Report

We present a case of a 65-year-old male, a lifelong nonsmoker and Vietnam War veteran, with a past medical history significant for aortic valve disease, aortic stenosis, hyperlipidemia, and a long-standing history of lower urinary tract obstruction owing to benign hypertrophy of the prostate. He started experiencing intermittent hematuria in the latter part of 2015 and was evaluated by

the urology department. His Eastern Cooperative Oncology Group performance status was 1. Examination revealed an abnormal prostate. A computed tomography (CT) of the pelvis showed a 10-cm prostatic mass invading the bladder (Figure 1). Also evident was a right common iliac, right internal iliac, and bilateral pelvic side wall lymphadenopathy. Thereafter, he underwent an enucleation procedure for the prostate gland. A histopathology examination of the prostate gland showed poorly differentiated prostatic adenocarcinoma, with Gleason score of 5 + 5 = 10/10 (Figure 2), with an initial prostate-specific antigen (PSA) of 77. There were no components or features of prostatic ductal carcinoma seen, with the absence of discrete gland or cribriform arrangement of tall pseudostratified columnar epithelium. He underwent staging scans with a bone scan and CT of the thorax, which did not reveal distant metastases. The diagnosis was made of locally advanced prostate cancer, stage IV-T4N1M0.

Owing to the rapidly progressing disease and significant hematuria, he was started on ADT along with bicalutamide 50 mg daily to prevent the flare phenomenon. In the meantime, he also experienced right-sided extensive common iliac vein thrombosis and was started on anticoagulation. Because of the huge local burden of the disease in the bladder and significant hematuria, he was started on docetaxel at 75 mg/m<sup>2</sup>, with the expectation of a rapid response. He had initial remarkable chemical and clinical response to chemotherapy after 3 cycles (Figure 3). However, after completing 6 cycles of docetaxel, his PSA started to rise, and his abdominal and pelvic CT scan showed progression of the disease in the pelvis without any distant metastases. At that point, a rebiopsy of the pelvic mass was

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# Refractory Prostate Cancer Responds to Single Agent Nivolumab

**Figure 1** Computed Tomography Image Demonstrating 10 cm Pelvic Mass on Presentation



**Figure 3** Computed Tomography Image Demonstrating a 5-cm Pelvic Mass Showing Response to 3 Cycles of Docetaxel



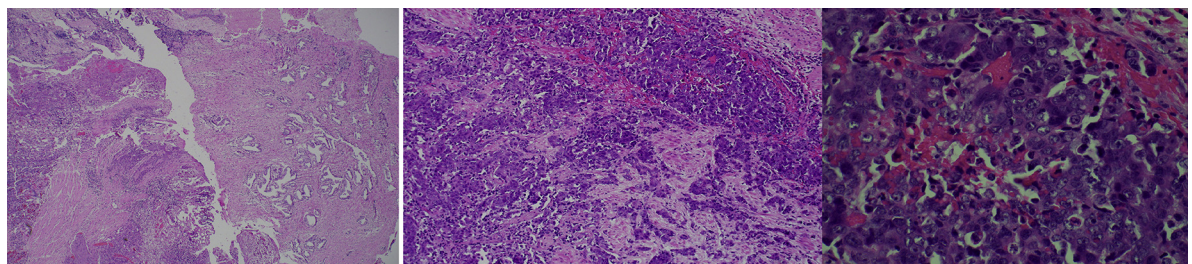
done to rule out small-cell anaplastic carcinoma transformation of the prostate carcinoma. Histopathology of the mass again showed prostatic adenocarcinoma. He was then started on enzalutamide. His case was thereafter discussed in the genitourinary tumor board, where radiation therapy was discussed as an option. However, the patient opted to continue with enzalutamide. Initially, the disease was stable for 3 cycles but then later progressed again in the right hemi pelvis. The patient was then referred to Johns Hopkins Institute. Enzalutamide was stopped, and he was started on cabazitaxel and carboplatin. He went on to complete 6 cycles of this treatment. Unfortunately, the disease progressed again in the pelvis after the treatment was finished (Figure 4). At that time, the patient was evaluated at Memorial Sloan Kettering Cancer Center for consideration of enrollment in a clinical trial exploring combination therapies together with nivolumab. The patient opted not to join the study. He was then started on nivolumab alone on a compassionate basis. After 3 cycles of nivolumab, the patient had significant clinical response. His PSA was undetectable. He had now

completed 19 cycles and continued to have an undetectable PSA. His pelvic mass had remarkably decreased to 7.9 cm  $\times$  1.7 cm (Figure 5) from 10 cm  $\times$  5.7 cm  $\times$  8.7 cm prior to the start of nivolumab. The mass was described as difficult to measure as it was almost unmeasurable in one dimension. His performance status also improved to 0 from 1. His PSA trend is outlined in Table 1. Programmed death-ligand 1 (PD-L1) testing was reviewed retrospectively in the tumor block, which revealed a PD-L1 immunohistochemical stain of  $< 1\%$  (Figure 6). Retrospectively, immunohistochemical analysis looking for the protein expression of MLH1, MSH2, MSH6, and PMS2 was performed on the tumor sample. The results showed the tumor cells to have loss of expression of MSH2 and MSH6, with retention of expression of MLH1 and PMS2. A germline mutation analysis was not performed.

## Discussion

In recent years use of docetaxel evolved from metastatic castrate resistant setting to hormone naive status and in locally advanced prostate cancer.<sup>6-9</sup> Despite these types of advances, metastatic

**Figure 2** From Left to Right Are Hematoxylin and Eosin Stains of the Prostate Biopsy. A Low-power View Shows Normal Benign Prostatic Tissue on the Right Side and a Malignant Infiltrate of Cells on the Left Side. The Next Image Is a Medium Power View Showing an Infiltrate Consisting of Clusters to Sheets of Malignant Pleomorphic Cells With High-grade Nuclei and Prominent Nucleoli. The Third Image Is a High-power View of an Infiltrate of Malignant Pleomorphic Cells With High-grade Nucleoli. Many Mitotic Figures Are Also Seen



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