Urology Case Reports 19 (2018) 67–69

Contents lists available at ScienceDirect

Urology Case Reports

journal homepage: www.elsevier.com/locate/eucr

Oncology

Case report: Incidental metastatic prostate cancer with undetectable PSA in pelvic lymphadenectomy

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A B S T R A C T

We report a patient that had a prior radical prostatectomy and negative PSA levels for two years and subsequently developed bladder cancer requiring radical cystectomy with mixed lymph nodes on final pathology. The nodes were found to be positive for both metastatic urothelial cell carcinoma and metastatic prostatic adenocarcinoma based on immunohistochemical staining. Treatment for metastatic bladder cancer was pursued after radical cystectomy recovery.

Introduction

Prostatic adenocarcinoma (Pca) and bladder cancer (BC) are common genitourinary malignancies that both carry significant morbidity and mortality.[1] Pca is common amongst men and one of the leading causes of cancer death in the United States. After active treatment for prostate cancer, PSA can be used to monitor disease status biochemically. Despite the high incidence and prevalence, a majority of incidentally found Pca are deemed to be clinically insignificant based on various factors including size, organ confinement, and absence of metastasis.[1,2] After radical prostatectomy, PSA is followed for many years to detect biochemical recurrence or metastatic disease.

Muscle invasive bladder cancer (MIBC) represents approximately 25% of bladder cancer diagnoses. Current guidelines support an individualized treatment course based on the patient and extent of disease. In patients with non-metastatic (M0) MIBC, there is a strong recommendation to offer a radical cystectomy with lymphadenectomy.[3]

Concomitant PCa and BC are often seen during radical cystectomies, but are not as frequently found to both be metastatic.[1,3] BCE and Pca can often be difficult to distinguish morphologically, but immunohistochemical stains aid in differentiating between the two malignancies, especially with metastasis of two topographically distinct primary tumors. Our literature review was unable to identify any other cases that discovered concomitant metastatic BC and metastatic Pca in the presence of undetectable PSA levels for several years following a radical prostatectomy.

Case report

A 63-year-old male with a history of radical prostatectomy with pT2cN0MX Gleason 3 + 3 prostatic adenocarcinoma with negative bilateral standard pelvic lymphadenectomy two years prior presented with new diagnosis of muscle invasive bladder cancer. His bladder cancer was diagnosed by transurethral resection of bladder after a two-week history of gross hematuria.

A staging work up prior to radical cystectomy showed no evidence of pelvic or retroperitoneal lymphadenopathy. A bone scan showed no evidence of bony metastatic disease. PSA was rechecked prior to surgery and confirmed to be < 0.01 ng/dL which is undetectable in the referenced lab. The patient was taken to operating room and a radical cystectomy, creation of ileal conduit and bilateral extended pelvic lymph node dissection was completed without intraoperative complications.

Pathology results from the urinary bladder revealed pT2aN1MX urothelial cell carcinoma with maximum tumor dimension of 10cm with lymphatic and perineural invasion. One left obturator lymph node and one right obturator lymph node were positive for metastatic carcinoma, as shown in Fig. 1. Immunohistochemical staining was performed. The left obturator lymph node was positive for Uroplakin and CK7, focally positive for CK20 and negative for PSA (Fig. 2). The right obturator lymph node was positive for PSA and CK7 and negative for Uroplakin and CK20 (Fig. 3). The patient's final diagnosis was metastatic urothelial carcinoma in the left obturator lymph node and metastatic prostatic adenocarcinoma in the right obturator lymph node.

After recovery from surgery, patient was referred for adjuvant chemotherapy but was unable to tolerate more than 2 cycles due to his

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https://doi.org/10.1016/j.eucr.2018.05.009
Received 3 May 2018; Accepted 10 May 2018
Available online 14 May 2018

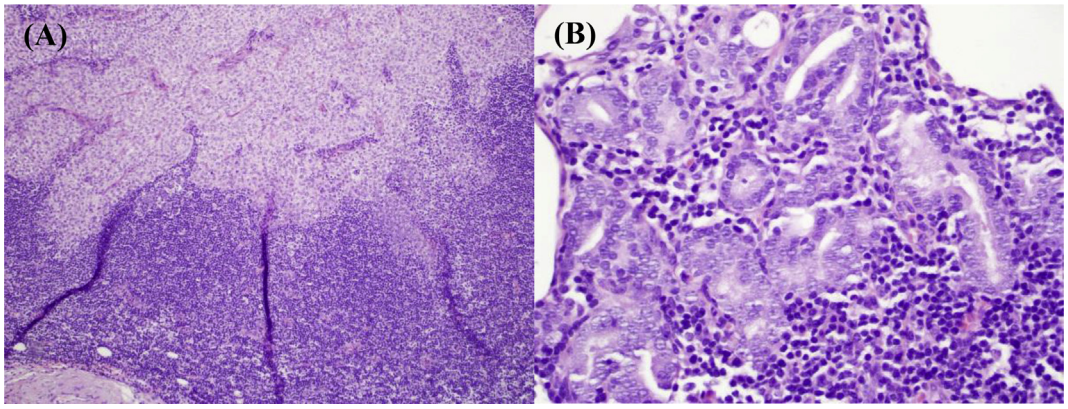

Fig. 1. Light microscopy slides from lymph node dissection. **(A) Left obturator lymph node.** Hematoxylin and eosin (H&E) stain, ×10 magnification, shows sheets of metastatic cell effacing normal lymph node architecture **(B) Right obturator lymph node.** H&E stain, ×20 magnification, shows metastatic cells forming glands near the capsule of lymph node.

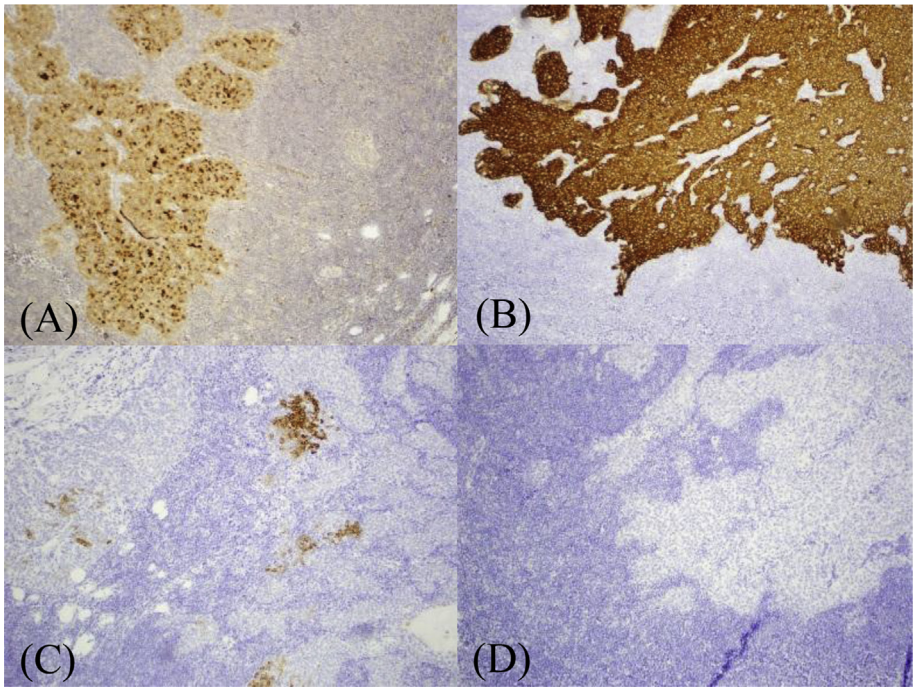

Fig. 2. Left obturator lymph node. (A) Uroplakin nuclear and cytoplasmic marker, ×10 magnification, expressed by tumor cells **(B)** CK7 cytoplasmic marker, ×10 magnification, expressed by tumor cells **(C)** CK20 cytoplasmic marker, ×10 magnification, focally expressed by tumor cells **(D)** PSA cytoplasmic marker, ×10 magnification, not expressed by tumor cells.

overall performance status. PSA remained undetectable post-operatively. Patient remained on surveillance protocol of his BC and ultimately succumbed to his disease after development of progressive metastatic BC.

Discussion

Pca and BC are found together in a large number of patients. It has even been suggested that there is an association between Pca and BC, but this is likely secondary to a detection bias from more extensive and numerous pathological evaluations. Several studies have demonstrated high rates of incidental discoveries of Pca in patients with BC at the time of radical cystectomy.[1,3] This is not an unexpected finding considering autopsy studies have demonstrated evidence of Pca in as high as 70% of 80-year-old men with the majority of cases being found incidentally and considered to have less aggressive behavior.[1]

While it is not uncommon to discover simultaneous disease, concomitant metastatic disease is much more rarely found.[1,3,4] Revelo et al. discovered 41% of their 121 patients with cystoprostatectomies had evidence of Pca. Approximately one-half of the discovered Pca were considered clinically significant; however, none demonstrated Pca involvement in the lymph nodes.[1] Bruins et al. further investigated 1476 radical cystoprostatectomies and of those, only 7 had evidence of Pca in the lymph nodes.[4] Dissimilar to our case, these patients were all studied before any active Pca treatment such as radical prostatectomy. Additionally, none of these studies investigated PSA levels before or after surgery and did not evaluate recurrence. However, they clearly demonstrated incidental Pca in lymph nodes as a rare finding.

This case consistently demonstrated undetectable PSA levels following a radical prostatectomy with negative lymph nodes 2 years prior. The kinetics of PSA, especially following radical prostatectomy, are very sensitive to detecting recurrence or residual malignancy. In patients with metastatic Pca, less than 1% are found to have undetectable levels making it the most accurate predictor of metastasis.[2] The absence of PSA levels could be explained by a minimal amount of disease, the inability to make PSA or clonal shift in the malignant cells that produce tumor markers other than PSA.

Obturator lymph nodes are known metastatic sites for both Pca and BC that can be histologically difficult to distinguish. There have been 5 reported cases of Pca and BC collision tumors found in the same lymph

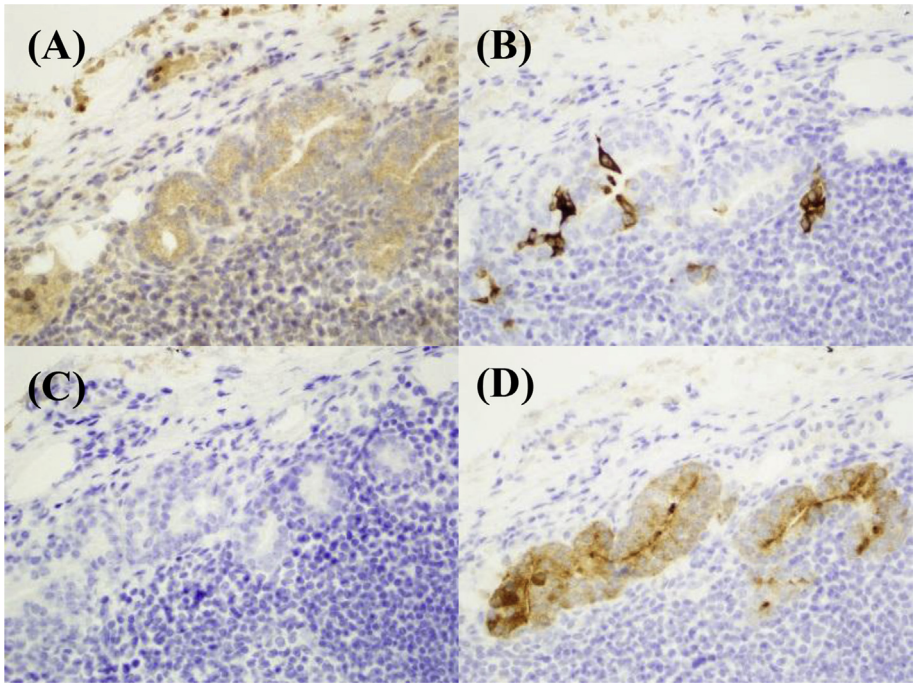

Fig. 3. Right obturator lymph node. (A) Uroplakin nuclear and cytoplasmic marker, × 40 magnification, high background staining present but not expressed by tumor cells **(B)** CK7 cytoplasmic marker, × 40 magnification, expressed by tumor cells **(C)** CK20 cytoplasmic marker, × 40 magnification, not expressed by tumor cells **(D)** PSA cytoplasmic marker, × 40 magnification, expressed by tumor cells.

node, but only two have utilized immunohistochemical stains. The use of CK7, CK20 and PSA has been both studied and supported in the differentiation of genitourinary carcinomas and were valuable in the identification and diagnosis.[5]

This discovery of such disease without any biochemical or radiological evidence of recurrence in the presence of metastatic high-grade BC, to the best of our knowledge, has not been described in previous literature.

Conclusion

This case report brings to our attention the possibility of indolent non-PSA producing prostate cancer in lymphadenectomy specimens at the time of radical cystectomy or other pelvic surgery. In addition, it demonstrates the importance of immunohistochemical stains in determining diagnosis. These stains can be vital in distinguishing between primary genitourinary tumors, as the pure morphology may be difficult to differentiate.

References

1. Revelo M, Cookson M, Chang S, Shook M, Smith J, Shappell S. Incidence and location of prostate and urothelial carcinoma in prostates from cystoprostatectomies: implications for possible apical sparing surgery. *J Urol.* 2004 May;171:646–651. http://dx.doi.org/10.1097/01.ju.0000107380.40481.bc.
2. Lee DK, Park JH, Kim JH, et al. Progression of prostate cancer despite an extremely low serum level of prostate-specific antigen. *Kor J Urol.* 2010 May;51(5):358–361. http://dx.doi.org/10.4111/kju.2010.51.5.358.
3. Sharma P, Zargar-Shoshtari K, Spiess P, Sexton W, Poch M. Undiagnosed prostatic malignancy at the time of radical cystoprostatectomy after prior prostatic radiation therapy. *Urol Ann.* 2016 Apr-Jun;8(2):151–156. http://dx.doi.org/10.4103/0974-7796.163797.
4. Bruins H, Djaladat H, Ahmadi H. Incidental prostate cancer in patients with bladder urothelial carcinoma: comprehensive analysis of 1,476 radical cystoprostatectomy specimens. *SJ Urol.* 2013 Nov;190(5):1704–1709. http://dx.doi.org/10.1016/j.juro.2013.05.034.
5. Bhavas T, Liu J, Huang Y. Collision metastasis of urothelial and prostate carcinomas to the same lymph node: a case report and review of the literature. *J Med Case Rep.* 2012;6:124. http://dx.doi.org/10.1186/1752-1947-6-124.