Case study

A Late Presenting Urachal Remnant Tumour: Rare Adenocarcinoma Originated from Developmental Defect

ABSTRACT

Occupying only 0.01% of all adult cancer patients, the rare entity urachal adenocarcinoma constitutes 22-35% of adenocarcinomas originating from urinary bladder. Though with the gradual descend of the bladder in the course of development urachus should turn into median umbilical ligament, exceptional persistence of it can give rise to urachal cyst or urachal adenocarcinoma in adulthood. With only 43% of survival rate for 5 years and mean survival between 12 and 24 months urachal carcinoma is a devastating disease. Diagnosis of it is based on the MD Anderson Cancer Centre (MDACC) criteria. Computed Tomography (CT) Scan and/or Magnetic Resonance Imaging (MRI) Scan of abdomen and pelvis are the major imaging modalities to proceed towards diagnosis and staging. Not only histopathological examination but also immune-histochemical expression of both CK7 and CK20 suffice to clinch the diagnosis. Though surgical intervention forms the mainstay of treatment, several regimens of chemotherapy have also been tried to fight against unresectable, residual, extensive urachal carcinomas.

This case took place in a 52 years old male patient who was presented with a gradually enhancing infra-umbilical swelling with slow growing urinary symptoms. By dint of

Ultrasonography(USG) and Contrast Enhanced CT(CECT) scan of whole abdomen the tumour was detected involving the bladder wall and the anterior abdominal wall. Cystoscopy was followed by upfront cytoreductive surgery. Histopathological examination revealed the diagnosis of an adenocarcinoma which was further confirmed to be an urachal remnant carcinoma with the help of immunohistochemistry. Post-operative CT scan showed residual disease involving bladder wall and was treated with an adjuvant platin based chemotherapy regimen.

INTRODUCTION

Urachal remnant tumour comprising 0.35 to 0.7% of all bladder malignancies is a rare entity [1]. We report a case of urachal adenocarcinoma treated with combined modalities, i.e. surgery followed by adjuvant chemotherapy. As ‘rare diagnosis is rarely right’, this case was even thought to be an adenocarcinoma of colonic origin with clinical and radiological resemblance with urachal remnant tumour. However, in spite of the confusing radiological features of the tumour the diagnosis was finally clinched on the basis of immunohistochemistry and treated accordingly to achieve a relatively prolonged disease free survival (DFS).

CASE REPORT

A 52 years old male patient, hypertensive, euglycaemic with past medical history of pulmonary tuberculosis in 1985, without any significant family history first attended the out patient department on with chief complaints of urinary

urgency and lower backache for last 15 days. While the present history of illness was cultivated, difficulty in micturition for last 6 months and gradually enhancing infra-umbilical swelling for last 5 months came in scene. On investigation, blood parameters including serum urea and serum creatinine were within normal limit. Serum Prostate Specific Antigen (PSA) was 1.03 ng/ml performed in the week of presentation which excluded prostatic pathology too. Ultrasonography of whole abdomen done on the same day revealed a 6.6 cm X 5.8 cm heterogeneous hypoechoic space occupying lesion (SOL) involving the anterior abdominal wall connected to urinary bladder which first evoked the suspicion for urachal remnant tumour. Subsequently, a Contrast Enhanced Computed Tomography (CECT) scan of whole abdomen was done within one week which clearly showed a septate cystic SOL measuring 5.8cm X 4cm in umbilical area attached to urinary bladder wall (Figure 1 & 2).

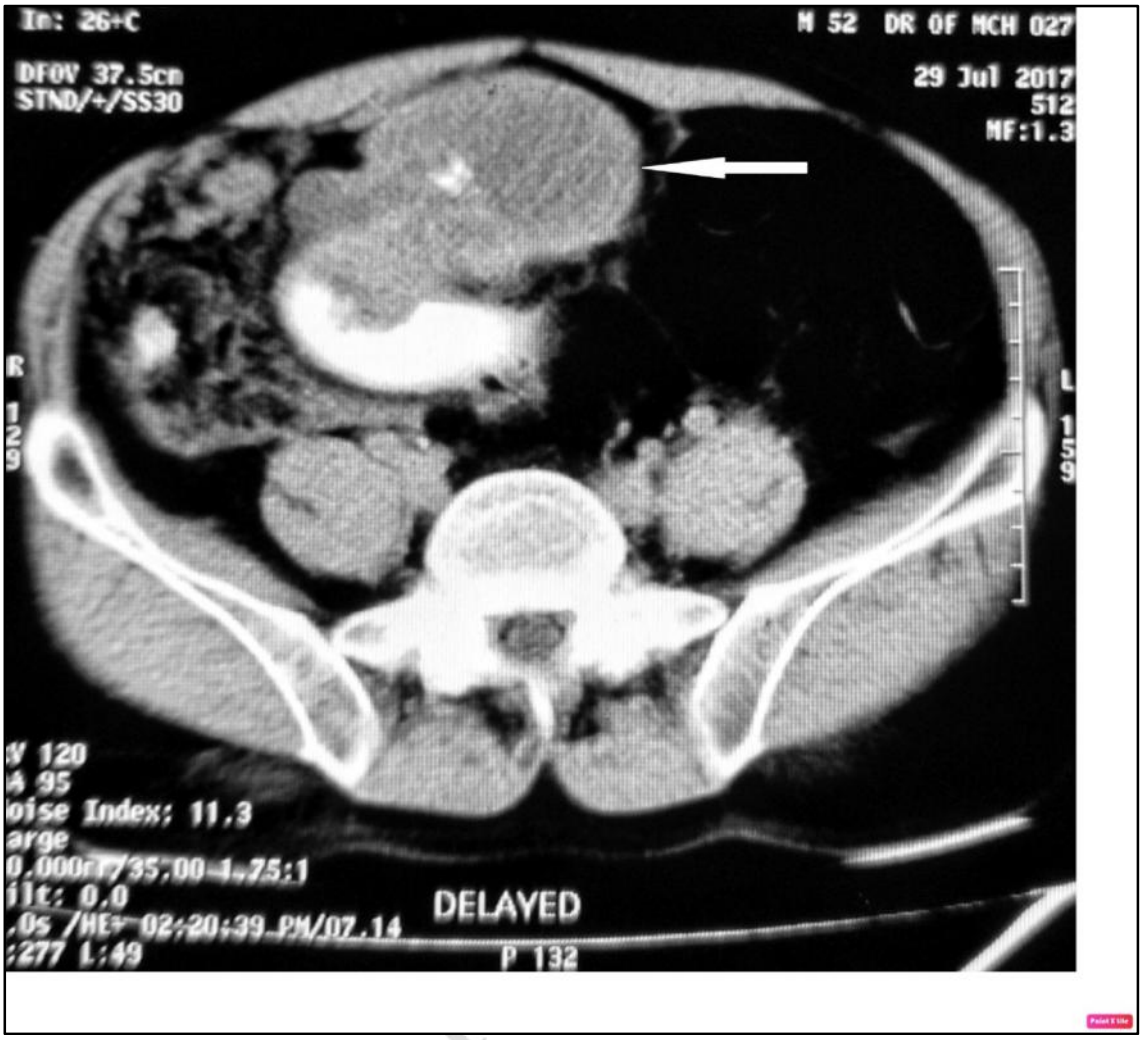

Figure 1: CECT scan shows cystic SOL involving bladder and anterior abdominal wall in axial view

Figure 2: Sagittal view in CECT scan shows SOL originated from bladder is attached to umbilical region of anterior abdominal wall

A colonoscopic report in search of origin revealed a firm extra-luminal mass at lower rectum. On the basis of imaging and symptoms, provisional diagnosis of an adenocarcinoma of colonic origin or a urachal neoplasm was done and patient

was operated within one month of presentation. Procedure was grossly cystoscopy followed by cytoreductive surgery. A cystic mass approaching from the supero-anterior region was found to have adherence and involvement with the wall of the bladder. Wide excision of the urachal cystic mass was done. A few nodular deposits were seen in bilateral paracolic peritoneum (Right>Left) evoking the need for bilateral paracolic peritonectomy. Infra-colic omentectomy was done as there were macroscopic omental deposits as well. It was followed by bladder peritonectomy. Further intraoperative observation revealed deposits in the form of tumour nodules over the small bowel mesentery which were excised and electro-dessicated. No other dissection of pelvic lymph node basin was performed. Finally, 2 layered closure of the bladder defect under general anaesthesia concluded the operative procedure of approximately four hours. Estimated blood loss was 450 ml which was managed by one unit of intraoperative whole blood transfusion. Another unit was transfused next morning. Low urine output and occasional moderate hypotension were the post-operative complication which was managed by adequate parenteral hydration only. The duration of post-operative hospital stay was 5 days. Obtained specimen of hypogastric mass with umbilicus and bladder wall along with omentum and peritoneum was sent for histopathological examination which opined for the existence of a tumour with greatest dimension of 11cm, microscopic examination of which showed mucinous adenocarcinoma of grade III with invasion of the bladder wall [Figure 3,4].

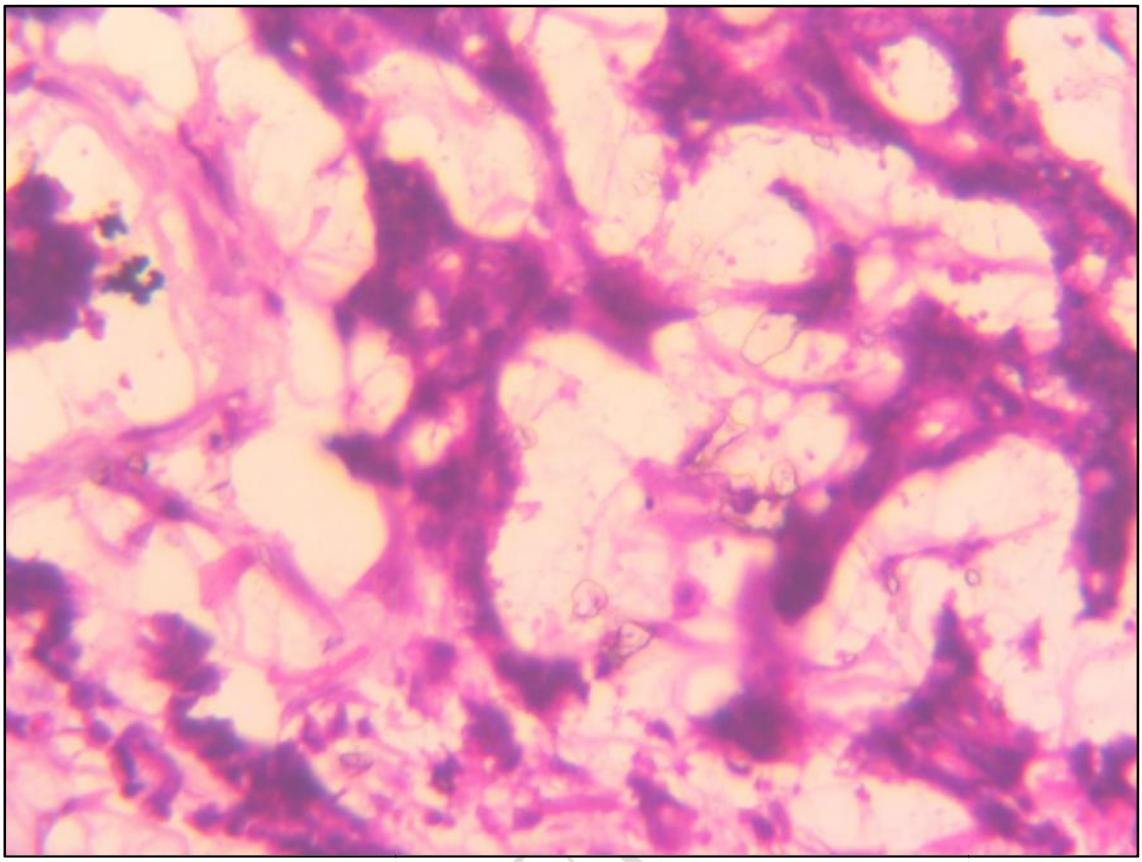

Figure 3: Clusters of malignant cells floating in pools of mucin. Transitional epithelium of urinary bladder is also seen in adjacent areas (low power view ;10x X 10; Haematoxylin and Eosin)

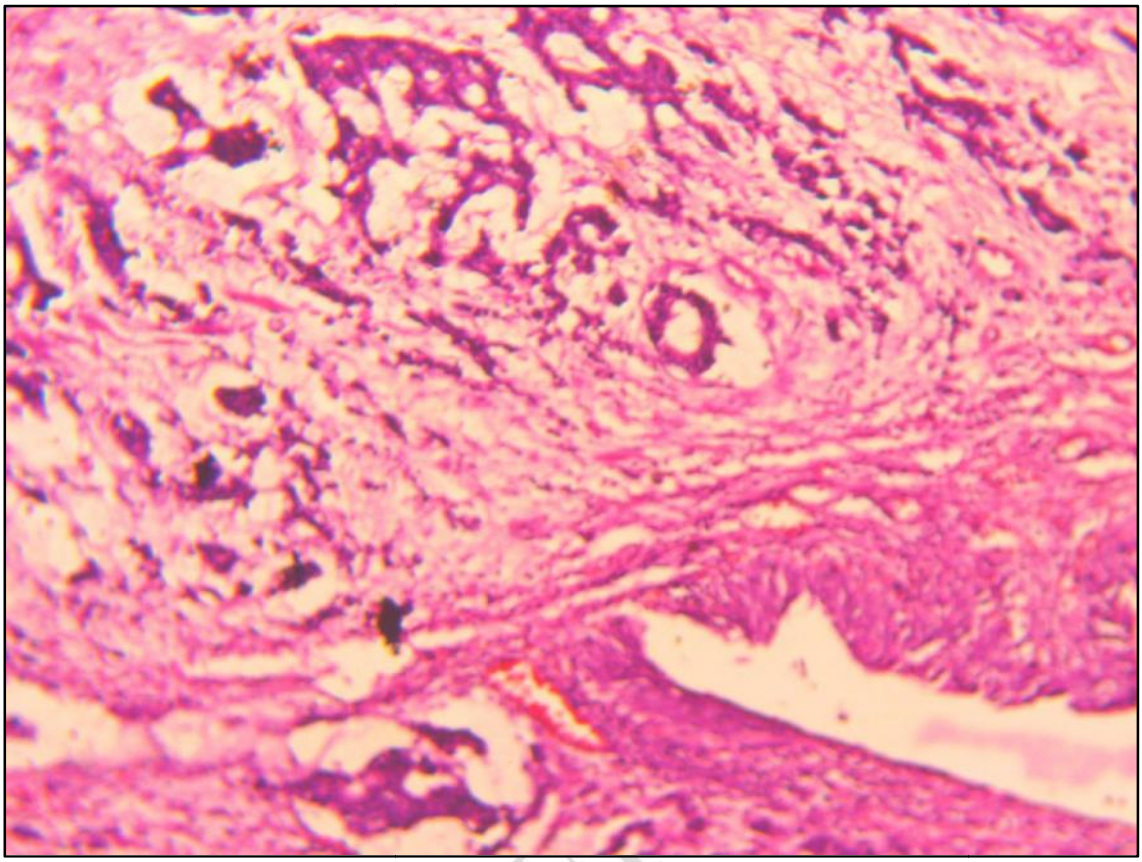

Figure 4: Mucin secreting adenocarcinoma is confirmed (high power view; 40x X 10; Haematoxylin and Eosin)

Though resected margins were negative, tumour deposits were found in right para-colic peritoneum, left para-colic peritoneum, omentum, bladder and pelvic peritoneum and mesenteric nodule obtained from small bowel resection. It established the pathological stage of the tumour to be IIIC. Following immunohistochemistry (IHC) report was positive for both Cytokeratin 7 and Cytokeratin 20. CDX2, CK 5/6 and anti-P63 was negative, which finally clinched the diagnosis of an urachal remnant tumour. Post-operative CECT scan was performed after three weeks following surgery which revealed

focal irregular thickening of urinary bladder pointing towards the residual tumour [Figure 5].

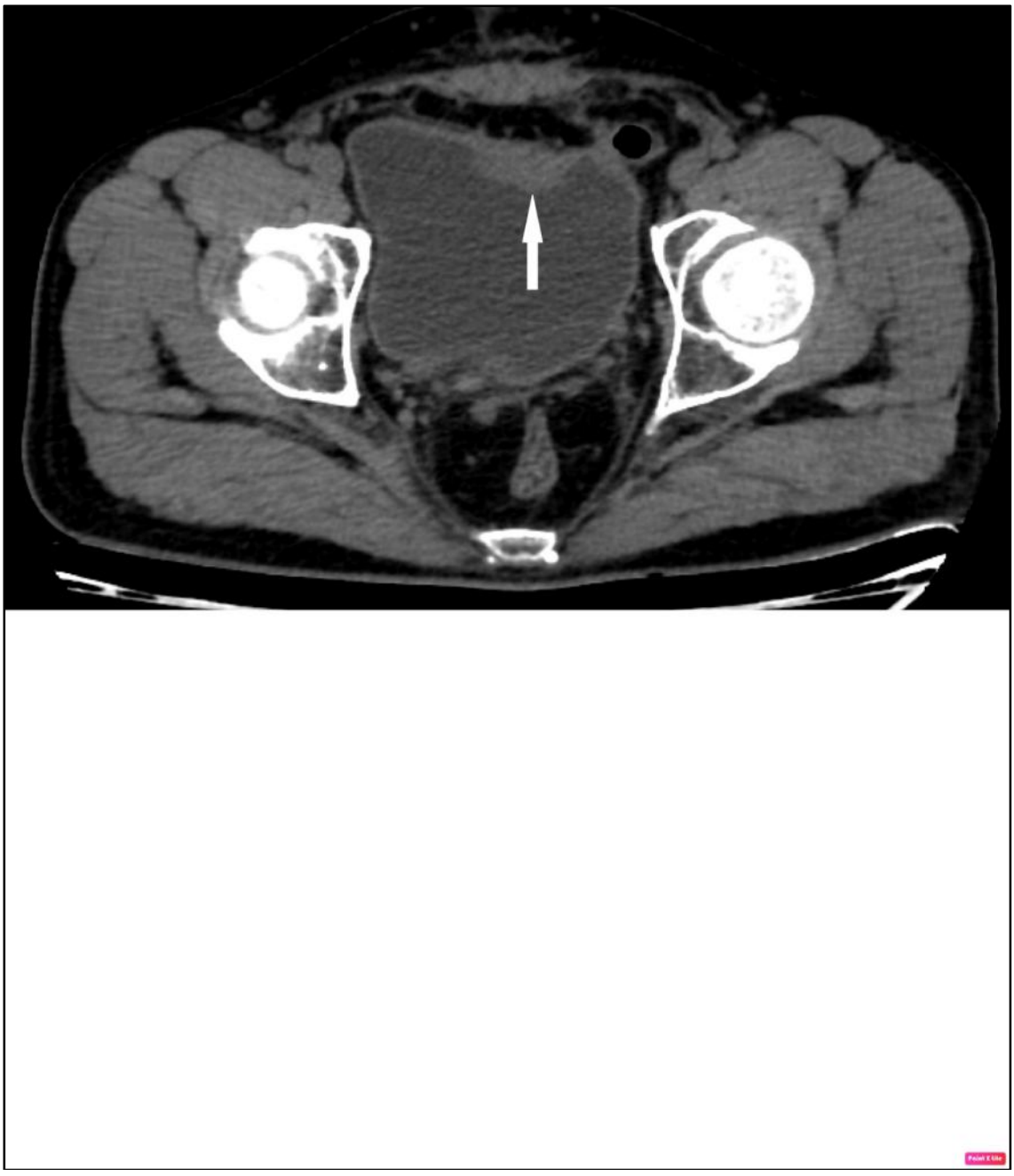

Figure 5: Post-operative CT scan showing residual tumour as irregular thickening of bladder wall

Hence, adjuvant chemotherapy was planned with cisplatin + 5FU regimen and patient received six cycles of the planned chemotherapy. The time elapsed after surgery is about 18 months till the last follow up. Patient was asymptomatic which established the disease free survival to be 11 months following completion of 6th cycle of chemotherapy i.e. the last day of active treatment.

DISCUSSION

Urachal carcinoma is a rare entity as it constitutes 0.35 to 0.7 % of all bladder cancers and 22-35% of adenocarcinomas taking place in bladder[1,2]. This devastating bladder malignancy accounts for an estimated 0.01% of all adult cancers [3].

Urachal cancer first described by Hue and Jacquin in 1863, was reported after translation and summarization by Sheldon [2]. Begg was the first who described the entity extensively in 1931[4].

Located in the space of Retzius, the urachus is a vestigial musculofibrous band of tissue. It is covered anteriorly by the fascia transversalis and posteriorly by the peritoneum [3]. The allantois is connected to the foetal bladder by the urachal canal during early phase of embryonic development [4]. Descend of the bladder takes place into the pelvis during the 4th month of fetal development. It is followed by the stretching of the urachus which turns into the median umbilical ligament, that joins the umbilicus to the dome of the

bladder. If remnants of the allantois remain within the ligament, they may develop themselves into neoplasms. Urachal remnants have been identified in the dome and anterior wall commonly and rarely in the posterior wall of the bladder in one third of cases in post mortem studies.[5]

The urachus has intramucosal, intramuscular and supravesical segments. It contains three distinct tissue layers:1) an epithelial canal lined by urothelium, 2) submucosal connective tissues and 3) an outer layer of smooth muscle. As urachal cyst or neoplasms can originate from any of these layers, it can be either epithelial or mesenchymal[5].

Though adenocarcinomas of the bladder have a relatively higher incidence in women as compared to urothelial carcinomas, urachal carcinomas have been reported at a higher incidence in men [6,7].

Dome-based urachal remnant neoplasms occupies the majority of tumors [8,9]. Urachal remnants have been observed in the midline or vertex in 54% and in the anterior wall in 2% of patients. Schubert, Pavkovic and Bethke-Bedurftig have also demonstrated it the posterior wall in 14% [5].

With mean survival between 12 and 24 months for a locally advanced or metastatic disease, and with a 5-year survival rate of only 43% urachal carcinoma establishes itself as a devastating disease [10,11]. By dint of late presentation of symptoms, early local invasion and propensity for distal metastasis urachal cancer concludes with a poor prognosis[12]. If and when bladder invasion takes place,

irritative voiding, mucous-like discharge, and haematuria like common urologic symptoms are presented [13].

MD Anderson Cancer Centre (MDACC) has fixed the diagnostic criteria for urachal remnant tumour including 2 main and 4 supportive criteria [14]. The main criteria are: 1) midline location of the tumour and 2) a sharp demarcation between the tumour and normal surface epithelium [13]. Supportive criteria include: a) an enteric histology, b) the absence of urothelial dysplasia, c) the absence of cystitis cystica and d) the absence of a primary adenocarcinoma of another origin [11,13].

Though investigation procedure often starts with an ultrasonography (USG) of whole abdomen, standard imaging work up including Computed Tomography (CT) Scan and/or Magnetic Resonance Imaging (MRI) Scan of abdomen and pelvis are the major imaging modalities to proceed towards diagnosis. Heterogeneity and calcification in a soft tissue mass is the general appearance of urachal remnant tumour in USG, while local staging and evaluation of distant metastasis are performed with imaging weapons like CT scan and/or MRI scan. Mixed solid and cystic tumors are demonstrated in 84% of cases of urachal tumour on CT scan [15], others appear solid. The visible cystic component is mucin. CT scan also reveals peripheral calcification, which is another remarkable feature [16].

In 88% of the cases the tumour bulk is seen outside the lumen of the bladder. On MRI, sagittal images are very important as they define the location of the tumour in details . On T2 sequence, focal areas of high intensity signify mucinous component, highly suggestive of adenocarcinoma. Whereas

the solid component is isointense to soft tissue on T1, and shows enhancement with contrast. For confirmation of diagnosis cystoscopy along with cystoscopic biopsy is performed [16]. Primary and secondary adenocarcinomas are differentiated with the help of immunohistochemistry (IHC). IHC positivity for both CK7 and CK20 coins the diagnosis of primary adenocarcinomas of the bladder, while only CK20 is expressed in colonic adenocarcinomas [17].

Three different staging systems of urachal cancer have been proposed, although they are yet to be validated: Sheldon, Mayo, and Ontario staging systems. Sheldon et al [2] proposed a staging system involving localization of the tumour (Table 1).

Table 1
The urachal cancer staging system as defined by Sheldon et al in 1984.

Stage	Definition
Stage I	Urachal cancer confined to urachal mucosa
Stage II	Urachal cancer with invasion confined to urachus itself
Stage IIIA	Local urachal cancer extension to bladder
Stage IIIB	Local urachal cancer extension to abdominal wall
Stage IIIC	Local urachal cancer extension to peritoneum
Stage IIID	Local urachal cancer extension to viscera other than bladder

Stage	Definition
Stage IVA	Metastatic urachal cancer to lymph nodes
Stage IVB	Metastatic urachal cancer to distant sites

The Ontario staging system is yet another simplified classification of urachal tumour involving 4 stages: confined to urachus (T1), confined to bladder (T2), invading surrounding fat (T3), and extending to the peritoneum (T4) [19].

The gold standard surgical approach for the management of localized urachal cancer is an excision of the urachus, umbilicus, and partial cystectomy combined with bilateral pelvic lymphadenectomy. One of the most significant predictors of urachal cancer prognosis is surgical margin status [18].

The choice of regimens has been based largely on case reports and single institution experiences. Tried regimens are depicted in List1[20].

List 1. Chemotherapy regimens tested in urachal cancers

Regimen
S-1+cisplatin ×5 courses
S-1+cisplatin
FOLFOX4

Regimen
Irinotecan
IFL
Cisplatin+paclitaxel+ifosfamide
5-FU+doxorubicin+VP16,doxorubicin+mitomycin-C+cisplatin
Doxorubicin+mitomycin-C+ cisplatin, uracil/ftorafur
5-FU+doxorubicin+mitomycin-C
Methotrexate+5-FU+epirubicin+cisplatin
Ifosphamide+5-FU+VP16+cisplatin
Cisplatin+5-FU
MVAC
Taxol+methotrexate+cisplatin
Gem-FLP

S-1: oral fluoropyrimidine; FOLFOX4: oxaliplatin 85 mg/m2 (D1), leucovorin 200 mg/m2 (D1,2), fluoruracil 400 mg/m2 (D1, D2), fluorouracil 600 mg/m2 CIV over 22 hours (D1,2); IFL: irinotecan 125 mg/m2, 5FU 500mg/m2, leucovorin 20mg/m2, once weekly for 4 to 6 weeks; MVAC: methotrexate, vinblastine, adriamycin, cisplatin; Gem-FLP: gemcitabine, 5FU, leucovorin, cisplatin.

CONCLUSION

Imaging modalities, even histopathological examination may not suffice to distinguish between urachal adenocarcinoma and adenocarcinoma colon, so immunohistochemistry remains as the mandatory tool to determine the diagnosis. Late

presentation of symptoms, early local invasion and propensity for distal metastasis make urachal remnant carcinoma a devastating disease for which surgery may not be adequate always and should be followed by adjuvant chemotherapy to proceed towards a favourable outcome.

CONSENT

All authors declare that written informed consent was obtained from the patient (or other approved parties) for publication of this paper and accompanying images.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCE

1. Reuter V., The urothelial tract: renal pelvis, ureter, urinary bladder and urethra. Lippincott Williams and Wilkins; Philadelphia.
2. Sheldon CA, Clayman RV, Gonzalez R, et al. Malignant urachal lesions. J Urol. 1984;131:1–8.
3. Scabini S., Rimini E., Romairone E., Scordamaglia R., Vallarino L., Giasotto V. Urachal tumour: case report of a poorly understood carcinoma. World J Surg Oncol. 2009;7:82.

4. Begg RC. The Urachus: its Anatomy, Histology and Development. J Anat. 1930;64:170–183.
5. Schubert G.E., Pavkovic M.B., Bethke-Bedurftig B.A. Tubular urachal remnants in adult bladders. J Urol. 1982;127(1):40–42.
6. Johnson DE, Hodge GB, Abdul-Karim FW, et al. Urachal carcinoma. Urology. 1985;26:218–221.
7. Kakizoe T, Matsumoto K, Andoh M, et al. Adenocarcinoma of urachus. Report of 7 cases and review of literature. Urology. 1983;21:360–366.
8. Johnson DE, Hodge GB, Abdul-Karim FW, et al. Urachal carcinoma. Urology. 1985;26:218–221.
9. Mostofi FK, Thomson RV, Dean AL., Jr Mucous adenocarcinoma of the urinary bladder. Cancer. 1955;8:741–758.
10. Molina J.R., Quevedo J.F., Furth A.F., Richardson R.L., Zincke H., Burch P.A. Predictors of survival from urachal cancer: a Mayo Clinic study of 49 cases. Cancer. 2007;110(11):2434–2440.
11. Siefker-Radtke A.O., Gee J., Shen Y., Wen S., Daliani D., Millikan R.E. Multimodality management of urachal carcinoma: the M. D. Anderson Cancer Center experience. J Urol. 2003;169(4):1295–1298.
12. Ashley R.A., Inman B.A., Sebo T.J., Leibovich B.C., Blute M.L., Kwon E.D. Urachal carcinoma: clinicopathologic features and long-term outcomes of an aggressive malignancy. Cancer. 2006;107(4):712–720.
13. Siefker-Radtke A. Urachal carcinoma: surgical and chemotherapeutic options. Expert Rev Anticancer Ther. 2006;6(12):1715–1721.
14. Gopalan A., Sharp D.S., Fine S.W., Tickoo S.K., Herr H.W., Reuter V.E. Urachal carcinoma: a clinicopathologic analysis of 24 cases with outcome correlation. Am J Surg Pathol. 2009;33(5):659–668.
15. Wong-You–Cheong J.J., Woodward P.J., Manning M.A., Sesterhenn I.A. Neoplasms of the urinary bladder: radiologic-pathologic correlation. Radiographics. 2006;26(2):553–580.

16. Ashley R.A., Inman B.A., Sebo T.J., Leibovich B.C., Blute M.L., Kwon E.D. Urachal carcinoma: clinicopathologic features and long-term outcomes of an aggressive malignancy. Cancer. 2006;107(4):712–720.
17. Singh I., Prasad R. Primary urachal mucinous adenocarcinoma of the urinary bladder. J Clin Diagn Res. 2013;7(5):911–913.
18. Pinthus J.H., Haddad R., Trachtenberg J., Holowaty E., Bowler J., Herzenberg A.M. Population based survival data on urachal tumors. J Urol. 2006;175(6):2042–2047. discussion 7
19. Herr H.W., Bochner B.H., Sharp D., Dalbagni G., Reuter V.E. Urachal carcinoma: contemporary surgical outcomes. J Urol. 2007;178(1):74–78. discussion 8.
20. Elser C, Sweet J, Cheran SK, Haider MA, Jewett M, Sridhar SS. A case of metastatic urachal adenocarcinoma treated with several different chemotherapeutic regimens. *Can Urol Assoc J.* 2012;6:E27–31.