Urology Updates

Review Article Open Access

Adenocarcinoma of the Urinary Bladder: A Literature Review of a Rare Tumor [Version 1, Awaiting Peer Review]

Mohammed S Al-Marhoon*

Urology Division, Department of Surgery, Sultan Qaboos University, Oman

***Corresponding authors:** Mohammed S Al-Marhoon, Urology Division, Department of Surgery, College of Medicine & Health Sciences, Sultan Qaboos University, P.O. Box 35, Al-Khoud 123, Oman, Tel: (+968) 95208801; Fax: (+968) 24143504; Email: msalmarhoon@gmail.com, mmarhoon@squ.edu.om

Original Submission

Received: November 01, 2016
Accepted: November 12, 2016
Published: November 16, 2016

Open Peer Review Status: Awaiting Peer Review

How to cite this article: Mohammed S Al-Marhoon. Adenocarcinoma of the Urinary Bladder: A Literature Review of a Rare Tumor [Version 1, Awaiting Peer Review]. Urol Updates. (2016) 1: 2.1

Abstract

Adenocarcinoma is an uncommon form of bladder carcinoma. Radical cystectomy remains the only satisfactory treatment option for primary bladder adenocarcinoma. Tumor stage, grade and lymph node involvement are the significant prognostic factors. The aim of this review is to educate treating physicians about this rare entity of bladder cancer.

Keywords

Adenocarcinoma; Urinary; Bladder; Review; Rare; Tumor

Incidence and Risk Factors of Bladder Adenocarcinoma

Adenocarcinoma of the urinary bladder is the third most common histologic type of bladder carcinoma. It accounts for 0.5% to 2.0% of all bladder tumors [1], with urachal carcinoma representing 0.34% to 0.7% [2]. The incidence of bladder adenocarcinoma is higher in patients with bladder exstrophy (90%) [3], and regions where schistosomiasis is endemic (10%) [4]. In addition, adenocarcinoma of the bladder may also occur in association with schistosomiasis, endometriosis, bladder augmentation, and other irritative conditions of the urinary bladder [5].

The prognostic factors for bladder adenocarcinoma outcomes have been reported to including tumor stage, grade, and lymph node metastasis [4]. Recently it has been identified that urachal and dome locations were associated with favorable survival and oncological outcomes, whereas basal location confers poorer outcomes [6].

Classification and Clinical Presentation of Bladder Adenocarcinoma

Adenocarcinoma of the urinary bladder is classified according to its site of origin as primary or secondary. The primary adenocarcinoma arises from the base of the bladder in 60% of cases (non-urachal adenocarcinoma) [7], and from the dome of the bladder in 40% (urachal adenocarcinoma) and 2% are the rare mucinous adenocarcinoma of the bladder [8]. The secondary (metastatic) adenocarcinoma, represents the direct extension of a primary colon, prostate, cervical and ovarian cancer [9]; or metastatis from a remote primary like melanoma, lymphoma, breast, kidney, lung, liver and stomach [10]. Urachal adenocarcinoma has been reported to metastasize to distant organs, including the lung, breast, brain, omentum, liver, bone, and lymph nodes [11]. In most patients, primary adenocarcinoma of the bladder presents with hematuria, which may be associated with irritative voiding symptoms and, occasionally, passage of mucus in the urine [12]. In addition, it shows a male predominance, with the sex ratio of males to females 2.7:1 [5].

Pathology and Diagnosis of Bladder Adenocarcinoma

The differentiation between primary and metastatic adenocarcinoma of the urinary bladder can be difficult, and may require immunohistochemical techniques [13]. Serum PSA can help in differentiating prostatic adenocarcinoma invading the bladder from bladder adenocarcinoma; vimentin can help to identify endometrial adenocarcinoma. For a diagnosis of primary adenocarcinoma of the bladder to be made, it must be distinguished from urothelial carcinoma with areas of glandular metaplasia. The pathogenesis of primary non-urachal adenocarcinoma is based on the ability of the urothelium to undergo metaplastic changes. Mostafi proposed that the metaplastic potential of the urothelium has two distinct patterns [14]. Progressive invagination of hyperplastic epithelial buds into the lamina propria (von Brunn's nests) leading to the formation of cystitis cystica. Subsequently, metaplasia of the urothelial lining of these cysts to columnar mucin-producing cells resulting in the production of cystitis glandularis, which is a premalignant lesion (follow-up is necessary). Alternatively, cuboidal or columnar metaplasia of the surface epithelium may occur with no downward invagination. Chronic vesical irritation and infection are the predisposing factors for these changes. This explains, at least in part, the higher incidence of these tumors among patients with bilharzial cystitis. Histologically, adenocarcinoma may be non–mucin producing or mucin producing. Most of these tumors are mucin secreting and the site of deposition is extracellular (interstitial) [15]. Less commonly, mucin is secreted within the lumen of the acini and, infrequently, excessive intracellular mucin displaces the nucleus to a peripheral crescent, giving the cells a signet ring appearance. It is generally believed that this variety has a poor prognosis [16].

On the basis of histopathologic findings, Anderstrom et al [17]. classified vesical adenocarcinoma into 5 patterns: glandular with columnar, sometimes enteric-appearing, cells; colloid carcinoma; papillary adenocarcinoma; signet ring cell carcinoma; and clear cell carcinoma. Several other histologic subtypes have been described, including mucinous; enteric (colonic); adenocarcinoma not otherwise specified; clear cell; hepatoid; and mixed type [18]. Unfortunately, no clear data have been gathered on whether these different varieties have an impact on survival or indicate prognosis, although signet ring cell carcinoma appears to impart a rapid course, resulting in death in most patients within 6 months of diagnosis [19]. Cystoscopically, the tumor is usually sessile, but it may be papillary. It can arise anywhere along the lateral walls, trigone, dome, and anterior wall of the bladder [19]. Multiple tumors are present approximately 50% of the time [15].

Adenocarcinoma of the bladder is virtually always invasive; only 1 series documented 2 tumors out of 27 that were Ta or T1 [19]. Primary adenocarcinoma of the bladder has a poor prognosis, regardless of the modalities used for treatment. The 5-year survival rates range from 0% to 31%; urachal and dome locations were associated with favorable survival and oncological outcomes, whereas basal location confers poorer outcomes [6].

Based on the morphology the histological growth patterns of bladder adenocarcinoma have been classified by WHO 2004 as: enteric (colonic), mucinous (colloid) [20], signet ring cell, and clear cell adenocarcinoma [21]. However, the WHO 2016 classification of bladder adenocarcinoma is as follows [22]: enteric, mucinous, mixed, and adenocarcinoma not otherwise specified.

Treatment Recommendations for Bladder Adenocarcinoma

Several treatment modalities have been used in the management of primary adenocarcinoma of the bladder including: a) Transurethral resection with or without radiotherapy, Kramer et al. [23] reported a poor 5-year survival rate of 19%; b) Partial cystectomy for localized disease in mobile parts of the bladder, the results attained with this procedure are dismal [24]. On the other hand, Anderstrom et al. [17] reported a 5-year survival rate of 54% among 15 patients treated with partial cystectomy; c) Radiotherapy, adenocarcinoma is not a radioresponsive and the reported 5-year survival is < 20% in patients treated with external irradiation alone [24]; d) Chemotherapy based on 5-fluorouracil, the response is unsatisfactory [25]; and e) Radical cystectomy with or without adjuvant therapy, reported 5-year disease-free survival rates range from 0% to 80% [24]. In a report of 185 cases the 5-year survival after radical cystectomy was 55% and Cox regression analysis proved that stage, grade, and lymph node involvement were all independent prognostic factors [15]. Therefore, based on a comprehensive review of the literature [26], the recommendations for treatment of the different types of adenocarcinoma of the bladder are as follows: Primary adenocarcinoma is poorly responsive to radiation and chemotherapy, and patients should be treated with radical cystectomy. Urachal adenocarcinoma should be treated with en-bloc resection of the urachus and umbilicus with partial cystectomy. The incidence of adenocarcinoma is much higher in patients with exstrophy. Any patient with bladder exstrophy who has retained his or her bladder should be closely followed, although an exact regimen cannot be prescribed on the basis of currently available evidence. Patients with metastatic adenocarcinoma involving the bladder should undergo complete resection of the involved portion of the bladder, with partial cystectomy with verified negative margins or with the use of radical cystectomy.

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