

Repeated Recurrences of Mucinous Prostate Carcinoma With Signet Ring Cells in the Urinary Bladder After Robotic-assisted Laparoscopic Radical Prostatectomy: a Case Report and Literatures Review

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Case report

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Abstract

Background: Mucinous prostate carcinoma (PCa) and signet-ring-cell PCa are two rare variants of prostate cancer, but the transformation of mucinous PCa into mucinous PCa with signet ring cells was extremely uncommon, little data of therapy was available.

Case presentation: We reported such a case that a man was pathologically considered as mucinous PCa after receiving transurethral resection of the prostate, then he underwent robotic-assisted laparoscopic radical prostatectomy (RARP), the pathological diagnosis was mucinous PCa (pT2cN0M0), without any adjuvant therapies, the man had received regular follow-up with serum total prostate-specific antigen level <0.003 ng/ml. Nevertheless, he received transurethral resection of bladder tumor (TUR-BT) at 13 months, 22 months and 31 months after RARP, respectively, the first TUR-BT specimens was mucinous PCa, where the two other present mucinous PCa with signet ring cells.

Conclusions: We reviewed the literatures and discussed the differential diagnosis, immunohistochemistry, prognosis of this rare carcinoma, emphasized the rarity of the histological change and demanded fundamental research clarifying the confusion of this change, which may be helpful to search for therapeutic targets and improve prognosis.

Background

Mucinous prostate carcinoma (PCa) is a variant of prostate cancer, which typically reveals cords of cuboidal epithelium and cribriform glands with bland cytology characteristic of prostate carcinoma floating in mucin(1). Of all prostate cancer types, the incidence of this rare malignancy is ~ 0.2%, which is pathologically defined by containing lakes of extra-cellular mucin comprising at least 25% of the primary prostatic tumor. Moreover, mucinous PCa with signet ring cells, defined as a disease in which at least 25% of the tumor consists of extra-cellular mucin and less than 25% of the tumor is composed of signet ring cells, is a rare morphologic variant of prostate cancer(2). There were very few clinical data available.

12 cases of mucinous PCa with signet ring cells were reported in two studies previously(3, 4), however, the transformation of mucinous PCa into mucinous PCa with signet ring cells which recurred repeatedly in urinary bladder has not been investigated. Because of the rarity of this interesting occurrence, herein we share the experience and discuss previously reported literatures concerning, hoping to arouse the attention of urologists on patients with mucinous PCa, so that early measures may be taken to improve outcomes.

Case Presentation

A 63-year-old man was referred to Mei Shan city hospital for complaining dysuria, urinary frequency and urgency for more than one year, the serum total prostate-specific antigen (t-PSA) was 3.600 ng/ml, he underwent a surgery of transurethral resection of the prostate (TUR-P) in December 2015 whereafter

pathologically considered as mucinous PCa postoperatively. Positron emission tomography examination indicated there were no clear evidence of metastatic malignancy except for the residual prostate.

The man was transferred to Department of Urology, West China Hospital of Sichuan University for recurrence of symptoms one month after the TUR-P and he was thoroughly examined. Computed tomography scan of abdomen and pelvic cavity was normal, and the serum t-PSA value was 0.186 ng/ml, f/t was 26.34%. Then he underwent robotic-assisted laparoscopic radical prostatectomy (RARP), the pathological diagnosis was mucinous PCa (pT2cN0M0) and surgical margin was negative. Immunohistochemical staining was positive for CK20, focally positive for PSA and PSAP but negative for CK7, CDX-2 [Figure 1.]. He then received regularly clinical follow-up (once a month for 3 months after RARP, and every three months for 3–12 months thereafter), the serum t-PSA level was < 0.003 ng/ml all the time without any adjuvant therapy.

He suffered lower urinary tract irritation symptoms at 13 months after RARP and the cystourethroscopy showed a cauliflower neoplasm in the trigone and suspicious lesions in the posterior wall of urinary bladder. Transurethral resection of bladder tumor (TUR-BT) was performed and pharmorubicin was applied as intravesical chemotherapy immediately post-operation in which the tissue origin had not been confirmed. Pathological and immunohistochemical examination of the specimen showed the same diagnosis as previously diagnosed, which indicated that it was mucinous PCa metastasizing to the urinary bladder. With regular reexamination (every three months after TUR-BT), his serum t-PSA level was always < 0.003 ng/ml.

Nevertheless, the patient still experienced the other twice TUR-BT at 22 months and 31 months after RARP, respectively, but differing from the first one, the second and the third TUR-BT presented mucinous PCa with signet ring cells in the examination of the specimens [Figure 2.]. Then he has experienced other twice TUR-BT in the Mei Shan city hospital since he left Department of Urology, West China Hospital of Sichuan University. Cystourethroscopy in Mei Shan city hospital revealed bladder tumors, radical cystectomy would not be implemented because the patient rejected urinary diversion, and he is undergoing chemotherapy and Chinese Herbs, the therapeutic effect couldn't be evaluated for lacking reliable evidence.

Discussion And Conclusions

Mucinous PCa is a rare variant of the prostate cancer, the differential diagnosis includes prostatic adenocarcinoma with mucinous features and secondary infiltration from a colonic or bladder adenocarcinoma. Proportion of the extra-cellular mucin component($\geq 25\%$) could exclude the prostatic adenocarcinoma with mucinous features. On the other hand, combined immunostaining for CK7 and CK20 has been widely used in surgical pathology to help determine the origin of epithelial neoplasms. A CK7(-) / CK20(+) / CDX-2(+) pattern is usually indicative of gastro-intestinal adenocarcinoma, particularly colorectal carcinoma, and 100% expression of CDX-2 was found in primary adenocarcinoma of the bladder(5–7). Furthermore, PSA and PSAP are the most reliable immunohistochemical markers

differentiating prostatic adenocarcinoma from primary adenocarcinoma of the bladder, which stain positive in most of the former and negative in the latter(8). Computed tomography scan of abdomen plus pelvic cavity and positron emission tomography examination both indicated that there were no clear evidence of gastrointestinal tumor or bladder tumor, absence of symptoms associated with them also excluded metastasis from adjacent organs.

Sousa et al(1). had practiced an actualization and a critical review of Elbadawi's criteria in 2000, they demonstrated a more practical criteria diagnosing mucinous PCa. The carcinoma herein reported, staining focally PSA(+) / PSAP(+) and CK7(-) / CK20(+) / CDX-2(-), should be mucinous PCa instead of secondary carcinoma from surrounding organs or distant sites, which metastasized to the urinary bladder and recurred repeatedly.

Clinically, the treatment for mucinous PCa is similar to that for typical acinar adenocarcinoma, includes androgen deprivation therapy, surgery, radiation therapy and chemotherapy. In the past, it was controversial about the prognosis of mucinous PCa. A study by Ro et al. comprising 12 patients found that mucinous PCa had aggressive biological behavior and a propensity to develop bone metastasis, but it should be noted that the 12 patients were with high-stage in diagnosis, metastasis was found in lymph node, liver, lung or bone. In contrast, some studies showed that mucinous PCa didn't implicate poor prognosis than typical prostate acinar carcinoma (n = 60)(9). The latter were supported by several recent studies(2, 10–12). The study by Bronkema et al(10). revealed similar 10-year estimated overall survival rate for a group of 1098 cases mucinous PCa compared with a group of 1340499 cases typical adenocarcinoma (78.0% vs 71.1%, p = 0.002). And study by Hemamali et al(11). of 73 cases mucinous PCa matched serum PSA, tumor volume, rate of extra-prostatic extension and 5-year biochemical recurrence rates, finally concluded similar prognosis between the two groups of tumors. Feng et al(12). found the same conclusion and indicated that patients did not receive radiation therapy had similar cancer-specific mortality with radiation therapy patients, confirmed the experience that mucinous PCa showed poor response to radiotherapy reported by previous study(13).

There were 12 cases of mucinous PCa with signet ring cells reported in two studies, which tended to in advanced stages, poor response to endocrine therapy and poor prognosis compared to mucinous PCa as well as typical adenocarcinoma(3, 10). Signet-ring-cell carcinoma of prostate was associated with forms of high-grade prostatic carcinoma: solid (4/8) and comedonecrosis (2/8)(14), which should be grade as Gleason pattern 5 according to The 2014 International Society of Urological Pathology Consensus Conference(15). Therefore, mucinous PCa with signet ring cells showed poor prognosis was not unexpected. But it is worth noting that clarifying the molecular mechanism or cause by which this transformation occurs is of great account, which may be helpful to search for therapeutic targets and improve prognosis, fundamental research is needed to eliminate the confusion.

Abbreviations

PCa: prostate carcinoma.

t-PSA: total prostate-specific antigen.

TUR-P: transurethral resection of the prostate.

RARP: robotic-assisted laparoscopic radical prostatectomy.

TUR-BT: transurethral resection of bladder tumor.

Declarations

Ethics approval and consent to participate.

Written informed consent was obtained from the patient to participate the study. The ethics approval was waived from the ethics committee of the West China Hospital of Sichuan University.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editors-in-Chief of this journal.

Availability of data and materials

The datasets used during the current study are available from the corresponding authors on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Author's contributions

SJB and HX reviewed all literatures available about mucinous PCa date to November in 2020, and SJB was major contributor in writing the manuscript. HRL, QW, XYX and WTZ performed the data acquisition and contributed to partial writing of the manuscript. LY provided guidance throughout the process and fund. All authors read and approved the final manuscript.

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Figures

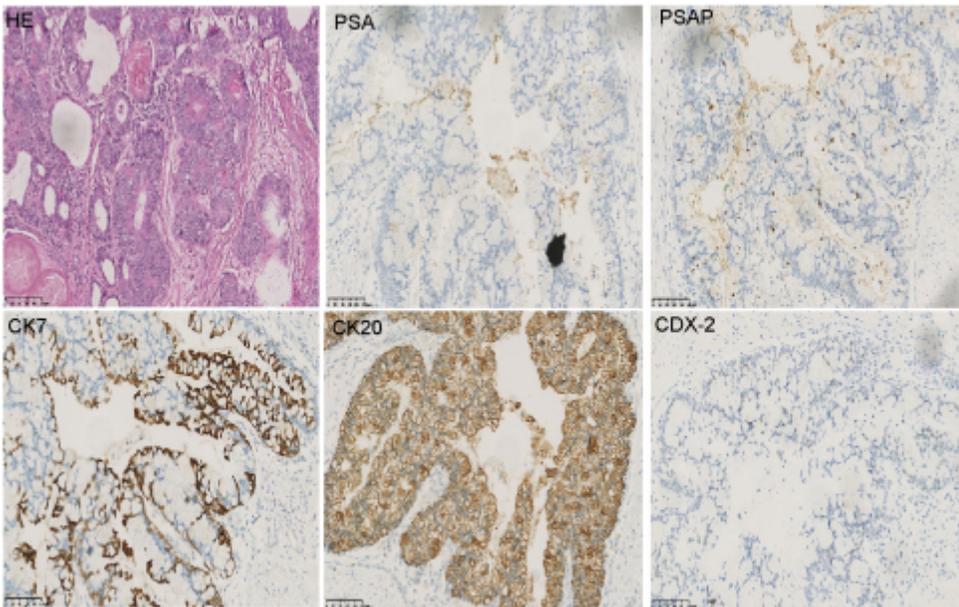


Figure 1

Histopathological and immunohistochemical examination of the prostate. Hematoxylin and eosin staining of the residual prostate tissue showed lakes of extra-cellular mucin (original magnification x200). Immunohistochemistry staining of the residual prostate tissue showed positive for CK20, focally positive for PSA and PSAP, while negative for CK7 and CDX-2 (original magnification x200)

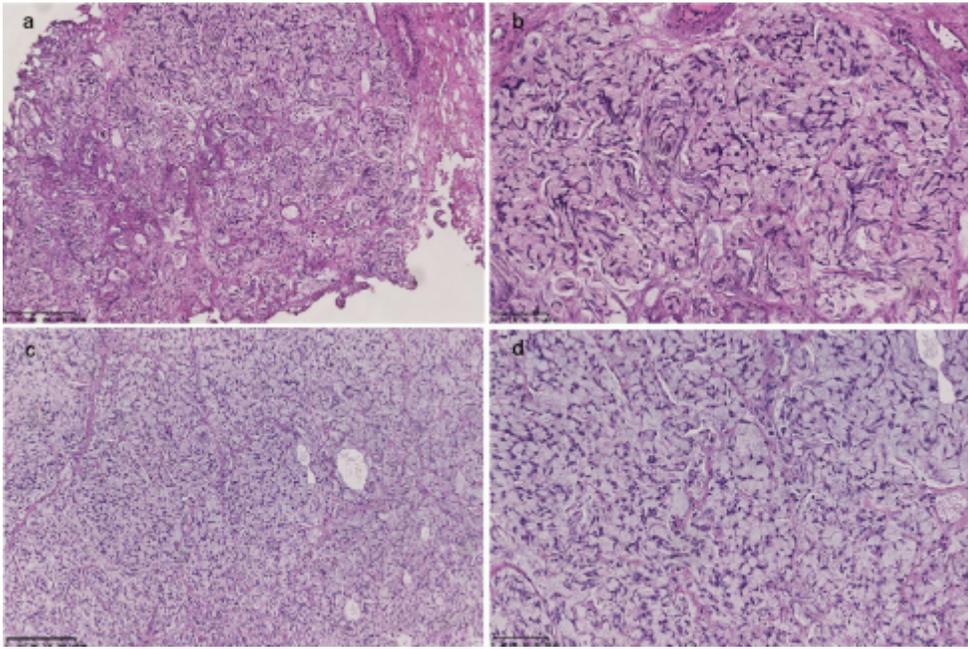


Figure 2

Histopathological and immunohistochemical examination of the bladder tumors. (a) and (b): Hematoxylin and eosin staining of the first TUR-BT specimen showed similar neoplastic cell feature compared with the RARP specimen (original magnification x100 and x200). (c) and (d): Hematoxylin and eosin staining of the second TUR-BT specimen showed lots of extra-cellular mucin lakes and a few signet-ring-cells (original magnification x100 and x200)