CASE REPORT

Non-invasive, low-grade papillary urothelial carcinoma in the urachus

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SUMMARY

The urachus is a duct connecting the allantois with the fetal bladder, forming the median umbilical ligament; it usually obliterates during fetal life. Carcinomas arising from urachal remnants are rare but associated with a poor prognosis. We present one case of non-invasive urachal papillary urothelial carcinoma, and through a systematic literature search, we identified 12 additional cases of urachal urothelial carcinoma reported in English literature in the past 20 years. The cases were compared according to the Sheldon Staging System and the Mayo Staging System presented by Ashley *et al* in 2006, and both Staging Systems tend to predict clinical outcome. The urachal carcinoma is an important differential diagnosis in patients presenting with haematuria or an infraumbilical mass, because the symptoms may be sparse and diagnosis at an early stage is essential for successful treatment.

BACKGROUND

The urachus is a duct connecting the allantois to the early fetal bladder. It is a three-layered structure with a luminal layer formed of cuboidal or transitional epithelium, an intermediate submucosal connective tissue layer and an outer smooth muscle layer. As the bladder descends to the pelvis at the fourth and fifth months of normal fetal development, the urachus is progressively stretched and the lumen obliterated. The remaining fibromuscular cord forms the median umbilical ligament.[1] Urachal remnants can give rise to pathology, such as infections or cancer. The most common carcinoma arising from urachal remnants is adenocarcinoma, but urothelial carcinoma, squamous cell carcinoma and neuroendocrine tumours have also been reported.[2 3] Urachal cancers constitute less than 1% of all bladder associated cancers,[2] and of all urachal carcinomas, 5–10% are of urothelial origin.[2–4] Several staging systems for grading urachal cancers are available, with the most used being the Sheldon Staging System [3] and the Mayo Staging System presented by Ashley *et al*[4] (table 1). Usually, urachal cancers are detected late due to sparse symptoms, and urachal carcinoma is associated with a poor prognosis if not diagnosed at an early stage.[5] The symptoms of urachal cancers, if present, are most commonly haematuria, mucosuria or a palpable infraumbilical mass. To our knowledge, non-invasive urachal urothelial carcinoma has not been reported previously.

CASE PRESENTATION

A 49-year-old woman developed a palpable, painless mass near the umbilicus that was resected by a general physician. She had no episodes of gross haematuria or umbilical secretion. Histological examination revealed a cystic process, containing a papillary lesion covered by dysplastic transitional-cell epithelium, suspicious of an urachal cyst (figures 1 and 2). No sign of invasive growth was seen. Immunohistochemical analysis showed a positive reaction with cytokeratin 7, cytokeratin 20 and P63, supportive of the diagnosis of papillary urothelial carcinoma (figures 3 and 4). The patient was then referred to the Department of Urology, Roskilde Hospital.

INVESTIGATIONS

- CT revealed an urachal remnant but an otherwise normal configuration of the urinary tract.
- Cystoscopy revealed a small area on the left side of the bladder, where the epithelium appeared slightly thickened but not obviously suspicious of malignancy.

Table 1 The Urachal Cancer Staging System

Stage	Definition
Defined by Sheldon *et al*	
Stage I	Urachal cancer confined to the urachal mucosa
Stage II	Urachal cancer with invasion confined to the urachus itself
Stage IIIA	Local urachal cancer extension to the bladder
Stage IIIB	Local urachal cancer extension to the abdominal wall
Stage IIIC	Local urachal cancer extension to the peritoneum
Stage IIID	Local urachal cancer extension to the viscera other than bladder
Stage IVA	Metastatic urachal cancer to the lymph node
Stage IVB	Metastatic urachal cancer to the distant sites
Defined by Ashley *et al*	
Stage I	Tumors confined to the urachus and/or bladder
Stage II	Tumors extending beyond the muscular layer of the urachus and/or the bladder
Stage III	Tumors infiltrating the regional lymph nodes
Stage IV	Tumors infiltrating the non-regional lymph nodes or other distant sites

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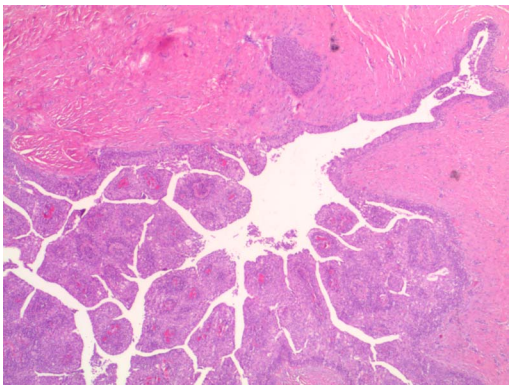

Figure 1 Subcutaneous cyst with papillary tumour—H&E×2.5.

- Urine cytology was normal.
- Gynaecological examination was normal.

DIFFERENTIAL DIAGNOSIS

The most important differential diagnoses for urachal cancer include the following:

- Non-neoplastic urachal remnants (sinus, diverticulum or cyst) with or without infection;
- Tumour in the upper or lower urinary tract;
- Lipoma or atheroma near or below the umbilicus;

Metastatic tumours, for example, from the ovaries.

TREATMENT

The patient underwent a laparoscopic partial cystectomy with en bloc resection of the urachus and umbilicus. The specimen contained mucosal surface, bladder muscle, subcutaneous tissue and skin from the abdominal wall. The bladder urothelium was hyperplastic but not dysplastic. A sinus/cyst extended continuously with the bladder mucosa (figure 5). There was no sign of carcinoma in the bladder mucosa. In the deep intramural tissue of the bladder wall, a small cyst was located; the cyst was lined with a two-layered epithelium, typical for an urachal remnant (figure 6). This cyst contained a papillary lesion of dysplastic urothelium that resembled the papillary lesion in the primarily resected subcutaneous tissue. The surgical margins were negative.

OUTCOME AND FOLLOW-UP

At 6 and 12 months we performed the following:

- CT revealed no sign of recurrence or metastases.

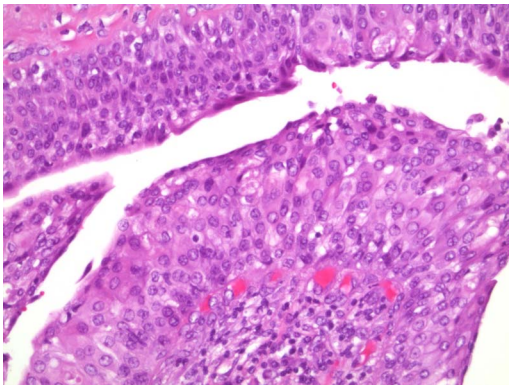

Figure 2 Hyperplastic epithelium with low-grade atypia—H&E×20.

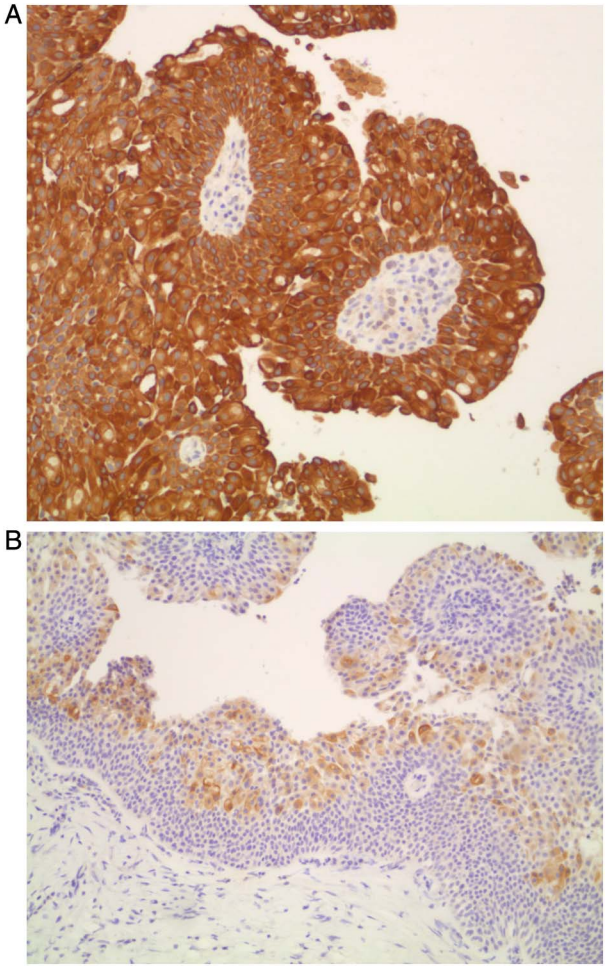

Figure 3 (A) Papillary tumour, positive reaction with cytokeratin 7×10 (brown cytoplasmic reaction). (B) Papillary tumour, positive reaction with cytokeratin 20×10 (superficial cells with brown cytoplasmic reaction).

- Flexible cystoscopy at 6 months was normal, and at 12 months showed a red, thickened and irritated area at the dome of bladder and recurrence was suspected.
- Urine cytology was normal at 6 and 12 months.

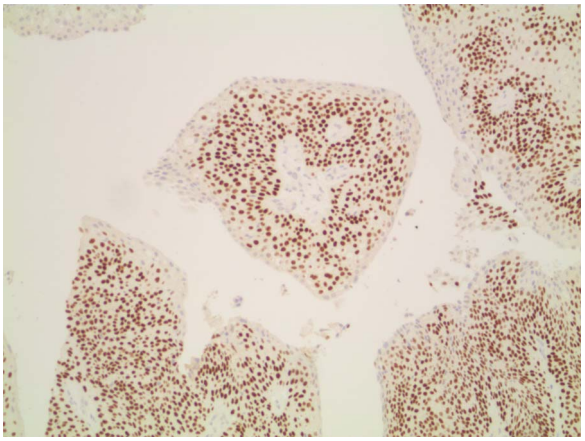

Figure 4 Papillary tumour, positive reaction with P63×10 (brown reaction in nuclei).

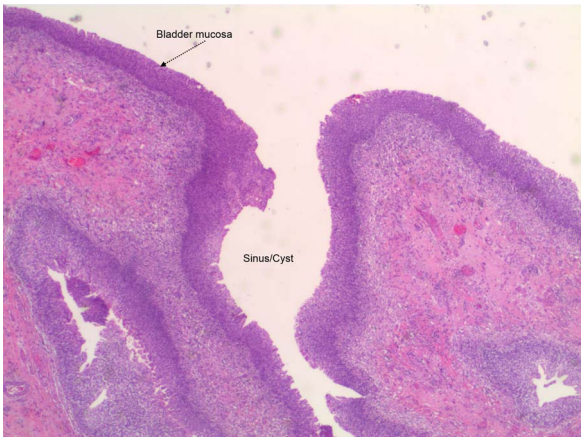

Figure 5 Bladder dome specimen, mucosal surface continuous with sinus.

Bladder biopsies at 12 months showed inflammatory changes and no sign of recurrence of disease.

DISCUSSION

In addition to the case presented, we identified 12 cases of urachal urothelial carcinoma published during the past 20 years in English language literature[2 6–13] (table 2).

There was a male predominance with a male/female ratio of 5.5:1, and the mean age at diagnosis was 52.8 years (range 21–85). Follow-up data were available for 11 cases. The mean follow-up period was 25.5 months (range 3–133). Of these 11 patients, 4had no sign of recurrence and 7 had recurrence of the disease of them 5 died of the disease, in the follow-up period. Of the 11 cases with follow-up data, only 3 were diagnosed at an early stage (I and II) using the Sheldon system; using the Mayo system, 7 of the patients were diagnosed at stages I and II. Of the patients diagnosed at Sheldon stages I and II, 66% had good outcomes, compared with 57% for patients diagnosed at Mayo stages I and II. The patients who were diagnosed at stages III and IV, according to the Sheldon Staging System and the Mayo Staging System had generally poor outcomes, that is, 75% vs 100%, respectively.

Eight patients, our case included, had a partial cystectomy with en bloc resection of the urachus and umbilicus performed. In four patients, total cystoprostatectomy with en bloc resection of the urachus and umbilicus was the treatment of choice. In one case, the surgical procedure was not described. Four of the 13 patients also had pelvic lymph node dissections. In one patient (Ref. 2, 59-year-old man) the tumour was inoperable at the time of diagnosis, and the initial treatment choices were chemotherapy and radiation therapy; when these treatments failed, surgery was performed.

We identified but excluded three other cases reported in Japanese, Chinese and Spanish.[14–16]

Several studies and case reports of urachal carcinoma are published based on the surgical pathology files and the tumour registry of the Mayo Clinic, and some cases of the urachal urothelial carcinoma seems to be subjects to more than one publication.[2 4 5 17] Another problem with collecting and comparing the case reports from the literature is the differences in the diagnostic criteria upon which the diagnosis was based; the former diagnostic criteria were based on urachal adenocarcinoma. Paner *et al* suggested a set of criteria for the pathological confirmation of urachal carcinoma other than adenocarcinoma. For the diagnosis to be confirmed, their system requires 1–3 and one of 4–6 of the following:

1. Located at the bladder dome or anterior wall and/or midline supravesical to the umbilicus.
2. Tumour epicentre away from the bladder surface.
3. No primary tumour of similar morphology elsewhere, except for a urothelial carcinoma in the genitourinary tract.
4. Close relationship with urachal remnant structures.
5. If no remnant urachal structure is identifiable, the tumour does not involve the intact bladder surface.
6. If no remnant urachal structure is identifiable and the tumour involves the bladder surface—for urothelial carcinoma only, a cavitary or cystic tumour with intraluminal papillary structures, or all non-glandular urachal carcinomas, the presence of a reverse invasive front.

Our case fulfils points 1–4 (figures 5 and 6).

Early and correct diagnosis of urachal carcinoma is essential because the prognosis of these cancers seems poor, especially when detected at a late stage.[4 5 18] Follow-up data were available for 11 of 13 patients and of these, 7 (64%) had recurrence of disease of them 5 (45%) died. Even though the number of patients is small, this is in overall concordance with previously reported data. Paner *et al*[2] reported an overall recurrence rate of 47% with a 27% mortality rate in their literature review of urachal urothelial carcinomas. In another series by Ashley *et al*[4], different histological types of urachal carcinoma were pooled together, which resulted in an overall 5-year cancer-specific survival rate of 49%. The most commonly used staging system for all histological types of urachal carcinoma is the Sheldon system, but the Mayo system

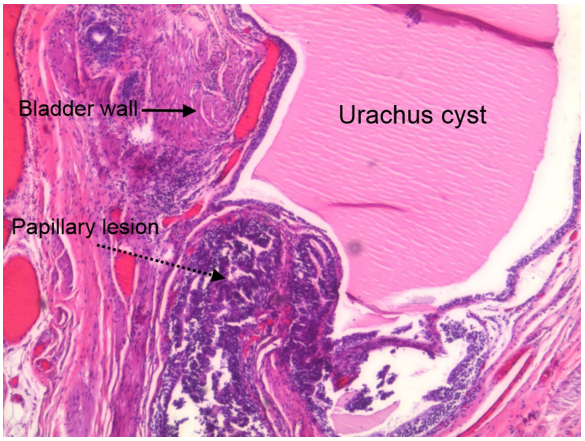

Figure 6 The remnant of urachus cyst with papillary lesion and bladder wall.

Learning points

- Urachal carcinoma is an important differential diagnosis in patients presenting with haematuria or an infraumbilical mass.
- The gold standard of treatment is a partial cystectomy with en bloc resection of the urachal remnants and umbilicus.
- A high tumour stage at diagnosis and positive surgical margin are the most consistent predictors of poor outcome.
- Owing to the high recurrence rate and mortality, we have decided that follow-up procedure after surgery at our institution has to include: CT, flexible cystoscopy and urine cytology every 6 months for at least 5 years.

Table 2 Distribution of cases

Reference	Age	Sex	Sheldon stage	Mayo stage	Treatment	Follow-up	Out-come
Pedersen, 2013	49	F	I	I	pc+en bloc	12 months	Aned
Satake, *et al*[12]	42	M	II	I	pc+en bloc	8 months	Aned
Lin *et al*[8]	50	M	II	I	pc+en bloc	19 months	Dod
Rubin *et al*[11]	21	F	II*	I	cp+en bloc	None	
Maletic *et al*[9]	49	M	IIIa	I	pc+en bloc	12 months	Aned
Paner *et al*[2]	68	M	IIIa	I	cp+pelvic lnd	60 months	Aned
Ichiyanagi *et al*[6]	48	M	IIIa	I	pc+en bloc, at recurrence ct	10 years+13 months	Awd
Nese *et al*[10]	66	M	IIIa	I	pc+rt, at recurrence ct	6 months	Awd
Soni *et al*[13]	33	M	IIIb	II	Resection	None	
Paner *et al*[2]	45	M	IVa	III	cp+pelvic lnd+en bloc+ct, palliative rt	6 months	Dod
Paner *et al*[2]	85	M	IVa	III	pc+pelvic lnd+ct	12 months	Dod
Paner *et al*[2]	59	M	IVb	IV	ct+rt, pc+en bloc+left inguinal mass resection	9 months	Dod
Paner *et al*[2]	72	M	IVb	IV	cp+pelvic lnd	3 months	Dod

*Estimated from informations available.
aned, Alive, no evidence of disease; awd, alive with disease; cp, cystoprostatectomy; ct, chemotherapy; dod, dead of disease; en bloc, en bloc resection of urachus and umbilicus; lnd, lymph node dissection; pc, partial cystectomy; rt, radiation therapy.

has also been used in the resent literature.[9] Both systems seems to predicts cancer-specific mortality equally well.[4] High tumour stage and positive surgical margin are the most consistent predictors of poor outcome of urachal carcinoma of all histological types.[4 19]

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Competing interests None.

Patient consent Obtained.

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