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Primary mesonephric adenocarcinoma of the bladder: A case report

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ABSTRACT

Primary mesonephric adenocarcinoma of the bladder is a very rare lesion. Only 9 cases have been reported since 1968, when it was first described. Due to its morphological diversity and variable immunohistochemical profile, mesonephric adenocarcinoma presents a diagnostic challenge, especially when seen in male patients, due to the rarity this entity in men. Here we present a rare case of a 63-year-old man who was found to have a bladder tumor and diagnosed with mesonephric adenocarcinoma of the bladder.

1. Introduction

Primary mesonephric adenocarcinoma of the bladder is rare, with only 9 reports published since 1968, when it was first described.[1] Mesonephric adenocarcinomas (MA) are far more reported in the uterine cervix, though they constitute less than 1% of all cervical carcinomas.[2] Fewer than 20 cases of benign mesonephric remnants have been described in the renal pelvis, prostate and periprostatic tissue. MA, due to its broad morphologic spectrum and immunohistochemical profile, presents a diagnostic challenge and should be differentiated from a variety of entities including clear cell adenocarcinoma (CCA), urothelial carcinoma with glandular differentiation, florid mesonephric hyperplasia, endometroid carcinoma, serous carcinoma, nephrogenic adenoma, and metastatic carcinoma.

2. Case presentation

Our patient was a 63-year-old Caucasian male with a history of BPH associated with mild lower urinary tract symptoms, erectile dysfunction on Viagra, kidney stones, and parathyroid removal over 30 years ago for a parathyroid adenoma. He had known renal cysts and had a renal bladder ultrasound for surveillance. In addition to revealing multiple simple appearing renal cysts this showed a bladder tumor with internal vascular flow measuring 1.1 × 1.1 × 0.8 cm. A follow-up CT urogram confirmed the presence of an avidly enhancing tumor measuring 1.5 cm involving the posterior lateral left bladder wall (Fig. 1). There was no associated hydronephrosis or concern for extravesical extension, regional or distant adenopathy, or evidence of metastasis. On cystoscopy, the tumor was identified in the left upper posterior wall of the bladder, well away from the ureteral orifices. It appeared to be submucosal, as smooth and intact appearing mucosa was overlying the mass. The tumor was resected in its entirety with bipolar electrocautery and fulguration of its base was performed.

Histologic sections showed an intramural cellular epithelial neoplasm centered in the lamina propria and composed of densely packed and focally confluent tubules and papillae. The overlying urothelium was uninvolved by tumor. Areas of the tumor showed follicular and tubular architecture with spaces containing homogeneous eosinophilic colloid-like material (Fig. 2). Cytologically, the lesional cells were monotonous and low-grade, with open chromatin and delicate nucleoli. Immunohistochemical stains showed the tumor cells were positive for pan-cytokeratin, PAX8, TTF-1, and CK7 and negative for NKX3.1, GATA3, P63, ER, PR, P16, and racemase. CD10 showed apical membranous positivity. Although the overall findings were consistent with the diagnosis of MA, it was noted that metastasis from a differentiated thyroid carcinoma could have overlapping features, and thus exclusion of a thyroid primary was recommended. Thyroid function tests were normal and a dedicated thyroid ultrasound was negative. A final diagnosis of MA was rendered.

The patient's post-operative course was unremarkable. Chest X-ray was clear, and no pleural effusions or nodules were visualized. Six weeks later, he underwent a repeat CT urogram, and TURBT, which revealed

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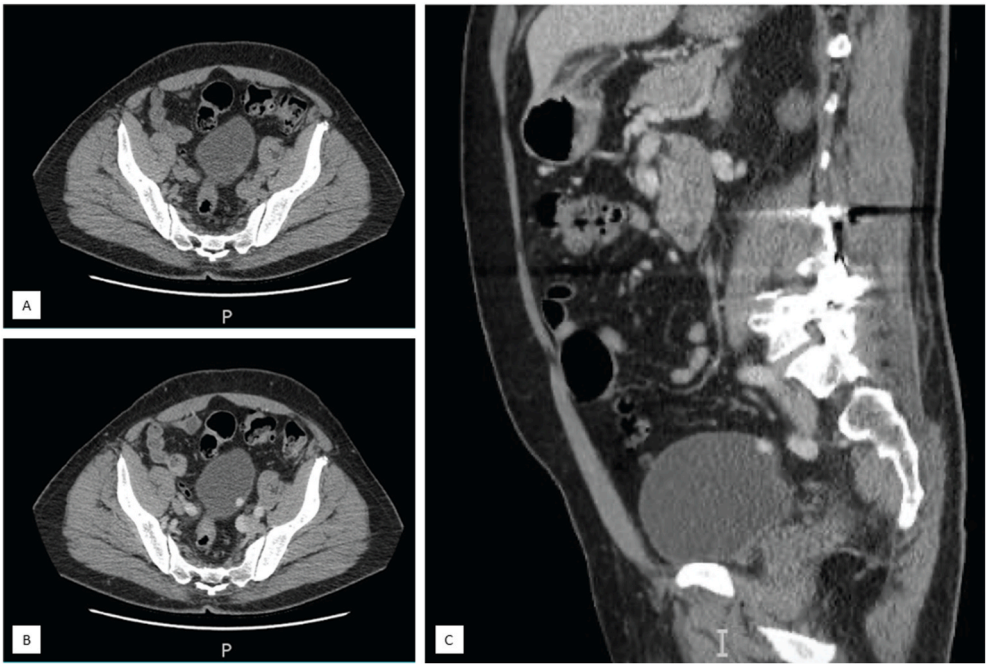

Fig. 1. CT of the abdomen and pelvis demonstrating a single enhancing intraluminal bladder tumor A-B. Pre- and post-contrast axial cuts. C. Post-contrast sagittal cut.

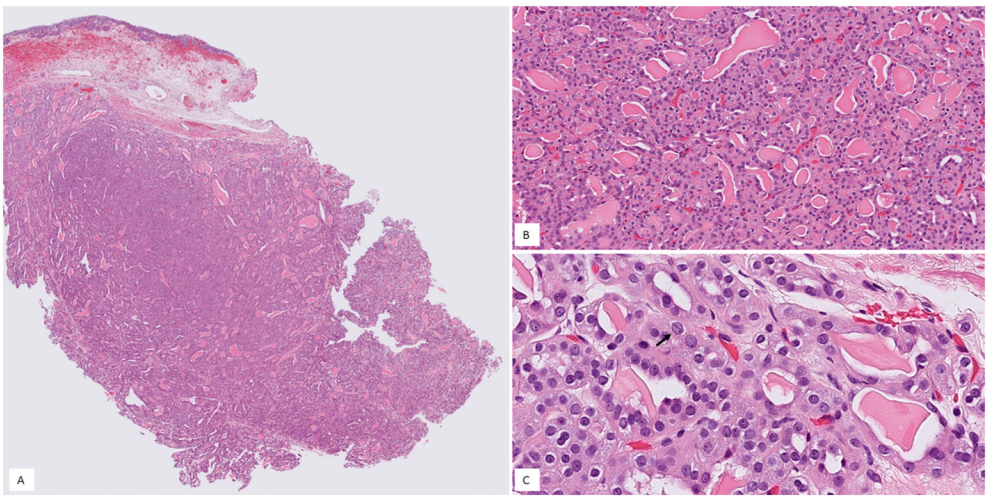

Fig. 2. Representative images of the tumor's histology A. Intramural neoplasm with normal overlying urothelium and lamina propria (H&E, 2x). B. The neoplasm shows confluent architecture with back to back tubules and follicles with associated eosinophilic material (H&E, 10x). C. Tubules are lined by cuboidal cells with eosinophilic cytoplasm, elongated nuclei with peripheral small nucleoli and scattered longitudinal nuclear grooves (arrow). (H&E, 40x).

no evidence of recurrence, and biopsies of the prior resection site didn't reveal residual tumor. Muscularis propria was present in the sample. The plan for future surveillance included a cystoscopy in 3 months and cross-sectional imaging in 6 months.

3. Discussion

Mesonephric ducts are paired embryologic structures that appear very early in fetal development. At around 11 weeks of gestation, in the absence of testicular anti-Müllerian hormone (AMH), mesonephric ducts regress and paramesonephric ducts develop into the fallopian tubes, uterus, and vagina in females. However, benign mesonephric remnants and hyperplasia aren't uncommon along the lateral wall of the cervix and may be found incidentally in up to 22% of hysterectomy specimens.[2] In males, AMH leads to the regression of the paramesonephric ducts, and the mesonephric ducts develop into the seminal vesicles, vas deferens, and ejaculatory ducts. The bladder is embryologically derived from both the endodermal cloaca and the intermediate mesodermal mesonephric ducts.

MA, when present in the bladder, must be differentiated from a variety of entities including mesonephric remnants and hyperplasia, CCA, urothelial carcinoma with glandular differentiation, endometroid carcinoma, serous carcinoma, nephrogenic adenoma, and metastatic carcinoma. Histologically, mesonephric remnants and hyperplasia appear lobulated collections of tubules lined by low cuboidal epithelium with dense eosinophilic intraluminal material, and uniform, bland nuclei.[3,4] However, mesonephric hyperplasia has larger glandular structure and more florid nature.[2] Like MA, CCA can show a predominantly tubular architecture with intraluminal eosinophilic secretions and may express PAX8. However, in contrast to MA, CCA typically demonstrates overtly

malignant nuclear cytology, often expresses Napsin-A, and may be associated with underlying endometriosis or urothelial carcinoma.[3,4]

Urothelial carcinoma with glandular differentiation can also demonstrate tubular architecture. Immunohistochemistry can differentiate between urothelial carcinoma with glandular differentiation (positive for P63, Uroplakin II/III, high molecular weight cytokeratin) and MA (positive for PAX-8, TTF-1) although both entities may express GATA3.

Endometroid adenocarcinoma may enter the differential diagnosis of MA. Most endometrioid adenocarcinomas express ER and PR, and lack expression of CD10, TTF-1, and GATA-3, as opposed to MA.[3] High-grade serous carcinoma may also be considered but will show aberrant P53 expression and often express WT1 and ER, in contrast to MA.[4]

MA must also be distinguished from nephrogenic adenoma with a tubular or papillary architecture.[5] A characteristic feature is the cuff of thickened basement membrane which often surrounds a subset of the tubules.[5] Although PAX8 is consistently expressed, nephrogenic adenomas lack TTF1 expression and wouldn't show the apical CD10 staining of mesonephric lesions.

Owing to the heterogeneity of non-urothelial bladder carcinomas, primary MA of the bladder has been historically treated like CCA. For patients presenting with localized disease the primary treatment involved radical cystectomy with lymph node dissection, a major surgery with adverse effects on quality of life. More recently it has been suggested that the course of MA is less aggressive, and treatment can include active surveillance following TURBT. Decisions for management of this rare entity must take into consideration the lack of prospective data on the benefits and risks of treatment types.

4. Conclusion

In summary, we present a unique case of primary MA of the bladder in an adult male. Though rare, MA should be considered part of the differential diagnosis for urinary bladder tumors. Morphologic and immunohistochemical features are critical in narrowing the differential diagnosis of this lesion.

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References

1. Dow JA, Young JD. Mesonephric adenocarcinoma of the bladder. *J Urol*. 1968;100(4): 466–469. https://doi.org/10.1016/S0022-5347(17)62554-0.
2. Ferry JA, Scully RE. Mesonephric remnants, hyperplasia, and neoplasia in the uterine cervix: a study of 49 cases. *Am J Surg Pathol*. 1990;14(12):1100–1111.
3. Cheriyan AM, Patel S, Krivak T, Lutins J, Horne Z, Liang S. A unique case of mesonephric adenocarcinoma of urinary bladder. *Hum Pathol: Case Rep*. 2021;24, 200519. https://doi.org/10.1016/j.ehpc.2021.200519.
4. Howitt BE, Nucci MR. Mesonephric proliferations of the female genital tract. *Pathology*. 2018;50(2):141–150. https://doi.org/10.1016/j.pathol.2017.11.084.
5. Venyo AK-G. Nephrogenic adenoma of the urinary bladder: a review of the literature. *Int Sch Res Notices. 2015*. 2015, 704982. https://doi.org/10.1155/2015/704982.

Abbreviations

Mesonephric Adenocarcinoma: (MA)
Benign Prostatic Hyperplasia: (BPH)
Transurethral Resection of Bladder Tumor: (TURBT)
Clear Cell Adenocarcinoma: (CCA)
Estrogen Receptor: ER
Progesterone Receptor: PR