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# Prostate cancer recurrence mimicking invasive urothelial cancer of the bladder

Kazuki Okubo [a], Fumiko Hamabe [b], Kosuke Miyai [c], Makoto Isono [a], Hiroshi Shinmoto [b], Akinori Sato [a,*]

[a] Department of Urology, National Defense Medical College, 3-2 Namiki, Tokorozawa, Saitama, 359-8513, Japan
[b] Department of Radiology, National Defense Medical College, 3-2 Namiki, Tokorozawa, Saitama, 359-8513, Japan
[c] Department of Basic Pathology, National Defense Medical College, 3-2 Namiki, Tokorozawa, Saitama, 359-8513, Japan

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ABSTRACT

A 74-year-old male patient with stage D1 prostate cancer with the initial prostate-specific antigen (PSA) level of 5570 ng/mL had received androgen deprivation therapy and the serum PSA level had decreased to 0.23 ng/mL when he developed macroscopic hematuria. MRI and cystoscopy suggested invasive urothelial cancer of the bladder, and transurethral resection was performed. The tumors were pathologically diagnosed as a Gleason score 9 prostate cancer with no PSA expression. Prostate cancer patients who develop novel symptoms should be screened for prostate cancer recurrence even if they have very low PSA levels.

## Introduction

Diagnosis of prostate cancer recurrence is generally made based on elevated PSA levels, but there have been reported cases of prostate cancer recurrence with no or only low PSA elevations.[1] In such cases, initiation of treatment against recurrence would be delayed. We report herein a case of prostate cancer recurrence with very low PSA levels, in which macroscopic hematuria led to prompt diagnosis and treatment of cancer recurrence.

### *Case presentation*

A 74-year-old male patient with stage D1 prostate cancer (PSA 5570 ng/mL, Gleason score 9) (Fig. 1A–C) had been treated with leuprorelin and bicalutamide for 10 months and subsequently with leuprorelin and enzalutamide for 4 months. The PSA nadir was 0.092 ng/mL and then his PSA had gradually increased to 0.23 ng/mL, when he complained of macroscopic hematuria. A computed tomography scan revealed disappearance of the lymph node metastasis (Fig. 2A). On MRI, novel bladder lesions were noted whereas the original bladder invasion was dramatically improved (Fig. 2B). Cystoscopy showed tumors protruding from the right lateral wall, suggesting invasive urothelial cancer (Fig. 2C). Transurethral resection was performed, and the tumors were pathologically diagnosed as a Gleason score 9 prostate cancer with no PSA expression (Fig. 2D). The patient subsequently received local radiotherapy. Enzalutamide was changed to abiraterone acetate plus prednisone against PSA progression. Although his PSA level has been gradually increasing, he has remained asymptomatic for 16 months.

## Discussion

Recurrence of prostate cancer is usually detected by elevated PSA levels, but there have been reported cases of prostate cancer recurrence with no or only slight PSA elevation.[1] In such cases, delay in starting the treatment against recurrence matters. In the present case, the patient had the PSA level of only 0.23 ng/mL, but concomitant gross hematuria led to prompt diagnosis of cancer recurrence and to subsequent successful treatment.

In the present case, the novel bladder lesion developed despite the successful control of the known metastatic lesions. There is tissue-specific quantification and localization of the androgen receptor (AR) in prostate cancer,[2] and its heterogeneity is associated with response to androgen deprivation therapy (ADT).[2,3] In our case, the resected tumor was found to have no PSA expression whereas the original biopsy specimen was positive for PSA. Because the expression of PSA is regulated by AR,[4] the AR expression and/or function is thought to be altered

* Corresponding author.
*E-mail addresses:* otti1104@gmail.com (K. Okubo), n.uf.fu.13@gmail.com (F. Hamabe), mykusu228@ndmc.ac.jp (K. Miyai), mktisn@hotmail.com (M. Isono), hshinmo@ndmc.ac.jp (H. Shinmoto), zenpaku@ndmc.ac.jp (A. Sato).

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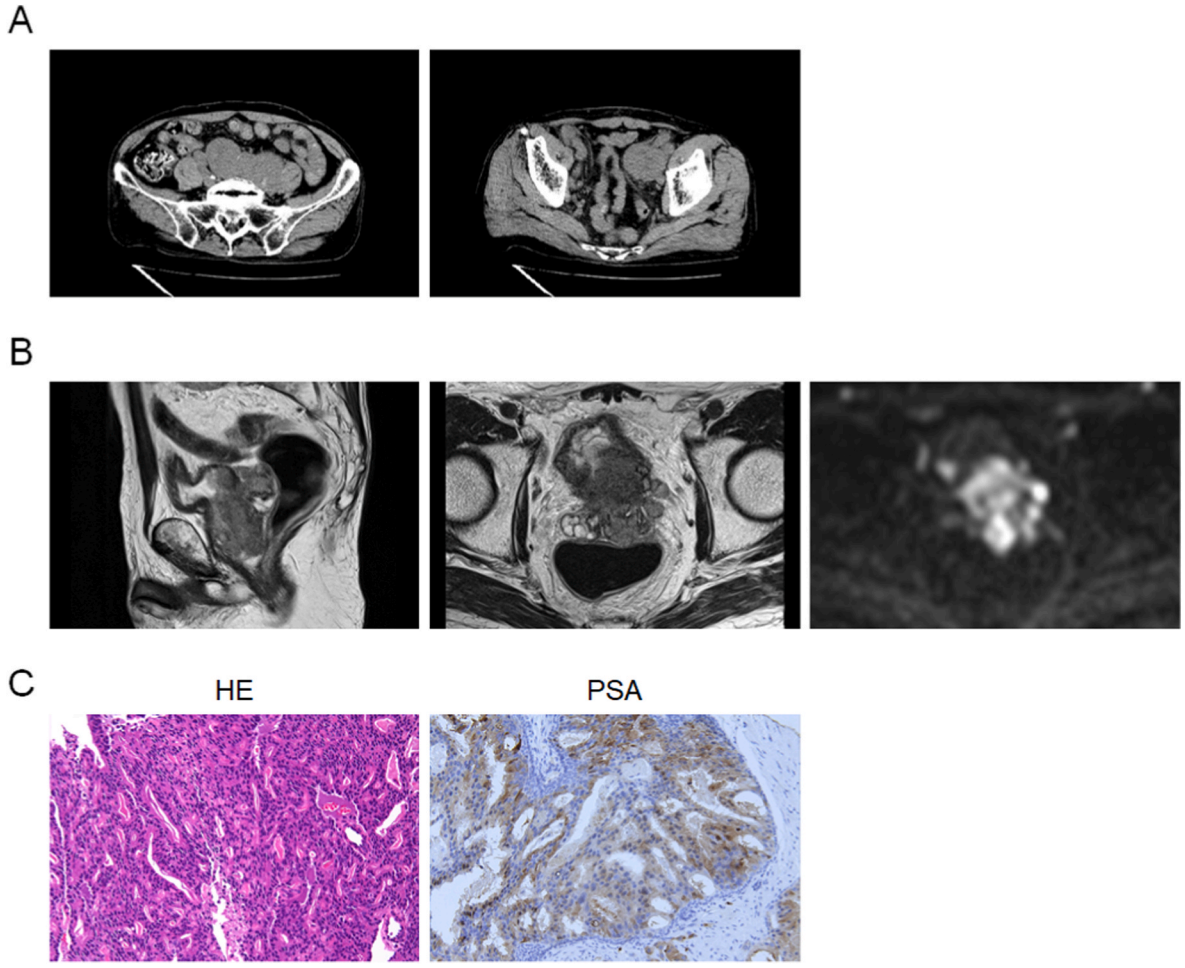


**Fig. 1. Initial presentation of the patient**. Computed tomography scan images. Massive paraaortic (left) and pelvic lymph node (right) metastases were noted (A). MRI images. Prostate cancer invasion of the bladder wall and the seminal vesicle was prominent. Left and middle, T2-weighted image; right, diffusion-weighted image (B). Histopathological findings of the biopsy specimen. A Gleason score 9 prostate cancer with positive prostate-specific antigen (PSA) expression was noted. Left, hematoxylin-eosin (HE) staining; right, immunohistochemical staining for PSA (C).

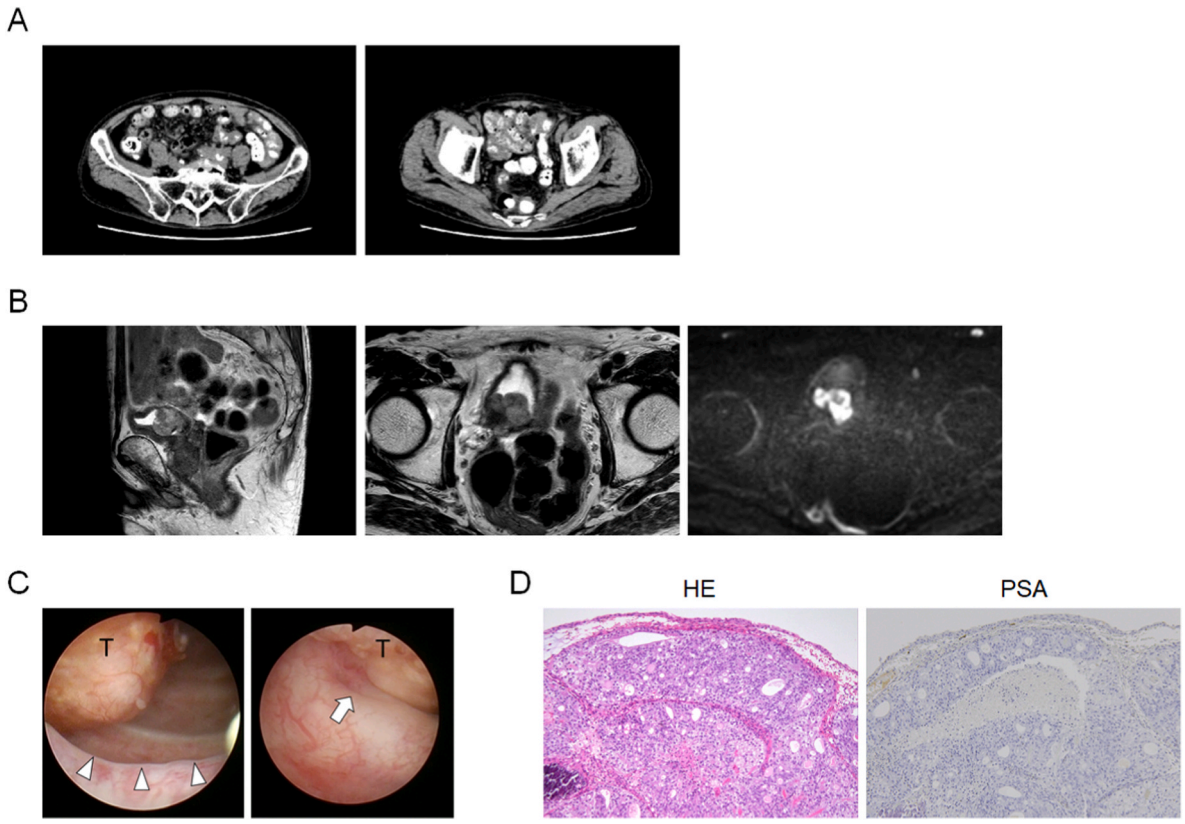


**Fig. 2. Prostate cancer recurrence mimicking invasive urothelial cancer of the bladder**. Computed tomography scan images. The lymph nodes disappeared after 14-month androgen deprivation therapy (A). MRI images. Novel bladder lesions were seen despite improvement of the original bladder invasion. Note that the novel lesions isolated from the prostate and had different signal intensity. Left and middle, T2-weighted image; right, diffusion-weighted image (B). Cystoscopy findings. Sessile bladder tumors were seen on the right lateral wall. T, tumor; arrowheads, bladder neck; arrow, right ureteral orifice (C). Histopathological findings of the resected tumors. The bladder tumors were diagnosed as a Gleason score 9 prostate cancer. Note that there was no prostate-specific antigen (PSA) expression. Left, hematoxylin-eosin (HE) staining; right, immunohistochemical staining for PSA (D).

in the novel bladder lesions. Thus, the heterogeneity of the AR might explain the ADT response difference between the novel bladder lesions and the primary sites in this case.

Recently, Triggiani et al.[5] showed in their retrospective analysis that stereotactic body radiotherapy had a 2-year local control rate of 90.2% in patients with oligoprogressive castration-resistant prostate cancer. So we applied radiotherapy to the bladder lesion to control the patient's local symptoms. Because of PSA progression, we also changed enzalutamide to abiraterone acetate plus prednisone. Although his PSA level still continued to increase, he has been asymptomatic for 16 months, suggesting that the radiotherapy itself successfully controlled the recurrent lesions.

## Conclusion

We reported a case of prostate cancer recurrence mimicking invasive urothelial cancer of the bladder. Despite very low PSA levels, patients with novel symptoms should be screened for prostate cancer recurrence so that they can receive appropriate treatment.

### *Consent*

Written informed consent was obtained from the patient for publication of this case report.

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## Declaration of competing interest

We have no conflict of interest to declare.

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