

Oncology

Occult mucin-producing urothelial-type adenocarcinoma of the prostate with elevated serum levels of carcinoembryonic antigen and carbohydrate antigen 19-9: Report of an autopsy-proven case



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ABSTRACT

Mucin-producing urothelial-type adenocarcinoma of the prostate (MPUAP) is a rare, aggressive neoplasm thought to originate from the prostatic urethral urothelium. Our case is the first reported to show significantly increased serum levels of carcinoembryonic antigen (CEA) and carbohydrate antigen (CA) 19-9 in MPUAP. An autopsy revealed occult MPUAP with prominent seminal vesicle, perineural, lymphatic vessel, and vascular invasion and extensive bone metastases. Duration of survival in this case was far shorter than average, and extensive bone metastases were rare in previously reported cases. This suggests serum CEA and CA19-9 levels can be an important prognostic factor in MPUAP.

Introduction

Mucin-producing urothelial-type adenocarcinoma of the prostate (MPUAP) is an exceedingly rare neoplasm. To date, only 23 cases have been reported in the English literature.¹ MPUAP shows normal serum prostate-specific antigen (PSA) levels as it arises through a process of glandular metaplasia of the prostatic urethra and subsequent in situ adenocarcinoma.¹ Gleason score, the grading system used to determine the aggressiveness of prostate cancer, should not be applied to MPUAP, as this neoplasm is not a usual acinar adenocarcinoma of the prostate.² Immunohistochemically, MPUAP is reportedly negative for PSA and caudal-related homeobox 2 (CDX2) and, in most cases, positive for cytokeratin 7 (CK7), CK20, high-molecular-weight cytokeratin (clone

34βE12), and carcinoembryonic antigen (CEA).^{1,2} We report an autopsy-proven case of occult MPUAP presenting with lymph node and extensive bone metastases.

Case presentation

An 81-year-old man was referred to our hospital for suspected hematological malignancy or occult cancer after management and investigation of a high fever and low back pain of unknown cause for 1 month in a previous hospital. His medical history was significant for hypertension. There were no urinary symptoms including urinary obstruction. The physical examination and urinalysis were unremarkable. Blood levels of white blood cells (13,590/μL), lactate dehydrogenase

Abbreviations: CA19-9, carbohydrate antigen 19-9; CDX2, caudal-related homeobox 2; CEA, carcinoembryonic antigen; CK, cytokeratin; 18F-FDG-PET, fluorine-18 fluorodeoxyglucose positron emission tomography; PSA, prostate-specific antigen

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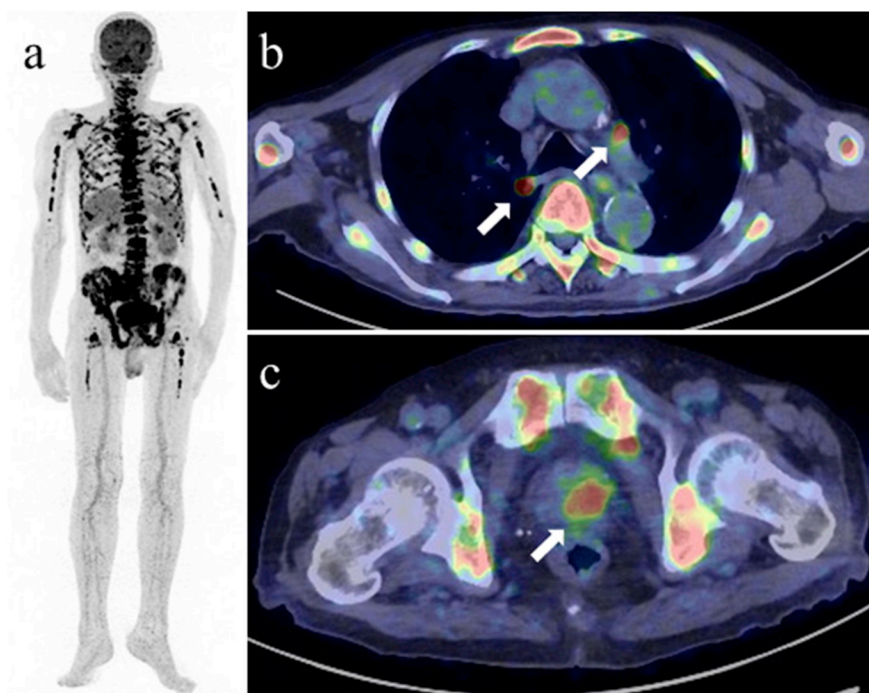


Fig. 1. Findings of fluorine-18 fluorodeoxyglucose positron emission tomography (^{18}F -FDG-PET) (a) Abnormal ^{18}F -FDG uptake in multiple bones, including ribs, vertebrae, pelvis, humeri, and femora was observed. (b) High ^{18}F -FDG uptake in the mediastinal lymph nodes (arrows) was seen. (c) There was an abnormal focus of ^{18}F -FDG uptake (arrow) in the prostate gland.

(663 IU/L), and soluble interleukin-2 receptor (2330 U/mL) were increased, whereas the hemoglobin (9.5 g/dL) level was decreased. The serum CEA and carbohydrate antigen (CA) 19-9 levels were significantly increased to 9849 ng/mL (normal, 0.7–4.2 ng/mL) and 1999 U/mL (normal, < 37 U/mL), respectively, whereas the serum PSA level of 0.55 ng/mL was within normal limits (normal, < 4.0 ng/mL). Upper and lower gastrointestinal endoscopy did not reveal any lesions. Whole-body computed tomography showed no evidence of malignancy. Fluorine-18 fluorodeoxyglucose positron emission tomography (^{18}F -FDG-PET) demonstrated abnormal ^{18}F -FDG uptake in multiple bones, including sternum, ribs, vertebrae, pelvis, humeri, and femora; mediastinal lymph nodes; and prostate (Fig. 1a–c). Bone marrow biopsy from the pelvic bone revealed poorly to moderately differentiated adenocarcinoma (Fig. 2a). There was only a small amount of extracellular mucin. On immunohistochemical examination, adenocarcinoma cells were positive for CK20, 34 β E12, CEA, and CA19-9 (Fig. 2b–e, respectively), and negative for CDX2, CK7, and PSA (Fig. 2f).

According to the ^{18}F -FDG-PET findings, normal serum PSA levels, and immunohistochemical panel, although extremely rare, occult MPUAP was suspected. The elderly patient with advanced-stage occult cancer denied chemotherapy and was transferred to the palliative care unit for pain management. Two weeks later, he died of respiratory failure with severe pancytopenia.

Autopsy revealed macroscopically a grayish-white mucinous mass, 25 × 15 mm in size, in a cross-section of the left transition and peripheral zone of the prostate (Fig. 3a). Microscopically, adenocarcinoma cells formed nests floating in extracellular mucus lakes (Fig. 3b). The tumor cells showed relatively strong nuclear atypia with cytoplasmic mucin. The mucus lakes were surrounded by fibrous stroma with

scattered adenocarcinoma cell nests. We also observed extracapsular extension as well as prominent seminal vesicle, perineural, lymphatic vessel, and vascular invasion. The prostatic urethral urothelium showed glandular metaplasia (Fig. 3c) and a transition between adenomatous epithelium and adenocarcinoma (Fig. 3d). Accordingly, the tumor was diagnosed as MPUAP. The immunohistochemical findings of adenocarcinoma cells in the prostate were identical to those of the biopsy specimen. There were multiple bone and mediastinal lymph node metastases, consistent with the ^{18}F -FDG-PET findings. Extracellular mucus lakes were occasionally seen in those metastatic lesions.

Discussion

Although the Gleason score should not be applied to MPUAP, it has been reported to be aggressive.² MPUAP is histologically identical to nonurachal adenocarcinoma of the urinary bladder and differ from mucinous adenocarcinoma of the prostate.² Thus, hormone therapy would be inappropriate. Among 23 previously reported cases, metastatic disease developed in the lung in four cases, liver in three cases, pelvic wall in two cases, testis in one case; bone metastases were seen in only one case.¹ Ten patients died of disease at an average of 44.3 months from presentation,^{1,2} suggesting progression to death is more common in MPUAP than in usual adenocarcinoma of the prostate. The difference in prognosis between MPUAP and usual adenocarcinoma of the prostate emphasizes the importance of differentiating between them.

Our case is the first reported to show significantly increased serum levels of CEA and CA 19-9 in MPUAP. To date, the clinical value of CEA and CA19-9 as tumor markers for MPUAP has been unknown. In some

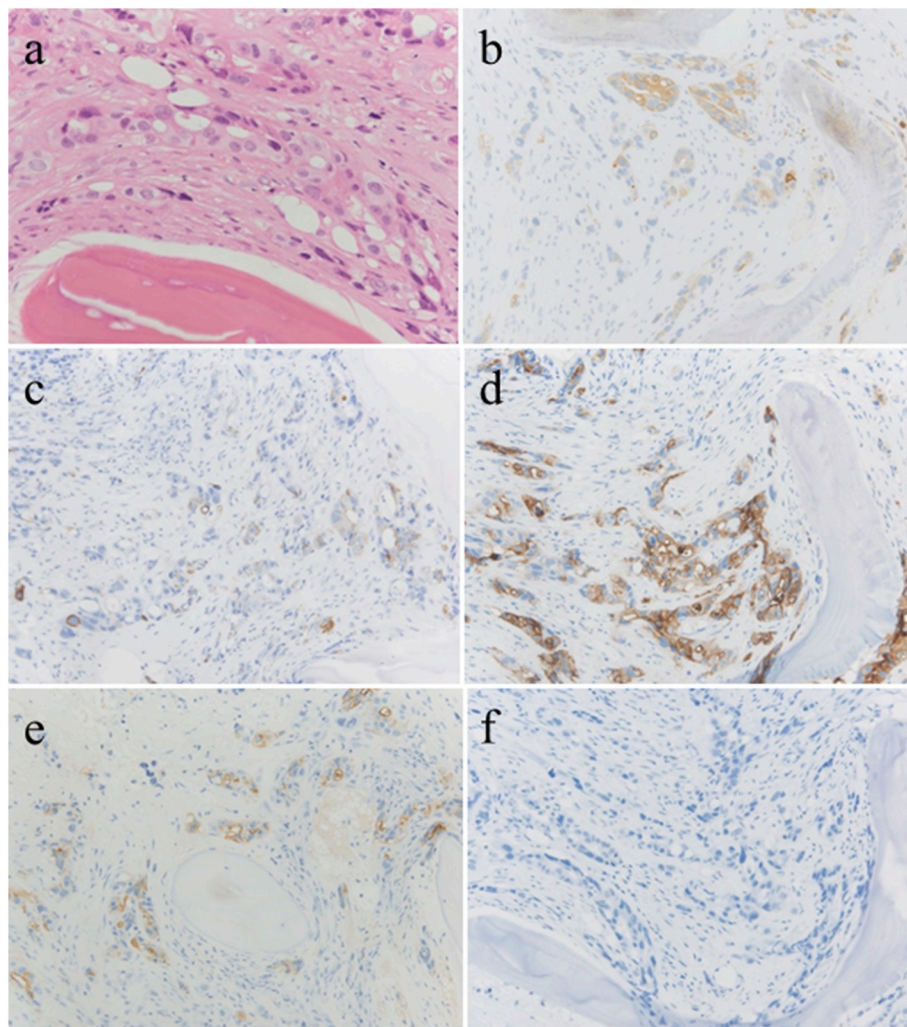


Fig. 2. Histological and immunohistochemical images of the bone marrow biopsy (a) Adenocarcinoma cells were seen. Hematoxylin and eosin staining. (b–f) Adenocarcinoma cells were positive for cytokeratin 20 (b), high-molecular-weight cytokeratin (34βE12) (c), carcinoembryonic antigen (CEA) (d), and carbohydrate antigen (CA) 19-9 (e), and negative for prostate-specific antigen (PSA) (f). (b–f) Immunohistochemistry with hematoxylin counterstaining.

cases, elevated serum levels of CEA and CA19-9 have been demonstrated in urothelial carcinoma of the bladder and the upper urinary tract.³ Hegele et al. reported that, in urothelial carcinoma of the urinary bladder, serum CEA and CA19-9 levels correlated with tumor invasion and malignancy grade.⁴ Thus, serum levels of CEA and CA19-9 may be associated with prognosis of MPUAP, as it is thought to originate from the prostatic urethral urothelium. In fact, our case showed extensive bone metastases, which were rare in previously reported cases, and died only 2 months from presentation, far shorter than the average duration in previous cases. This suggests that serum CEA and CA19-9 levels can be an important prognostic factor in MPUAP.

¹⁸F-FDG-PET can be valuable for detecting MPUAP. It has often been stated that ¹⁸F-FDG-PET is not useful in prostate cancer. However, a recent study reported that aggressive primary prostate tumors with a Gleason score greater than 7 tended to show high FDG uptake.⁵ As

mentioned, MPUAP has been reported to be aggressive. In fact, high ¹⁸F-FDG uptake in the prostate shown using ¹⁸F-FDG-PET allowed us to consider occult MPUAP in the differential diagnosis. Therefore, ¹⁸F-FDG-PET may be quite useful in localizing the site of MPUAP.

Conclusion

MPUAP, originating from the prostatic urethral urothelium, is thought to be aggressive compared with usual adenocarcinoma of the prostate. Our case is the first to show significantly elevated serum levels of CEA and CA 19-9 and presented with prominent seminal vesicle, perineural, lymphatic vessel, and vascular invasion, extensive bone metastases, and far shorter duration of survival than average in previous cases. This suggests serum CEA and CA19-9 levels can be an important prognostic factor in MPUAP.

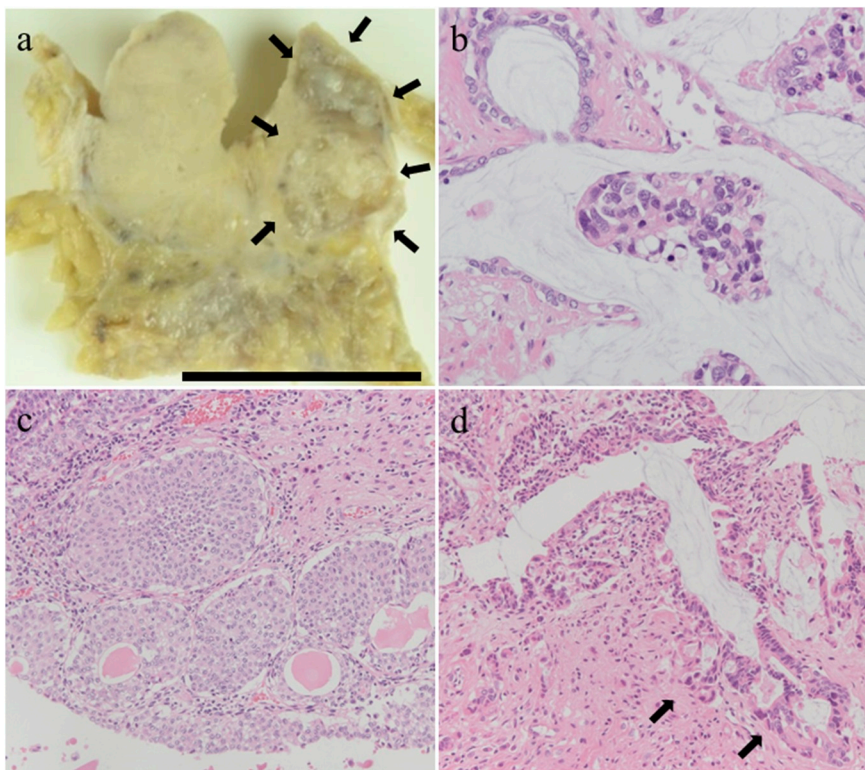


Fig. 3. Macroscopic and histological images of the prostate (a) Cross-section of the prostate at the level of the verumontanum showed a grayish-white mucinous mass (arrows) in the left transition and peripheral zone (scale bar: 3 cm). (b) Adenocarcinoma cell nests floated in mucus lakes. (c) The prostatic urethral urothelium showed glandular metaplasia. (d) Transition between adenomatous epithelium and adenocarcinoma (arrows) was seen in the prostatic urethra. (b–d) Hematoxylin and eosin staining.

Consent

Informed consent was obtained from his family for the publication of this report.

Conflicts of interest

None.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.eucr.2018.11.005>.

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