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Urachal Carcinoma – A rare entity: Review of Literature

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Abstract

Urachal carcinoma is a rare and highly aggressive tumor that develop in the urachal remnant. Because of its location and its rarity, the diagnosis of UrC is often difficult. Although surgery is the treatment of choice for UrC, with a high incidence of local recurrence and distant metastasis and therefore the treatment of local recurrence and distant metastasis of UrC following surgery has been a challenge. We review the clinical diagnosis and therapy of UrC and factors related to its prognosis.

Keywords: Urachal Carcinoma, Urachus, Surgery, Chemotherapy.

Introduction

Urachal cancers (UrC) are rare and aggressive cancers of the bladder which were originally described by Hue and Jacquin in 1863. They account for only 0.5% of all bladder cancers, and 20% to 40% of primary bladder adenocarcinomas.[1,2,3] The first extensive description of this entity was made by Begg in 1931.[4]

Currently, there is no consensus on the diagnostic criteria for UrC, and thus its diagnosis is a challenge. For the treatment of UrC, surgery is the treatment of choice, including partial cystectomy and radical resection.[3,5,6,7] The role of neoadjuvant or adjuvant chemotherapy in the treatment of UrC has not been confirmed and the standard regimens for chemotherapy are still undecided for these patients.[8] Chemotherapy is used only for patients with unresectable cancer or with metastasis.[9] In the present study we reviewed the literature for analysis of the clinical diagnosis, therapy and prognosis of UrC.

We conducted MEDLINE and PUBMED search of the literature on the Urachal carcinoma, urachus, criteria to define urachus cancer. References of all publication were also searched.

The urachus is the main excretory organ of the fetus located anatomically in a region from the umbilicus to upper bladder, and traversing the endo-abdominal fascia and abdominal membrane in the Retzius crevice. The urachus is present in all children at birth and then gradually degenerates into a single fibrous band connecting the umbilicus to the dome of bladder after birth. It has become a closed epithelial canal in about 30% of adults. It is about 5-6 cm long. The urachal remnant may persist with tubular or cystic structures in approximately one-third of subjects.[6,10] UrC usually develops in the remnant urachus,[6,8] which is found in urachal remnant in about 64% (16/25) of patients and in the non-urachal remnant in about 36% (9/25).[6,8] Thus, the urachal remnant is important for pathological lesions of the urachus.[10]

Different series on UrC has shown that it is more common in males as compared to females.[5-10] The mean age of onset of UrC ranges from 47 to 64 years in different reports and most patients are older than 50 years.[5-10,11,12]

Pathology

The urachus is composed of three layers: an outer muscular layer, middle connective tissue layer and an inner layer usually lined with transitional cell epithelium. Urachal cancer usually is an adenocarcinoma (about 90%) mostly with mucinous/ colloidal histology. The histology can be difficult to distinguish especially from colorectal cancer and primary adenocarcinoma of the urinary bladder. Immunohistochemistry in this situation is of little help with stains for beta-Catenin and Cytokeratin 7 can be helpful. Other rare types include urothelial carcinoma, squamous cell carcinoma, neuroendocrine carcinoma and sarcoma.[3,13,14]

Clinical Presentation

The most frequent initial symptom is hematuria but mucinuria (mucin in the urine), local pain or swelling, recurrent local or urinary tract infections, abdominal lump and umbilical discharge can be seen.[15,16]

Diagnosis

A cystoscopy is essential for the visualization and histological diagnosis of UrC because most lesions are located in the dome and anterior wall of the bladder.[5,6,9] Other adjunctive measures for assessment include computed tomography (CT), ultrasonography (US) and magnetic resonance imaging (MRI), which can guide the selection of therapeutic strategies.[5,6,16] Immunohistochemistry showed the expression of CK20 in 15/24 patients and CK7 and 34BE12 in a smaller proportion of patients.[6] Most patients showed a cytoplasmic membranous staining pattern for b-catenin. Immunostaining did not unequivocally discriminate between an UrC and a colorectal carcinoma, but diffuse positivity for 34BE12 would support a UrC diagnosis, and diffuse nuclear immunoreactivity for b-catenin would militate against. Enteric urachal adenocarcinoma

can have features of colonic cell differentiation with goblet cells and positive staining for acid mucin and CK20, but these features were absent in non-neoplastic urachal epithelial cells.[17]

The MD Anderson Cancer Center (MDACC) criteria helps in the diagnosis of urachal cancers (Table 1).

Table 1: Criteria for diagnosis of Urachal carcinoma

Criteria for diagnosis of Urachal carcinoma
Main criteria: a) Location in the bladder dome or elsewhere in the midline of the bladde. b) Sharp demarcation between tumour and normal surface epithelium.
Supportive criteria: a) Enteric type histology. b) Absence of urothelial dysplasia. c) Absence of cystitis cystica or cystitis glandularis transitioning to tumour. d) Absence of primary adenocarcinoma of another origin.

Staging

Staging is an important factor to choose the treatment modality and to predict clinical outcome. Several staging systems have been developed in UrC.[5,11,18] (Table 2) the most common applied staging system is the Sheldon System.

Table 2: Staging systems

Stage	Sheldon System	Mayo Clinic system	TNM system
Stage I	Confined to urachal mucosa	Confined to urachus and bladder	Invasion of basal membrane
Stage II	Confined to urachus, invasive	Tumor extending beyond urachus or bladder	Bladder invasion 1. Outer muscle layer of bladder 2. Inner bladder muscle and mucosa
Stage III	Local extension to: a) Bladder muscle b) Abdominal wall c) Peritoneum d) Other viscera	Infiltration of regional lymph nodes	Extravesical tumor, bladder fat, abdominal wall
Stage IV	Metastasis to a) Regional lymph nodes b) Distant sites/Peritoneal Carcinoma	Distant lymph nodes or metastasis/Peritoneal Carcinoma	Peritoneal carcinoma

Prognostic factors

Some factors may affect the prognosis of UrC patients, including the status of surgery margin, local lymph node status, tumor grade and clinical stages, metastasis on diagnosis and resected umbilicus, pathological type.[6,11,14,15] TNM stage is a main predictor of UrC outcome after surgery.[11] Nakanishi et al.28 analyzed the relations of DNA status, proliferating cell-nuclear antigen expression and argyrophilic nucleolar-organizer region count to the prognosis of UrC in 14 patients.[19]

Treatment

Surgery

Surgical resection is main strategy for the treatment of UrC,[5,20] Proper surgical resection might require partial cystectomy, radical cysto prostatectomy or cystectomy. Partial cystectomy is a common option and is performed in about 92% of patients with UrC.[5] In a study by Gopalan et al. The incidence of local recurrence was higher in 9/24 patients undergoing a partial cystectomy alone (38%) than in 11/24 patients treated by radical resection (27%).[6] There is no evidence supporting the benefits of lymphadenectomy on the survival of UrC patients.[11]

Chemotherapy

Chemotherapy is administered in case of locally advanced or metastatic UrC. Siefker-Radtke et al. Reported on seven of 42 patients with clinically evident metastasis on admission, with Sheldon staging of stage III UrC in 27 patients (64%) and stage IV UrC in 12%.[20] Although chemotherapy has been proposed as an adjunctive treatment for UrC, no standard and highly effective regimens have been developed and the overall response rate is about 48% .[5,9,16,20,21,22] 5-fluorouracil (5-FU) has been used as a component, but the response rate to 5-FU alone is still poor.[5] First-line regimens for chemotherapy of UrC include gemcitabine and cisplatin (GP), 5-FU and cisplatin (FP), paclitaxel and cisplatin (TP), methotrexate, vinblastine, doxorubicin and cisplatin (MVAC), methotrexate, vinblastine and cisplatin (CMV), etoposide, ifosfamide and cisplatin (VIP).[5,6,20] Second-line regimens include paclitaxel and carboplatin (TC), etoposide and cisplatin (EP), bleomycin, vincristine, mitomycin, and cisplatin

(BOMP), VP-16 and ifosfamide (VI) and paclitaxel.[9] Other regimens consist of 5-FU alone, oxaliplatin, 5-FU and leucovorin, 5-FU plus leucovorin plus irinotecan, ifosfamide plus 5-FU and etoposide plus cisplatin, and irinotecan alone.

Radiotherapy

Radiotherapy is rarely used in the treatment of UrC. For patients receiving radiotherapy as an adjuvant treatment, the median survival time was 19.5 months (range: 4–28.5 months). When radiotherapy in combination with chemotherapy was performed the median survival time was 21 months (range: 6–32.5 months).[5]

Conclusion

Urachal carcinoma is a rare, highly malignant and difficult to treat tumor. Surgery is the treatment of choice. Chemotherapy is given as adjuvant therapy in case of locally advanced and metastatic disease. But no standard regimens have been developed. The prognosis is still poor due to local recurrence and distant metastasis.

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