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Urachal carcinoma: a pathologic and clinical study of 46 cases

Jasreman Dhillon, MD^{a,d}, Yu Liang, MD, PhD^a, Ashish M. Kamat, MD^b, Arlene Siefker-Radtke, MD^c, Colin P. Dinney, MD^b, Bogdan Czerniak, MD, PhD^a, and Charles C. Guo, MD^{a,*}

^aDepartment of Pathology, The University of Texas MD Anderson Cancer Center, Houston, TX 77030, USA

^bDepartment of Urology, The University of Texas MD Anderson Cancer Center, Houston, TX 77030, USA

^cDepartment of Genitourinary Medical Oncology, The University of Texas MD Anderson Cancer Center, Houston, TX 77030, USA

Summary

Urachal carcinoma is a rare tumor that has not been well studied. To determine the pathologic and clinical features of this disease, we retrospectively evaluated 46 cases from our surgical pathology files. The patients included 16 women and 30 men, with a mean age of 53.4 years (range, 28–82 years). Forty patients had undergone cystectomy, and the remaining 6 had undergone transurethral bladder biopsy. Most tumors were located at the dome (n=44); only 2 were located at both the dome and anterior wall. All tumors consisted of adenocarcinoma, including mucinous (n=36), enteric (n=7), not otherwise specified (n=2), and signet ring cell (n=1) types. Focal areas of signet ring cell features were present in 23 cases, but urothelial carcinoma in situ was not identified in any cases. The tumors invaded the muscularis propria (n=8), perivesical adipose tissue (n=27), and abdominal wall (n=3). Twenty-five patients had died of cancer at a mean of 32 months (range, 12–74 months), and 21 patients were alive at a mean of 65 months (range, 7–230 months). The median cancer-specific survival time of urachal adenocarcinoma patients was 45 months, which was significantly longer than that of bladder urothelial carcinoma patients with similar-stage disease (p=0.047). Patients' cancer-specific survival was associated with tumor stage according to the Sheldon, Mayo, and TNM staging systems. In conclusion, urachal carcinomas are predominantly composed of invasive adenocarcinomas, which commonly demonstrate mucinous features. Most tumors present at advanced stages but are still associated with a better survival rate than bladder urothelial carcinomas.

*Corresponding author. Department of Pathology, Unit 85, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Boulevard, Houston, TX 77030-4009. ccguo@mdanderson.org; tel: (713) 792-3094; fax: (713) 792-4049.

^dCurrently Department of Pathology, Moffitt Cancer Center, Tampa, FL 33612, USA.

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Keywords

Urachus; urachal carcinoma; adenocarcinoma; tumor staging system

1. Introduction

The urachus is a vestigial structure of the allantois that generally loses its function after birth [1]. During embryogenesis, the allantois regresses to form the urachus, a tubular structure that connects the urinary bladder and the umbilicus. After the third trimester, the urachus usually involutes as a fibrous cord, which coalesces with the obliterated umbilical arteries and forms the median urachal ligament. However, a urachal remnant, which is characterized by a tubular or cystic muscular structure that is lined by epithelium, can still be found in about a third of adults [2]. Although it is most commonly found at the bladder dome, the urachal remnant can also be found anywhere along the bladder midline, including the posterior and anterior walls [1]. It can be divided into 3 segments: intramucosal, intramuscular, and supravescical [3]. The urachal wall is usually composed of the urothelium, subepithelial connective tissue (or lamina propria), and muscularis propria layers. The urachal urothelial lining frequently undergoes metaplastic changes, mostly glandular metaplasia [4].

Carcinoma can arise from the urachal epithelial lining. Although the urachal remnant is generally lined with urothelium like the bladder, urachal carcinomas demonstrate pathologic and clinical features that are distinct from those of bladder carcinomas [5–12]. While most bladder carcinomas are urothelial carcinoma, the vast majority of urachal carcinomas are adenocarcinoma, which typically produces abundant extracellular mucin and exhibit focal signet ring cell features. Most bladder urothelial carcinomas present as non-invasive papillary urothelial carcinomas and do not invade the muscular wall [13]. In contrast, the majority of urachal adenocarcinomas mainly involve the muscularis propria and perivesical soft tissues, with a sharp demarcation from the bladder surface urothelium [5–12]. In urachal carcinomas, the bladder urothelium is usually intact or ulcerated and lacks papillary urothelial carcinoma or urothelial carcinoma in situ.

Urachal carcinomas are rare, accounting for less than 1% of all bladder cancers [5–7]. Although most urachal carcinomas are adenocarcinoma, urachal adenocarcinoma is far less common than is non-urachal adenocarcinoma in the bladder [8]. A previous study from our institution reported that urachal adenocarcinomas accounted for one-third of all adenocarcinomas of the bladder, but this figure may have been high because of the referral-based nature of our institution [14]. A recent multi-center study reported that urachal adenocarcinomas account for about 10% of bladder adenocarcinomas, which may reflect their true incidence in the general population [15]. Because of the rarity of urachal tumors, there have been limited studies of this malignancy reported in the medical literature; most studies have been single-case and small-series reports. Here, we determined the pathologic and clinical features of urachal carcinoma in a large series of cases from a single institution.

2. Patients and Methods

With the approval of the institutional review board, we retrospectively reviewed our surgical pathology report databases to identify all patients with urachal carcinoma who had been treated at The University of Texas MD Anderson Cancer Center (Houston, Texas) from 1990 through 2010. The following diagnostic criteria were used to diagnose primary carcinoma of the urachus: 1) the tumor was located in the dome or midline of the bladder; 2) the tumor predominantly invaded the muscularis propria and perivesical soft tissues with either intact or ulcerated bladder epithelium; 3) there was a sharp demarcation between the tumor and the bladder surface urothelium; 4) there was no extensive cystitis glandularis or cystitis cystica, particularly atypical intestinal metaplasia, in the bladder wall; 5) urothelial carcinoma or urothelial carcinoma in situ was not found in the bladder; and 6) there was no primary adenocarcinoma of another organ.

Forty-six patients with urachal carcinoma were identified. All patients had undergone transurethral biopsy of the bladder, and 40 had undergone partial or radical cystectomy, including partial cystectomy with removal of the urachus and umbilicus (n=14), partial cystectomy with removal of the urachus (n=10), partial cystectomy (n=9), cystoprostatectomy with removal of the urachus and umbilicus (n=2), cystoprostatectomy (n=2), cystectomy with removal of the urachus (n=1), cystectomy with removal of the urachus and umbilicus (n=1), and total pelvic exenteration with removal of the umbilicus (n=1). The 6 patients who had not undergone cystectomy presented with metastases. The biopsy and cystectomy specimens from all 46 patients were routinely processed for histologic examination. Usually, more than 40 sections were taken from a cystectomy specimen, including the tumor (one block per centimeter of the largest tumor dimension), resection margins (ureter, urethra, umbilicus and soft tissue), and noncancerous bladder, medial ligament and other associated organs. Three sections were typically taken from the noncancerous areas of the bladder dome and the median umbilical ligament, respectively. Hematoxylin-eosin-stained slides were used for morphologic analysis. The reviewed pathologic parameters included tumor size, location, histologic type, tumor stage, signet ring cell features, lymphovascular invasion, resection margin, urachal remnant, and other urothelial changes.

The following demographic and clinical information was obtained from patients' charts: age, sex, clinical presentation, cystoscopic findings, clinical stage, treatment, and clinical outcome, including metastasis. Clinical stages were evaluated using 3 different staging systems. The Sheldon staging system was defined as follows [5]: stage I, tumors were limited to the urachal mucosa; II, tumors invaded into but not beyond the urachal muscular layer; III, tumors extended to the bladder, abdominal wall, and other adjacent organs; and IV, tumors metastasized to the lymph nodes or other distant organs. The Mayo staging system was defined as follows [9]: stage I, tumors were confined to the urachus or bladder; II, tumors extended beyond the muscular layer of the urachus or bladder; III, tumors metastasized to the regional lymph nodes; and IV, tumors metastasized to non-regional lymph nodes or other distant sites. The TNM clinical staging system was defined as follows [16]: stage I (T1N0M0), tumors invaded the subepithelial connective tissue; II (T2N0M0), tumors invaded the urachal or bladder muscularis propria; III (T3M0N0 or T4aM0N0),

tumors invaded the perivesical soft tissue, prostate, uterus, or vagina; and IV (T4b and any T with N1-3 or M1), tumors invaded the abdominal wall and metastasized to the lymph nodes or other distant sites.

The outcome for urachal carcinomas was analyzed and compared with that of bladder urothelial carcinomas (n=106) at similar TNM stages who were treated at our institute. Kaplan-Meier curves that reflected patients' cancer-specific survival rates were generated using the GraphPad Prism 6 software package (GraphPad Software, Inc., La Jolla, CA). The log-rank test was used to calculate 2-tailed *P* values. *P* values < 0.05 were considered statistically significant.

3. Results

3.1. Patient demographics and clinical findings

Of the 46 patients in our study, 16 were women and 30 were men. Their mean age at initial diagnosis was 53.4 years (range, 28–82 years), and 24 (52%) were under the age of 50 years. The most common presenting symptom was hematuria (n=29); other symptoms included tenderness around the umbilicus (n=4), mucinuria (n=3), pelvic pain or pressure (n=3), and weight loss (n=1). In 4 patients, the urachal tumors were incidentally found on a radiographic study for other diseases. In 2 patients, the presenting symptom was unclear. Forty patients underwent partial (n=33) or radical (n=7) cystectomy, and 29 also underwent resection of the urachus or umbilicus. The 6 patients who did not undergo cystectomy presented with metastases.

3.2. Pathologic findings

Most urachal tumors were located at the dome (n=44); only 2 tumors were located at the dome and anterior area (n=2). The average tumor size was 3.7 cm (range, 1–10.5 cm). On cystoscopic examination (data were available for 12 cases), the tumors appeared as exophytic masses (n=4), sessile masses (n=3), grape-like lesions (n=1), nodular masses (n=1), mucoid discharge (n=1), fulgurated areas (n=1), or papillary lesions (n=1). On microscopic examination, all urachal tumors were composed of invasive adenocarcinoma. The majority of adenocarcinomas were of the mucinous type (n=36), which was characterized by abundant extracellular mucin with single tumor cells and small malignant glands (Fig. 1). Seven tumors exhibited enteric features, closely resembling adenocarcinoma of the colon (Fig. 2). In 2 cases, the adenocarcinomas showed a non-specific glandular growth pattern or were of the not otherwise specified type (Fig. 3). Only 1 case was composed of pure signet ring cells (Fig. 4), and focal areas of signet ring cells were observed in 23 other cases. On cystectomy specimens (n=40), the tumors invaded the muscularis propria (n=7), perivesical tissue (n=29), and abdominal wall or other adjacent organs (n=4). Lymphovascular invasion was present in 7 cases. The resection margins were positive in 7 cases. The urachal remnant was identified in 7 cases. Focal cystitis cystica or cystitis glandularis was identified in 9 cases. Urothelial carcinoma in situ was not present in any case.

3.3. Clinical follow-up

Follow-up data were available for all patients, with a mean follow-up time of 47 months (range, 7–230 months). Twenty-five patients died of cancer in a mean of 32 months (range, 12–74 months), and 21 patients were alive in a mean of 65 months (range, 7–230 months). Twelve patients presented with metastases at the time of cystectomy, and 22 developed metastases after cystectomy. The common sites of metastases included the lungs (n=13), bones (n=11), peritoneum (n=10), lymph nodes (n=9), liver (n=5), intestines (n=5), and brain (n=3). Of the 29 patients who had undergone cystectomy with removal of the urachus and umbilicus, 10 died of cancer (34%) in a mean of 35 months (range, 13–74 months). Of the 11 patients who had undergone cystectomy without removal of the urachus and umbilicus, 7 died (64%) in a mean of 31 months (range, 12–71 months).

According to the Sheldon staging system [5], the tumors were stage III (n=27) or IV (n=19) (Table 1). Among patients with stage III tumors, 9 (33%) had died of cancer at 41 months (range, 13–71 months) and 18 (67%) were alive at 55 months (range, 7–230 months). Among those with stage IV tumors, 11 (58%) had died at 22 months (range, 12–45 months), and 8 (42%) were alive at 29 months (range, 13–92 months).

On the basis of the Mayo staging system [9], the tumors were stage I (n=6), II (n=21), III (n=1), and IV (n=18). Among patients with stage I tumors, 1 (17%) had died of cancer at 46 months and 5 (83%) were alive at a mean of 47 months (range, 7–168 months). Among those with stage II tumors, 8 (38%) had died at a mean of 40 months (range, 13–71 months) and 13 (62%) were alive at 59 months (range, 8–230 months). Among those with stage III and IV tumors, 11 (58%) had died at 22 months (range, 12–45 months) and 8 (42%) were alive at 30 months (range, 12–92 months).

On the basis of the TNM clinical staging system [16], the tumors were stages II (n=5 [11%]), III (n=19 [41%]), and IV (n=22 [48%]). Among patients with stage II tumors, 1 (20%) died of cancer in 46 months and 4 (80%) were alive at a mean of 47 months (range, 17–81 months). Among those with stage III tumors, 9 (47%) had died of cancer at a mean of 39 months (range, 13–74 months) and 10 (53%) were alive at 80 months (range, 7–230 months). Among those with stage IV tumors, 15 (68%) had died at 26 months (range, 12–54 months) and 7 (32%) were alive at 55 months (range, 12–102 months). A log-rank test demonstrated that the cancer-specific survival rate was significantly associated with cancer stage ($p=0.024$) (Fig. 5A)

The outcome of urachal adenocarcinoma patients was compared with that of bladder urothelial carcinoma patients (n=106) at similar tumor stages. The urothelial carcinomas had all been treated at our institution and included TNM stages II (n=14 [13%]), III (n=40 [38%]), and IV (n=52 [49%]) tumors. The stage distribution of bladder urothelial carcinoma was similar to that of urachal adenocarcinoma (see above). The median cancer-specific survival of urachal adenocarcinoma patients was 45 months, while the median survival of bladder urothelial carcinoma patients was 27 months (Fig. 5B). A log-rank test revealed that the median survival duration of urachal adenocarcinoma patients was significant longer than that of bladder urothelial carcinoma patients at similar stages ($p=0.047$). Cancer-specific survival was also compared between bladder urothelial carcinoma and urachal

adenocarcinoma at similar stages. The survival rates in the urachal adenocarcinoma cohorts were higher than those in bladder urothelial carcinoma counterparts at similar stages (Fig. 5C); however, the differences were not significant in the log-rank test, probably due to the limited number of patients at each stage in this study.

4. Discussion

The diagnostic criteria for urachal tumors have undergone modifications. Initially, Wheeler and Hill proposed a set of strict criteria, which included the following [17]: 1) tumor in the dome of the bladder, 2) absence of cystitis cystica and cystitis glandularis, 3) predominant involvement of the muscularis or deeper tissue by tumor with intact or ulcerated epithelium, (4) presence of urachal remnants, (5) presence of a suprapubic mass, (6) sharp demarcation between the tumor and the normal surface epithelium, and (7) tumor growth in the bladder wall, extending into the space of Retzius. However, these criteria were too restrictive and would have excluded most reported cases of urachal carcinoma. Subsequently, Johnson et al modified the criteria and included the following [6]: 1) tumor in the dome or elsewhere in the midline of the bladder, 2) sharp demarcation between the tumor and the surface epithelium, and 3) absence of primary adenocarcinoma of another organ. Urachal adenocarcinoma may be associated with areas of cystitis cystica and cystitis glandularis in the adjacent or distant bladder mucosa, but it usually does not show dysplastic intestinal metaplasia. As the modified criteria are more practical, we have used them at our institution, including in the current study.

Although the urachal remnant is lined with urothelium, the vast majority of urachal carcinomas are composed of adenocarcinoma. It is unclear why adenocarcinoma is the predominant histologic type of urachal carcinoma. It has been postulated that the oncogenesis of urachal adenocarcinoma involves a metaplastic process, as the urachal urothelium often exhibits glandular metaplasia [11]. An alternative theory is that some urachal adenocarcinomas, particularly the enteric type, arise from the enteric rest left behind in the urachus from the cloaca during embryogenesis [14]. Although all the urachal carcinomas in the current study were composed of adenocarcinoma, other histologic types, such as urothelial, squamous, and sarcomatoid carcinomas, have been reported [18,19]. However, non-adenocarcinomatous histologic types, particularly urothelial carcinoma, should be viewed with caution when diagnosing urachal carcinoma; urothelial carcinoma can also arise in the bladder dome and may involve the urachal remnant at an advanced stage.

It is important to differentiate urachal adenocarcinoma from non-urachal adenocarcinoma of the bladder, as they may require different treatment strategies. Urachal carcinoma often responds favorably to a partial cystectomy with en bloc resection of the urachus and umbilicus, as the tumor predominantly involves the muscularis propria and perivesical soft tissue and the bladder surface urothelium is usually not affected [7]. In contrast, non-urachal primary adenocarcinoma of the bladder responds poorly to partial cystectomy because of the widespread tumor field effect in the surface epithelium of the bladder. Although it is not difficult to distinguish urachal from non-urachal adenocarcinoma in cystectomy specimens, it is challenging to differentiate them on small biopsy specimens because of the significant

overlapping histologic features. Furthermore, both urachal and non-urachal adenocarcinomas are commonly positive for CK7, CK20, and CDX2 and lack nuclear positivity for beta-catenin [20]. Thus, immunohistochemical studies have limited value in the differential diagnosis. To reach a correct diagnosis, it is necessary to combine the pathologic findings on a biopsy specimen with the patient's radiographic study (tumor located in the bladder dome) and cystoscopic (intact or ulcerated urothelium) findings.

Adenocarcinoma from other organs, particularly the prostate and colorectum, should also be considered in the differential diagnosis of urachal adenocarcinoma. Advanced prostatic and colorectal adenocarcinomas may invade the bladder but usually involve the bladder neck or posterior wall rather than the dome. Furthermore, prostatic adenocarcinomas usually express prostate-specific markers, such as prostate-specific antigen, prostate-specific acid phosphatase, prostatein and NKX3.1; colorectal adenocarcinomas do not express high molecular weight cytokeratin 34 beta E12, and CK7 but express nuclear positivity for beta-catenin [20,21]. Nuclear localization of β -catenin can rarely occur in urachal adenocarcinomas; however, diffuse nuclear reactivity argues against its diagnosis. Metastasis from the kidneys, breasts, endometrium, and other organs may involve the bladder but are extremely rare [22–25]. A correct diagnosis is usually not difficult if the patient's clinical history and radiographic findings are carefully considered.

Several staging systems have been used for urachal carcinomas [5,9,16]. Sheldon et al proposed a staging system in which stage I and II tumors were defined on the basis of urachal confinement [5]. However, studies have found that the urachal remnant is only identified in a minority of patients. The low frequency by which the urachal remnant is identified in cystectomy specimens is probably because most urachal carcinomas present at an advanced stage, when the remnant has been obliterated by the tumor. In addition, only selected regions of the median umbilical ligament and bladder dome are submitted for histologic examination. In the current study, the urachal remnant was identified in only 17.5% (7 of 40) of cystectomy specimens. Therefore, most urachal tumors were stage III or higher according to the Sheldon system. Ashley et al at the Mayo Clinic proposed another staging system, but its distinction between stages III and IV seems arbitrary [9]. The TNM staging system for bladder carcinomas was initially thought to be of limited value for urachal carcinomas, as urachal tumors do not arise from the bladder surface urothelium [16]. Nonetheless, the TNM staging system can still assess the extent of disease, such as tumor confinement to the bladder wall (most urachal carcinomas are centered in this location) and metastasis to the lymph nodes or distant organs. We used the TNM staging system to analyze patient outcome in the current study and found that overall survival of patients was associated with the tumor TNM stage. These results indicate that the TNM staging system may also be useful for urachal carcinoma.

Most urachal carcinomas present at advanced stages, with widespread metastasis; patients generally have a poor clinical outcome [26]. It has been difficult to compare the prognoses of patients with urachal and non-urachal adenocarcinomas because of the rarity of these tumors.

Using data from multiple cancer registries, which included 151 urachal adenocarcinomas and 1374 non-urachal adenocarcinomas, Wright et al found that the overall survival and cancer-specific survival for patients with urachal adenocarcinoma were significantly better than those with non-urachal adenocarcinoma in a multivariate analysis, after adjusting for tumor stage, tumor grade, histologic type, patient age, and treatment [15]. Although overall survival is usually used to estimate the patient's prognosis, cancer-specific survival is a more insightful endpoint to study the impact of cancer on patients, as it takes into account deaths from other unrelated causes. Deaths from other unrelated causes are considered to be withdrawn alive rather than death from cancer. In the current study, we compared the cancer-specific survival rates of patients with urachal adenocarcinoma and bladder urothelial carcinoma at advanced stages and found that patients with urachal carcinoma had significantly longer median survival durations than did those with bladder urothelial carcinoma. One factor that likely contributed to the favorable outcome of urachal adenocarcinoma was the demographic difference: patients with urachal carcinoma were significantly younger (mean, 53 years; range, 28–82 years) than were those with urothelial carcinoma (mean, 68 years; range, 32–90 years). We also compared the survival rates of urachal adenocarcinoma and bladder urothelial carcinoma at similar stage. Although the survival rates of urachal adenocarcinoma were higher than those of bladder urothelial carcinomas at similar stages, the differences were not significant, probably due to the limited number of patients at each stage in this study. Our analysis was also limited by a relatively short followup time (47 months on average) when compared with other studies [10,11,19]. A longer followup may be needed to further assess the outcomes of urachal adenocarcinomas and bladder urothelial carcinomas at similar stages.

In summary, we evaluated the pathologic and clinical features of urachal carcinoma in a large series of patients at a single institution. Our study demonstrates several notable differences between urachal carcinoma and bladder carcinoma, despite the proximity of their locations. Urachal carcinoma occurs at a relatively younger age than bladder carcinoma, and the male predominance in urachal carcinoma is not as pronounced as it is in the bladder carcinoma. All urachal carcinomas in our series are composed of invasive adenocarcinoma, most commonly the mucinous type. The majority of urachal adenocarcinomas present at advanced stages and spread out of the urachus and bladder. Although the prognosis of urachal carcinoma is poor, it is significantly better than that of bladder urothelial carcinoma at similar stages. The mortality rate is associated with the tumor stage in Sheldon, Mayo and TNM staging systems.

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References

1. Begg RC. The urachus: its anatomy, histology and development. *J Anat.* 1930; 64:170–83. [PubMed: 17104266]
2. Schubert GE, Pavkovic MB, Bethke-Bedurftig BA. Tubular urachal remnants in adult bladders. *J Urol.* 1982; 127:40–2. [PubMed: 7057501]

3. Hammond G, Yglesias L, Davis JK. The urachus, its anatomy and associated fasciae. *Anat Rec.* 1941; 80:271–8.
4. Tyler DE. Epithelium of intestinal type in the normal urachus, a new theory of vesical embryology. *J Urol.* 1964; 92:505–7. [PubMed: 14226479]
5. Sheldon CA, Clayman RV, Gonzalez R, Williams RD, Fraley EE. Malignant urachal lesions. *J Urol.* 1984; 131:1–8. [PubMed: 6361280]
6. Johnson DE, Hodge GB, Abdul-Karim FW, Ayala AG. Urachal carcinoma. *Urology.* 1985; 26:218–21. [PubMed: 4035835]
7. Siefker-Radtke AO, Gee J, Shen Y, Wen S, Daliani D, Millikan RE, Pisters LL. Multimodality management of urachal carcinoma: the M. D. Anderson Cancer Center experience. *J Urol.* 2003; 169:1295–8. [PubMed: 12629346]
8. Ayala, AG.; Tamboli, P. Urachal Adenocarcinoma. In: Eble, JN.; Sauter, G.; Epstein, JI., et al., editors. *Pathology and genetics of tumours of the urinary system and male genital organs. World Health Organization Classification of Tumours*; Lyon: IARC Press; 2004. p. 218–249.
9. Ashley RA, Inman BA, Sebo TJ, Leibovich BC, Blute ML, Kwon ED, Zincke H. Urachal carcinoma: clinicopathologic features and long-term outcomes of an aggressive malignancy. *Cancer.* 2006; 107:712–20. [PubMed: 16826585]
10. Herr HW, Bochner BH, Sharp D, Dalbagni G, Reuter VE. Urachal carcinoma: contemporary surgical outcomes. *J Urol.* 2007; 178:74–8. [PubMed: 17499279]
11. Gopalan A, Sharp DS, Fine SW, Tickoo SK, Herr HW, Reuter VE, Olgac S. Urachal carcinoma: a clinicopathologic analysis of 24 cases with outcome correlation. *Am J Surg Pathol.* 2009; 33:659–68. [PubMed: 19252435]
12. Amin MB, Smith SC, Eble JN, Rao P, Choi WW, Tamboli P, Young RH. Glandular neoplasms of the urachus: a report of 55 cases emphasizing mucinous cystic tumors with proposed classification. *Am J Surg Pathol.* 2014; 38:1033–45. [PubMed: 25025366]
13. Dinney CP, McConkey DJ, Millikan RE, Wu X, Bar-Eli M, Adam L, Kamat AM, Siefker-Radtke AO, Tuziak T, Sabichi AL, Grossman HB, Benedict WF, Czerniak B. Focus on bladder cancer. *Cancer Cell.* 2004; 6:111–6. [PubMed: 15324694]
14. Grignon DJ, Ro JY, Ayala AG, Johnson DE, Ordóñez NG. Primary adenocarcinoma of the urinary bladder. A clinicopathologic analysis of 72 cases. *Cancer.* 1991; 67:2165–72. [PubMed: 1706216]
15. Wright JL, Porter MP, Li CI, Lange PH, Lin DW. Differences in survival among patients with urachal and nonurachal adenocarcinomas of the bladder. *Cancer.* 2006; 107:721–8. [PubMed: 16826584]
16. Edge, SB.; Byrd, DR.; Compton, CC.; Fritz, AG.; Greene, FL.; Trotti, A, III. Chapter 45: Urinary Bladder. In: Edge, SB.; Byrd, DR.; Compton, CC.; Fritz, AG.; Greene, FL.; Trotti, A., III, editors. *AJCC Cancer Staging Manual. 7.* New York, NY: Springer; 2010. p. 497–505.
17. Wheeler JD, Hill WT. Adenocarcinoma involving the urinary bladder. *Cancer.* 1954; 7:119–135. [PubMed: 13126906]
18. Paner GP, Barkan GA, Mehta V, Sirintrapun SJ, Tsuzuki T, Sebo TJ, Jimenez RE. Urachal carcinomas of the nonglandular type: salient features and considerations in pathologic diagnosis. *Am J Surg Pathol.* 2012; 36:432–42. [PubMed: 22301493]
19. Molina JR, Quevedo JF, Furth AF, Richardson RL, Zincke H, Burch PA. Predictors of survival from urachal cancer: a Mayo Clinic study of 49 cases. *Cancer.* 2007; 110:2434–40. [PubMed: 17932892]
20. Paner GP, McKenney JK, Barkan GA, Yao JL, Frankel WL, Sebo TJ, Shen SS, Jimenez RE. Immunohistochemical analysis in a morphologic spectrum of urachal epithelial neoplasms: diagnostic implications and pitfalls. *Am J Surg Pathol.* 2011; 35:787–98. [PubMed: 21572312]
21. Wang HL, Lu DW, Yerian LM, et al. Immunohistochemical distinction between primary adenocarcinoma of the bladder and secondary colorectal adenocarcinoma. *Am J Surg Pathol.* 2001; 25:1380–1387. [PubMed: 11684954]
22. Zhang M, Wah C, Epstein JI. Metastatic renal cell carcinoma to the urinary bladder: a report of 11 cases. *Am J Surg Pathol.* 2014; 38:1516–21. [PubMed: 25140895]
23. Xiao GQ, Chow J, Unger PD. Metastatic tumors to the urinary bladder: clinicopathologic study of 11 cases. *Int J Surg Pathol.* 2012; 20:342–8. [PubMed: 22134629]

24. Raymond KW, Hin TS, Fai KC, Steve CW. Urinary bladder metastasis from lung adenocarcinoma: A rare cause of hematuria. *Urol Ann.* 2014; 6:359–62. [PubMed: 25371617]
25. Bates AW, Baithun SI. Secondary neoplasms of the bladder are histological mimics of nontransitional cell primary tumours: clinicopathological and histological features of 282 cases. *Histopathology.* 2000; 36:32–40. [PubMed: 10632749]
26. Siefker-Radtke A. Urachal adenocarcinoma: a clinician's guide for treatment. *Semin Oncol.* 2012; 39:619–24. [PubMed: 23040259]

Highlights

- A large series of urachal carcinomas from a single institution are studied
- Detailed pathologic features of urachal carcinoma are analyzed
- Clinical outcome is associated with tumor stage in three different staging systems
- Urachal carcinomas have better outcome than bladder urothelial carcinomas at similar stages

Figure 1. Urachal adenocarcinoma, mucinous type. A. Small malignant glands in abundant mucin. B. Cords of tumor cells in abundant mucin. C. Rare tumor cells in a pool of mucin. D. Metastasis produces abundant mucin in a lymph node. (Hematoxylin and eosin; original magnification x 40 [A, B, D], x 100 [C]).

Figure 2. Urachal adenocarcinoma, enteric type. (Hematoxylin and eosin; original magnification x 100).

Figure 3.
Urachal adenocarcinoma, not otherwise specified type. (Hematoxylin and eosin; original magnification x 100).

Figure 4. Urachal adenocarcinoma, signet ring cell type. (Hematoxylin and eosin; original magnification x 200).

Figure 5A

Figure 5B

Figure 5C

Figure 5.

Kaplan-Meier analysis of cancer specific survival in patients with urachal adenocarcinomas. A. Urachal adenocarcinomas by stage. B. Urachal adenocarcinomas in comparison with bladder urothelial carcinomas. C. Urachal adenocarcinomas in comparison with bladder urothelial carcinomas by stage. (UAD = Urachal adenocarcinoma; BUC = Bladder urothelial carcinoma).

Table 1
Patient mortality rates in relation to tumor stage according to different staging systems^{*}

Stage	Sheldon		Mayo		TNM	
	n	Mortality rate	n	Mortality rate	n	Mortality rate
I	0	-	6	17%	0	-
II	0	-	21	38%	5	20%
III	27	33%	1	100%	19	47%
IV	19	58%	18	56%	22	68%

^{*} The Sheldon, Mayo, and TNM staging systems were used as described in Patients and Methods [5,9,16].