CASE REPORT

Enteric type urachal adenocarcinoma: a case report

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Urachal pathology is rare. The most frequently reported lesion is urachal adenocarcinoma. The pathogenesis of urachal adenocarcinoma is unknown. We report a case of a 55-year-old man who presented with microscopic hematuria. Clinical work up showed a tumor involving the urinary bladder with extravesical extension. Masses or tumors involving other organs were excluded. Partial cystectomy revealed a distended bladder wall with the formation of a cystically dilated mass filled with mucoid material. Microscopic examination showed enteric type adenocarcinoma with abundant mucin formation. The neoplastic urachal epithelium showed features of colonic differentiation as evidenced by the presence of goblet cells and positive staining for acid mucin and cytokeratins 20 (CK 20). Such features are absent in non-neoplastic urachal epithelium. This was a rare case of urachal adenocarcinoma, enteric type, with abundant mucin formation. The urachal adenocarcinoma had morphological features and an immunohistochemical profile that were similar to that of adenocarcinoma of the colon.

Key Words: urachus, urinary bladder adenocarcinoma, urachal adenocarcinoma. mucocele, CK7, CK20

Introduction

Urachal adenocarcinoma is rare and accounts for 0.3%-0.7% of all urinary bladder carcinomas.[1] The pathogenesis of urachal adenocarcinoma is not fully understood. Intestinal metaplasia has been well documented as a premalignant condition in gastric and esophageal adenocarcinomas and has recently been recognized in gall bladder adenocarcinoma.[2] Although intestinal metaplasia was postulated 76 years ago as a possible cause of urachal adenocarcinoma,[3] this theory is still controversial. Evolution of urachal adenocarcinoma through a sequence of events proceeding from intestinal metaplasia to dysplasia to carcinoma has not been fully studied.

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Case

Clinical summary

A 55-year-old male presented with microscopic hematuria during a routine checkup. His past medical history included hiatus hernia, sciatica, alcohol abuse, and smoking. Laboratory results showed a normal prostate-specific antigen (PSA) level. An abdominal CT scan with contrast revealed an exophytic mass measuring 1.8 cm x 2.1 cm. The mass occupied the anterior and the right walls of the urinary bladder and showed an extravesical component, Figure 1. It had a centrally higher attenuation relative to the rest of the bladder wall, denoting a complex cystic lesion and peripheral hyper-attenuating foci consistent with calcifications.

Cystoscopy confirmed the presence of a mass in the right dome, and a transurethral resection of the bladder tumor revealed colonic type adenocarcinoma with lamina propria invasion. Colonoscopy and gastroscopy identified a small hiatus hernia but no other lesions. Further clinical workup confirmed the absence of masses in other organs. A right partial cystectomy was performed.

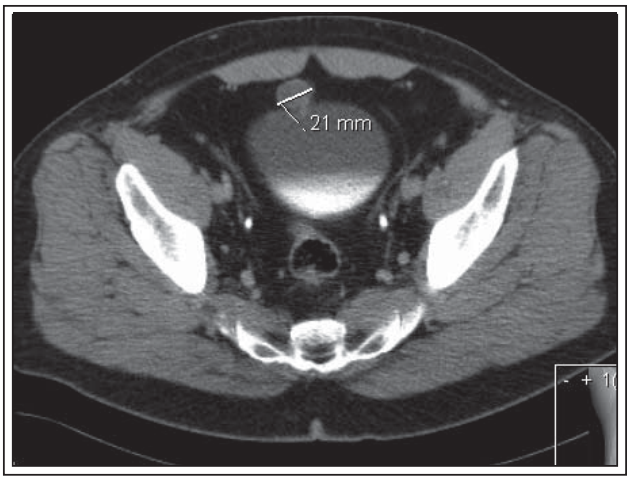

Figure 1. Urinary bladder tumor involving the dome with extravesical extension (CT scan with contrast).

Pathological findings

The surgery revealed distention of the urinary bladder wall with a 5 cm x 3 cm x 2 cm mass. The mass had a gelatinous, soft cut surface. Microscopic examination showed a urachal remnant focally involved by villous adenocarcinoma, enteric type, Figure 2. The overlying surface urothelium was intact with no evidence of cystitis cystica, cystitis glandularis, or connection to the urachal remnant. The muscularis propria, adventitia, and perivesical adipose tissue contained dissecting mucin pools inducing foreign body giant cell reaction, Figure 3, and faint calcifications. Within the mucin pools, portions of malignant glands were identified. Antibodies against cytokeratins 7 (CK7) and 20 (CK20) showed reciprocal expression within the urachal remnant with CK7 expression in non-neoplastic urachus and CK20 expression in neoplastic urachus, Figures 4 and 5. Focal nuclear expression of caudal-related homeobox transcription factor (CDX2) was noted in the neoplastic urachus but not in the non-neoplastic urachus. Mucin stains using colloidal iron, mucicarmine, and periodic acid Schiff with diastase (PAS/D) highlighted the presence of goblet cells and confirmed the presence of acidic mucin in the neoplastic urachus versus the non-neoplastic urachus, which was devoid of goblet cells and acidic mucin. The final diagnosis was invasive, well

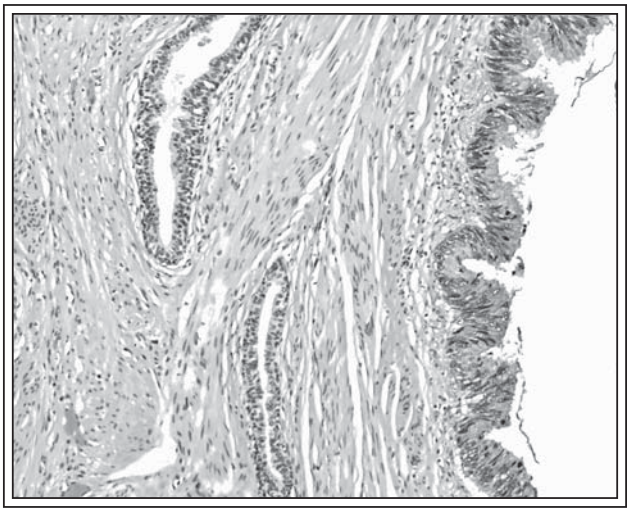

Figure 2. Urachal remnant with adenocarcinoma, enteric type (HE X400).

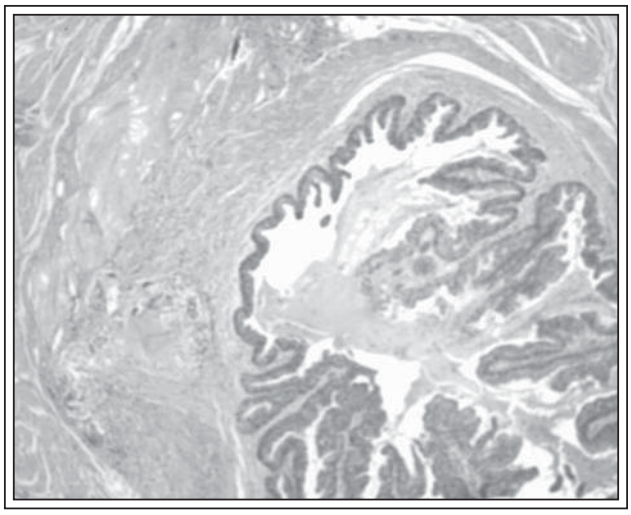

Figure 3. Urachal adenocarcinoma with abundant mucin and giant cell reaction, (HE X400).

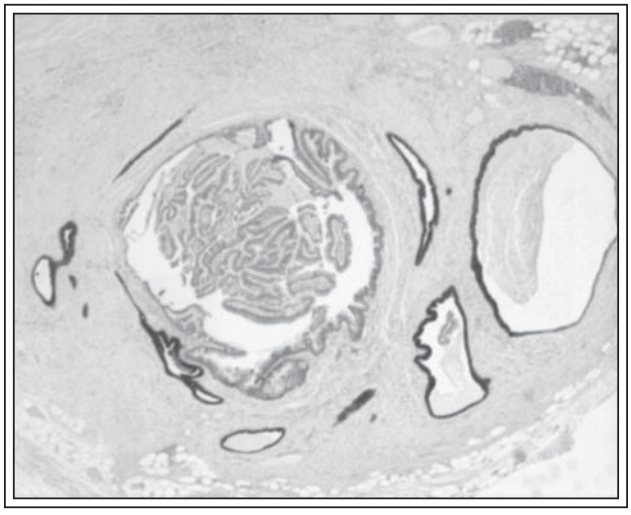

Figure 4. Reciprocal expression of CK7 with positive staining in the non-neoplastic urachus but not in its neoplastic counterpart (CK7 X200).

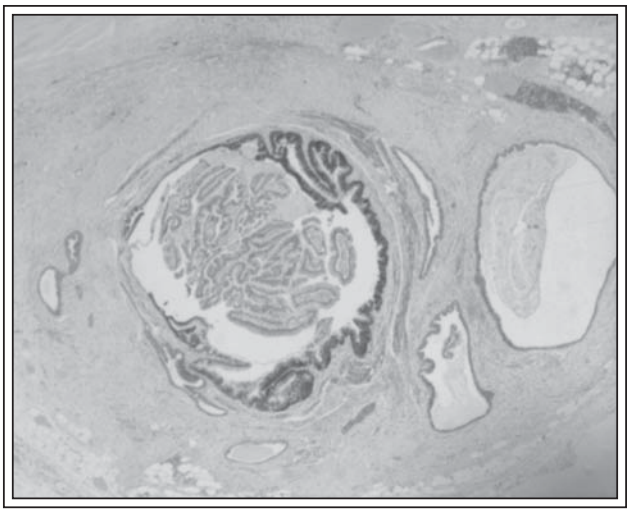

Figure 5. Reciprocal expression of CK20 with absent staining in the non-neoplastic urachus but positive expression in its neoplastic counterpart (CK X200).

differentiated urachal adenocarcinoma, enteric type, with abundant mucin production. The patient received systemic chemotherapy and remained well during a 6 month follow up.

Discussion

Although urachal adenocarcinoma is a rare pathologic entity accounting for < 1% of bladder tumors, one third of urinary bladder adenocarcinomas are of urachal origin.[4] The most frequent presentations are hematuria and a suprapubic mass. Less common symptoms are mucosuria and umbilical discharge.[5] The strongest predictors of malignancy are the presence of hematuria and age > 55 years.[6] Both features were present in the current case.

The urachus is an embryological structure that connects the cloaca with the allantois. It involutes during the 32nd week of gestation, and after birth it is represented by the medial umbilical ligament. In most adults, microscopic remnants of a patent lumen can be identified, and in about a third of cases, these remnants are in continuity with the bladder lumen. Urachal remnants may be lined by transitional, squamous, or glandular epithelium. The latter is devoid of goblet cells. Urachal pathology includes cyst formation, infection, and benign and malignant tumors. Malignant urachal tumors include adenocarcinomas, squamous cell carcinomas, and sarcomas. Mostofi[7] postulated the following criteria for the diagnosis of urachal adenocarcinoma: tumors located at the dome or anterior wall of the bladder, coming from outside in, with intact or ulcerated bladder mucosa and no evidence of cystitis cystica or glandularis and with the presence of a urachal remnant. As the latter is rarely identified, urachal adenocarcinoma is diagnosed in most cases without the presence of a urachal remnant. In the current case, all of Mostofi's proposed criteria were fulfilled.

The differential diagnosis of adenocarcinoma of the urinary bladder includes primary vesical adenocarcinoma, urachal adenocarcinomas, and metastasis to the bladder. The latter is commonly of prostatic, ovarian, or colonic origin. In the current case, metastatic origin was excluded based on the patient's complete work up. Primary vesical origin was excluded based on the presence of the tumor within and external to the muscle propria, absence of cystitis cystica or glandularis, and fulfillment of Mostofi's diagnostic criteria.[6]

Mucocele is a descriptive term that implies viscus distention with mucin. The term is commonly used to describe the gastrointestinal tract, particularly the appendix and the gall bladder. Urachal mucoceles are extremely rare. A urachal mucocele can be a sequela of various precursors including mucinous adenocarcinoma, mucinous adenoma, and intestinal metaplasia of the urachal remnant. In contrast to adenocarcinoma, the cells of intestinal metaplasia lack nuclear anaplasia and rarely involve the muscularis propria.[8]

In rare cases, lesions resembling intestinal metaplasia may infiltrate the lamina propria of the bladder or even the detrusor muscle.[9] Mucin pools are not uncommon in cases of intestinal metaplasia, and their presence in a tissue sample in the absence of epithelial cells within the mucin pools is not diagnostic of adenocarcinoma.[8] In the current case, we prefer to describe the tumor as a cystic mucinous carcinoma with large pools of mucin rather than use the generic term of mucocele. The presence of malignant glands within the mucin was sufficient to document invasion. Pseudomyxoma peritonei may complicate urachal adenocarcinoma.[10] Although this was absent in the current case, the tumor extended extravesically, so this complication could develop later in the disease course.

The pathogenesis of urachal adenocarcinoma is unknown. Urachal adenocarcinoma may arise from a villous adenoma of the urachus.[11] The current case showed focal surface villous architecture. As early as 1931, intestinal metaplasia of urachal epithelium has been postulated as a predisposing factor for urachal adenocarcinoma.[2] Its role as a precursor lesion of urachal adenocarcinoma is still controversial, however, despite being documented as a preneoplastic lesion that can lead to gastric, esophageal, and gall bladder adenocarcinomas. The acquisition of goblet cells, acid

mucin, and CK20 expression in neoplastic urachus, as well as CDX2 expression and loss of CK7 expression in neoplastic urachus but not in non-neoplastic urachus may support the concept that some urachal adenocarcinomas arise through the intestinal metaplasia and dysplasia carcinoma sequence. However, this needs to be studied further in more cases. Awareness of the morphological and immunohistochemical overlap between adenocarcinomas of urachus and colonic origins is crucial to avoid diagnostic pitfalls, particularly at metastatic sites.

Urachal adenocarcinoma is usually at an advanced stage before the patient is symptomatic and presents.[12] Extension of carcinoma beyond the bladder at the time of diagnosis is seen in 34% of cases.[12] Common sites for metastasis are lymph nodes, the lung, and the peritoneum.[13] In the current case, extravesical extension was documented clinically but metastasis was absent. In general, survival is poor for urachal adenocarcinomas, with a 25%-45% 5 year survival rate (5YSR).[14] Urachal signet ring carcinoma is similar to signet ring carcinoma elsewhere in the body,[15] and the 5YSR is reported to be 27%.[16] The urachal adenocarcinoma in our patient lacked signet ring cells, and despite the abundant mucin production was well-differentiated.

Early and complete extended partial cystectomy including umbilicalectomy is crucial for survival in patients with urachal adenocarcinoma.[17] Recently, laparoscopy has been increasingly used to treat bladder and urachal pathology efficaciously.[18] Laparoscopic en-bloc partial cystectomy and bilateral extended pelvic lymphadenectomy and/or combined endoscopic-laparoscopic surgical en bloc resection of the urachus and bladder dome[19] are reported to be safe and feasible minimally invasive alternatives to open partial cystectomy for urachal tumors. Chemotherapy with 5 fluorouracil, doxorubicin and mitomycin C is considered to be the regimen that should be tried for cancer patients with advanced urachal carcinoma.[15] The patient in the current case received this regimen, and despite the extravesical tumor extension, he remained well during a 6 month follow up.[8]

Summary

We report a rare case of urachal adenocarcinoma that illustrates aberrant phenotypic expression of colonic epitope in neoplastic urachus in contrast to non-neoplastic urachus. This suggests that further study in a larger case series is needed to determine whether some urachal adenocarcinomas arise through intestinal metaplasia and dysplasia. □

References

1. Sheldon CA, Clayman RV, Gonzalez R, Williams RD, Fraley EE. Malignant urachal lesions. *J Urol* 131(1);1984:1-8.
2. Maesawa C, Ogasawara S, Yashima-Abo A et al. Aberrant maspin expression in gallbladder epithelium and its association with intestinal metaplasia in patients with cholelithiasis. *J Clin Pathol* 59(3);2006:328-330.
3. Begg RC. The colloid adenocarcinoma of the bladder arising from the epithelium of the urachal canal : with a critical survey of tumors of urachus. *Br J Surg* 1931;18:422-464.
4. Taylor S, Bacchini P, Bertoni F. An isolated veretebral metastasis of urachal adenocarcinoma. *Arch Pathol Lab Med* 2004;128(9):1043-1045.
5. Fiter L, Gimeno F, Martin L, Gomez Tajeda L. Signet ring carcinoma of bladder. *Urology* 1993;41(1):30-33.
6. Ashley AR, Inman BR, Sebo TJ, Leibovich BC, Blute ML, Dwon ED, Zincke H. Urachal carcinoma: clincopathological features and long term outcomes of an aggressive malignancy. *Cancer* 2006;107(4):712-720.
7. Mostofi FK, Thomson RV, Dean A Jr. Mucous adenocacinoma of the urinary bladder. *Cancer* 1955;8(4):741-758.
8. Murphy WM, Grignon JD, Perlman. In AFIP atlas of tumor pathology, tumors of the urinary bladder –American Registry of Pathology-Washington-DC. P. 309.
9. Jacobs LB, Brooks JD, Epstein JI. Differentiation of colonic metaplasia from adenocarcinoma of urinary bladder. *Human Pathol* 1997;28:1152-1157.
10. Pseudomyxoma peritonei due to mucinous cystadenocarcinoma in situ of the urachus presenting as an inguinal hernia. *Int J Clin Oncol* 2006;11(5):416-419.
11. Lucas DR, Lawrence WD, McDewitt WJ. Mucinous papillary adenocarcinoma of the bladder arising within a villous adenoma urachal remnant : an immunohistochemical and ultrastructural study. *J Urol Pathol* 1994;2:173-182.
12. Henry DR, Farrow GM, Zincke H. Urachal cancer: role of conservative surgery. *Urology* 1993;42(6):635-639.
13. Kakizoe T, Matsumoto K, Andoh M, Nishio Y, Kishi K. Adenocarcinoma of urachus: report of 7 cases and review of literature. *Urology* 1983;21(4):360-366.
14. White head ED, Tessler AN. Carcinoma of urachus. *Br J Urol* 1971;43(4):468-476.
15. Morii A, Furuya Y, Fujiuchi Y, Akashi T, Ishizawa S, Fuse H. Urachal signet ring carcinoma. *Int J Urol* 2007;14(4):360-361.
16. Chen KTK, Workman RD, Rainwater G. Urachal signet ring cell carcinoma. *Urology* 1990;36(4):339-340.
17. Satoshi O, Shigeki S, Karuko I et al. Urachal adenocarcinoma metastatic to ovaries: case report and literature review. *Int J Gynecol Pathol* 2003;22(2):189-193.
18. Wadhawa P, Kolla SB, Hemal AK. Laparoscopic en bloc partial cystectomy with bilateral pelvic lymphadenectomy for urachal adenocarcinoma. *Urology* 2006;67(4):837-843.
19. Porpiglia F, Cracco CM, Terrone C et al. Combined endoscopic and laparoscopic en bloc resection of the urachus and the bladder dome in a rare case of urachal carcinoma. *Int J Urol* 2007;14(4):362-364.