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CASE REPORT

Case Report: Bladder adenocarcinoma: primary or urachal?

[version 1; peer review: 2 approved, 1 approved with reservations, 1 not approved]

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Abstract

Background: Bladder adenocarcinoma (AC) is a scarce histological variant and there are few studies on its proper management. No previous case reports present the management of a urachal tumor and the incidental finding of bladder adenocarcinoma.

Clinical case: We present the case of a young woman with nonspecific symptoms, who presented with a prior history of dysuria, bladder tenesmus, suprapubic pain and urinary urgency for one year, which had been treated as recurrent urinary tract infection. A partial cystectomy plus extended lymphadenectomy was scheduled. We found a bladder tumor with characteristics of a urachal tumor and the pathological report indicated a primary bladder AC. The patient had a complete recovery at one year of follow-up.

Conclusions: A patient can present with a tumor with urachal characteristics; however, the pathology report can show primary AC. The decision to perform partial cystectomy was an appropriate option for the location of this tumor, with optimal surgical results. Still, a long-term follow-up is necessary. More specific management guidelines are required for the treatment of AC.

Keywords

Urinary Bladder Neoplasms, Adenocarcinoma, Surgical Pathology

Open Peer Review

Approval Status

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Any reports and responses or comments on the article can be found at the end of the article.

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Author roles: **Tejeda-Mariaca JE:** Conceptualization, Data Curation, Project Administration, Supervision, Writing – Original Draft Preparation, Writing – Review & Editing; **Ordoñez-Alcantara M:** Conceptualization, Investigation, Project Administration, Writing – Original Draft Preparation, Writing – Review & Editing; **Bello-Sedano A:** Conceptualization, Project Administration, Writing – Original Draft Preparation, Writing – Review & Editing; **Perez-Cornejo V:** Conceptualization, Project Administration, Writing – Original Draft Preparation, Writing – Review & Editing; **Grande-Urbina JA:** Data Curation, Project Administration, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing

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Background

Within bladder tumors, adenocarcinoma (AC) is a histological variant that represents only 0.5–2% of cases. Its prognosis is the poorest, given that it is diagnosed in more advanced stages due to its rarity. There is little literature about its management and there are no standard treatment guidelines.

Its association with a history of bladder exstrophy, schistosomiasis and chronic bladder irritation has been described. Due to intramural growth, the symptoms occur later in disease progression and AC is diagnosed in more advanced stages, so the prognosis is worse. Only 5% of cases are diagnosed during the initial stages. Hematuria is the most frequent symptom (60–100% of cases), and irritative symptoms and mucosuria are also common (25–80% of cases)¹.

Bladder AC can be classified as primary or secondary, the latter occurring by direct extension or by metastasis from a distant site like the colon, prostate, endometrium, cervix or breast. Strictly, the urachus is not an intrinsic component of the bladder. However, urachal AC is usually described with bladder tumors because they share pathological and clinical features. Therefore, bladder AC can be classified as urachal AC (10–30%) and non-urachal AC (70–90%).

Primary bladder AC shows a pure glandular phenotype. It usually arises from the trigone and the posterior wall but can be found anywhere in the bladder. It usually presents as a solitary lesion². Histologically, it shows several growth patterns: enteric, morphologically identical to its colonic counterpart; or mucinous, with abundant extravasated mucin, including signet ring cells.

Urachal AC develops from the remnant of urachus. It presents as a solitary polypoid mass in the dome of the bladder, although it can be seen anywhere along the anterior midline, and it can affect the Retzius space and the anterior abdominal wall. Microscopically, it is very similar to primary AC, the mucinous variant being the most frequent.

Here, we report an incidental case of a patient with bladder AC treated as urachal AC who presented good oncological results at one year of follow-up. What is unique about this case is that urachal AC tumor management was proposed because of the clinical findings; however, the urachus was ultimately found to be tumor-free.

Clinical case

Patient information

The patient was a 35-year-old mestizo woman, who works as a junior manager, with no clinical history of hematuria, bladder tumors or prior surgical interventions and no family history of bladder tumors. The patient presented to the urology practice with a prior history of dysuria, bladder tenesmus, suprapubic pain and urinary urgency for one year, which had been treated as recurrent urinary tract infection with broad spectrum antibiotics. The patient presented negative cultures; however, the symptoms did not disappear. A timeline of the major timepoints

in the patient's history, diagnosis and treatment is provided (Figure 1).

Clinical findings

A physical abdominal and genitourinary exploration was carried out. There were no positive findings upon physical examination and no painful trigger points were found. There were no signs of vulvar irritation or palpable abdominal mass.

Diagnostic assessment

A bladder screening ultrasound was performed in order to identify any abnormal structure or urinary retention. During the exam the bladder was full, and a bladder dome mass was noted. A unique, polypoid mass with mucoid characteristics of 4.0cm was found using urethrocytoscopy. A lower abdomen contrasted CT scan was performed and a collection/mass was located on the anterior and superior edge of the bladder of 60 by 40mm, which was cystic and solid (density of 30UH) and had peripheral calcifications (Figure 2). Following this, a transurethral resection was performed. In the transurethral resection pathological report, moderately differentiated muscle invasive mucinous AC was reported. Taking into account these findings, an endoscopy, colonoscopy and mammography were performed, but there was no evidence of tumor in the exams. A solid or cystic mass in the midline with calcifications is considered a major finding indicative of urachal AC and so the diagnosis of urachal AC was proposed.

Therapeutic interventions

Mobile solitary tumors that are away from the base may potentially benefit from partial cystectomy, so a partial cystectomy

Figure 1. Lower abdominal CT scan showing superior and anterior bladder mass and cystic lesions with peripheral calcifications.

Figure 2. Partial cystectomy with urachal resection plus omphalectomy. A bladder dome mass of approximately 5cm was resected.

plus extended lymphadenectomy was scheduled (Figure 3). There were no pre-intervention considerations. The patient was placed in dorsal decubitus position and spinal anesthesia plus epidural catheter, with bupivacaine hydrochloride at 0.5%, without adrenaline and without preservatives, was administered without any complications.

The surgical intervention was performed by an experienced surgeon without complications. A bladder dome mass of approximately 5cm was resected. In the partial cystectomy pathology report, an invasion of the proximal third of muscle layer was described. Clear surgical margins were reported, and no positive lymphatic nodules were found. There was no evidence of infiltration in the area corresponding to the remnant of urachus. Immunohistochemical analysis showed the tumor tested positive for Cytokeratin 20 (CK20) and Cytokeratin 7 (CK7) that are distributed in epithelia and their neoplasms. However, the test for carcinoembryonic antigen (CEA), which is a marker of colon carcinoma cells, was negative.

The urachus was tumor-free (Figure 4). However, the bladder layer presented a tumor in its dome without any evidence of secondary AC. Therefore, the final diagnosis was primary bladder AC.

Follow-up and outcomes

The patient was discharged 10 days after the surgical intervention. Cephalixin 500mg three times a day was prescribed for five days after discharge. The Foley catheter was removed 14 days after surgery. No complications and no urinary fistula were

Figure 3. a) Primary adenocarcinoma (AC) and infiltrated muscle layer (M) (blue arrows). **b)** Tumor-free urachus.

reported. No chemotherapy was administered. No signs of recurrence were observed during a CT scan and urethrocystoscopy performed after a follow-up period of one year.

Discussion

Although the bladder is not a common site of metastasis, secondary AC is more frequent than primary AC. Cancer cells can spread by direct extension or by the hematogenous/lymphatic route. During diagnosis, ultrasound is useful as an initial imaging test; however, CT scanning and MRI provide solid information to determine the extent of the disease, rule out metastases and evaluate if it is potentially resectable. In our case report there was evidence in the CT scan that a collection/mass was located on the anterior and superior edge of the bladder; however, it may have been interesting perform an MRI in order to precisely identify any urachal involvement.

A mass in the midline, solid or cystic, with calcifications is considered a major finding indicative of urachal AC. Cystoscopy and transurethral resection of the tumor confirms the diagnosis. Peritoneal carcinomatosis, as well as peritoneal pseudomyxoma, can be a finding in patients with metastatic disease. The analysis of CEA, CA125 and CA19-9 antigen levels should be carried out, which may be elevated in 40%–60% of these patients. The diagnosis of primary bladder AC should be made only after the exclusion of a secondary AC. Therefore, it is necessary to perform colonoscopy, endoscopy, mammography and colposcopy. The histopathological findings are difficult to use to differentiate between the types of AC and immunohistochemistry has limited utility for the differential diagnosis. The diversity of AC means that cytological preparations are a challenge because immunohistochemistry has limited utility.

The low frequency of AC and the absence of large studies explain the absence of clearly established therapeutic guidelines. In primary AC, radical cystectomy and dissection of pelvic lymph nodes are the first option. However, mobile solitary tumors that are away from the base may potentially benefit from partial cystectomy¹. In urachal AC, partial cystectomy is the standard procedure, with block resection of the bladder dome, urachal ligament, and umbilicus^{3,4}. Lymphadenectomy (LD) is necessary when the incidence of lymph node metastasis in AC is high at the time of diagnosis. LD improves survival, time

Figure 4. Timeline of major timepoints in the patient's history, diagnosis and treatment.

before recurrence and staging. Therefore, performing extended LD would be the most appropriate option in these patients⁵.

The role of chemotherapy is not yet clear. However, some cohort studies have shown benefit in high-risk patients (advanced stage, positive margins, positive nodes). This is

based on cisplatin and 5-fluorouracil⁴. The use of radiotherapy is also not clear in bladder AC. Some studies showed better oncological results with positive nodes and recurrence. Despite this, its advantage in terms of oncological results has not been established with adequate studies. It can be recommended for local control only⁶.

Conclusions

1. A patient can present with a tumor with urachal characteristics, however, the pathology report can show primary AC.
2. The decision to perform partial cystectomy was an appropriate option for the location of this tumor, with optimal surgical results. Still, a long-term follow-up is necessary.

3. More specific management guidelines are required for AC.

Data availability

All data underlying the results are available as part of the article and no additional source data are required.

Consent

Written informed consent for publication of their clinical details and clinical images was obtained from the patient.

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Alejandro Carvajal Obando

Universidad CES, Medellín, Colombia

It is an interesting work and an unusual find in that geography. It is valuable in keeping urologists aware of the possibility of such a differential diagnosis.

However, I make several clarifications:

1. The abstract is not clear, it is not understood why the surgical treatment is noted (partial cystectomy) and the full text must be read to understand it
2. During the discussion, they focused little on the pathophysiology and epidemiology of the type of tumor, I think it should be expanded further because they discussed the diagnosis and treatment options.
3. The conclusions of the work should not justify the findings of the case, but rather contextualize the analysis of the case

Is the background of the case's history and progression described in sufficient detail?

Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

Partly

Is the case presented with sufficient detail to be useful for other practitioners?

Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: General Urology, Andrology, MAle Infertility

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 07 August 2020

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Oriana Rivera

Vicerrectorado de Investigación, Universidad Norbert Wiener, Lima, Peru

- The article is well structured and fulfills one of the educational functions.
- The introduction expresses the reason why it is intended to publish, there is a review of the topic and explains the relevance of the topic.
- The case description has important antecedents, the interrogation, the physical examination, the diagnostic support studies, and the results.
- In the discussion, the authors emphasize why the case is remarkable and explains or clarifies the important aspects and compares themselves with other students.

In conclusion, the document is suitable for indexing.

Is the background of the case's history and progression described in sufficient detail?

Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

Yes

Is the case presented with sufficient detail to be useful for other practitioners?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: EPIDEMIOLOGY AND PUBLIC HEALTH

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 06 July 2020

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Marlon Perera

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The authors provide a case report on the management of muscle-invasive adenocarcinoma of the bladder with partial cystectomy. As discussed by the authors, this is not standard or recommended treatment for this disease. This treatment strategy has been well addressed in the literature.

Background:

- Schistosomiasis and chronic bladder irritation are associated with squamous cell carcinoma of the bladder (not adenocarcinoma).

Case report:

- It is unclear the duration of followup. It would be useful to know longer-term oncologic outcomes. Specifically, the authors are advocating for partial cystectomy in T2 adenocarcinoma of the bladder without a clear report of the oncologic outcome.

I'm not entirely sure of the novelty of this case and its' suitability for publication.

Is the background of the case's history and progression described in sufficient detail?

Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

No

Is the case presented with sufficient detail to be useful for other practitioners?

No

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Urology, urooncology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to state that I do not consider it to be of an acceptable scientific standard, for reasons outlined above.

Reviewer Report 21 February 2020

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Orsolya Módos

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This report presents a case of a young woman with adenocarcinoma presented in the bladder. With endoscopic procedures, secondary involvement of the bladder was excluded. Based on imaging findings the presence of urachal carcinoma was supposed, therefore partial cystectomy with extended lymphadenectomy and the removal of the umbilical remnant and the umbilicus was performed. The pathological examination of the tumor found primer bladder adenocarcinoma.

The case report is well written, the train of thought is traceable, but there are some diagnostic tools which could suggest the presence of urachal cancer before open surgical treatment.

Therefore I have some minor point to discuss:

1. Serum tumor markers as CEA, CA-19-9, CA125 and CA-724 can be elevated in urachal cancer.
^{1,2} What was the level of these serum tumor markers before and after partial cystectomy?
2. However, there is no reliable immunohistochemical marker which can distinguish between urachal and primary bladder adenocarcinoma, some of them can suspect the origin of the examined adenocarcinoma. Were immunohistochemical examinations performed of the TURB tumor sample (e.g. AMACR, CK34bE12, GATA3)? This should be mentioned in the manuscript.
3. Histological examination of partial cystectomy resulted primary bladder adenocarcinoma. What was the TNM-stage of this?
4. In the case of primary bladder adenocarcinoma, radical cystectomy is suggested. In this case, urachal cancer was supposed before surgical treatment, therefore partial cystectomy was performed, however the final diagnosis was primary adenocarcinoma. In the future, is radical cystectomy proposed and if so, when?

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Is the background of the case's history and progression described in sufficient detail?

Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Partly

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

Yes

Is the case presented with sufficient detail to be useful for other practitioners?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: urachal cancer, urological cancer

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

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