Case Report

Rare Case of Primary Clear Cell Carcinoma of the Urinary Bladder

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Abstract

Cancers of the urinary bladder account for about 3.2% of all cancers worldwide. Clear cell adenocarcinomas (CCAs) of urinary bladder are rare. CCA must be differentiated from benign condition such as nephrogenic adenoma (NA) as well as malignant conditions such as urothelial carcinoma with clear cells, metastasis from ovary and kidney, and urinary bladder myomelanocytic tumor. The diagnosis is based on characteristic histopathological and immunohistochemical features. We present a rare case of CCA of urinary bladder with aggressive clinical behavior in a 72-year-old female.

Keywords: Clear cell carcinoma, immunohistochemistry, urinary bladder

Introduction

Cancers of the urinary bladder account for about 3.2% of all cancers worldwide and are considerably more common in males than in females.[1] Nearly 90% of bladder tumors are transitional cell carcinomas.[1] Clear cell adenocarcinomas (CCAs) of urinary bladder are rare.[1]

However, patients with CCA are typically females with age range from 22 to 83 years and commonly present with hematuria and/or dysuria.[2] CCAs frequently grow as polypoid or papillary mass.

Histopathologically, the differential diagnosis of CCA includes benign tumor such as nephrogenic adenoma (NA) as well as various malignant tumors such as urothelial carcinoma with clear cells, metastatic renal cell carcinoma, and cervical or vaginal CCA.[2]

Case Report

A 72-year-old female was admitted in the surgery ward to investigate for increased frequency of micturition for 3 months. There were no other systemic complaints. Urine routine and microscopy examinations did not show any significant pathology. Blood sugar level was normal. On cystoscopy, a solid mass was seen occupying the bladder base and lateral wall. Computed tomography abdomen and pelvis showed neoplastic growth involving the urinary bladder wall causing obstructive uropathy in the right kidney. Diffuse urinary bladder wall thickening was noted with a maximum thickness of 1.6 cm in the posteroinferior wall of the bladder and bladder base. Transurethral resection of bladder tumor (TURBT) was done along with deep muscle biopsy. Sections studied from TURBT specimen and deep muscle biopsy showed similar histomorphological features. Sections from polypoidal growth [Figure 1a] seem to be composed of cells arranged in tubules, papillae, and tubulocystic areas and at places trabeculae [Figure 1b]. Tumor cells had high nuclear-cytoplasmic ratio and hyperchromatic, pleomorphic nuclei with moderate amount of eosinophilic cytoplasm. Many cells showed clear cytoplasm [Figure 1c]. Abnormal mitotic figures were noted. There were areas of necrosis. The surrounding stroma showed moderate amount of inflammatory cell infiltrate. Lining epithelium surrounding the tumor showed urothelial carcinoma *in situ* [Figure 1d]. Immunohistochemical study was performed. Tumor cells showed immunoreactivity for CEA and CK7 [Figure 2a]. Ki67 labeling index [Figure 2b]

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Table 1: Differential diagnosis of clear cell adenocarcinoma[5]

Histopathological features	NA	Urothelial carcinoma	Metastasis from renal cell carcinoma	Metastasis from CCA ovary	CCA of urinary bladder
Microscopy	Small tubules and cysts that resemble renal tubules	Papillae with thin cores	Nests with vascularity	Solid with cystic areas, sometimes papillae formation	Solid, glandular, tubulocystic, and tubulopapillary
Mitosis	Absent	Variable	Low mitosis	Abnormal mitosis	High mitoses
IHC					
CK7	+	+	-	+	+
CK20	±	+	-	+	±
Vimentin	-	-	+	-	-

NA – Nephrogenic adenoma; IHC – Immunohistochemistry; CCA – Clear cell adenocarcinoma; + – Immunopositivity; - – Immunonegativity; ± – Immunopositivity or immunonegativity

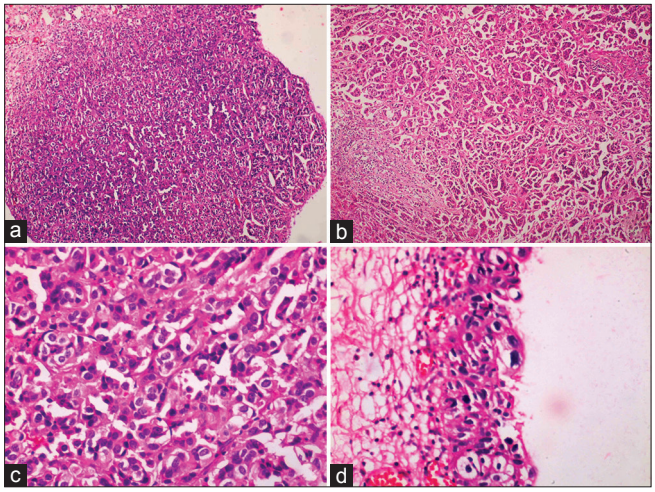

Figure 1: (a) Photomicrograph showing tumors cells in polypoidal growth (H and E, ×100) and (b) photomicrograph showing tumors cells arranged in tubules and micropapillary fashion (H and E, ×100), (c) photomicrograph showing sheets of tumor cells with clear cytoplasm (H and E, ×100), (d) photomicrograph showing urothelial carcinoma *in situ* (H and E, ×100)

and p53 [Figure 2c] immunoreactivity were 90% and 95%, respectively. Tumor cells did not show immunoreactivity for vimentin, HMB45, CK20, and synaptophysin. Based on histomorphology and immunohistochemical studies, a diagnosis of CCA of urinary bladder was made. The patient underwent total cystectomy. Pathological tumor stage was pT2bNxMx. Postoperatively, the patient died after a week due to respiratory complications.

Discussion

CCA of urinary tract is rare, with only sporadic cases reported in literature.[3] Till date, less than fifty cases have been reported.[3] In one study of 38 cases, the authors reported the mean age at presentation as 62.2 years and the median age as 63 years with a female preponderance (22 females vs. 16 males). The most common presenting symptoms were gross hematuria, dysuria, recurrent urinary tract infection, and suprapubic pain.[4] Based on the available data, the most common sites of origin of this tumor type were bladder neck and posterior wall.[4]

CCA must be differentiated from benign conditions such as NA and malignant conditions such as urothelial carcinoma with clear cells, metastasis from ovary and kidney, and urinary bladder myomelanocytic tumor. These differences are summarized in Table 1.[5] In NA, mitoses are absent and p53 and ki67 labeling index is not high.[6] Renal cell carcinoma shows vimentin positivity. In the index case, both ovaries were normal. Clear cell myomelanocytic tumor of urinary bladder consists of nests of clear-to-eosinophilic epithelioid cells with delicate vascular stroma.[7] These are positive for HMB45 and smooth muscle actin, whereas CCAs are negative for these markers.[6] Urothelial carcinoma with clear cells shows papillae with thin cores and absent hobnail cells.

Various theories have been proposed for the origin and histogenesis of CCA of bladder.[2] These tumors were initially thought to arise from mesonephric rests in trigone area and were designated as mesonephric adenocarcinoma.[2] However, convincing evidence for mesonephric origin was lacking.[2] Some authors believe that it arises from Mullerian elements in the bladder and are histogenetically identical to the female genital tract because in some cases, the neoplasms have been associated with vesical endometriosis or have arisen in Mullerian duct cysts or remnants in the bladder.[4] This also explains the female preponderance in CCA.[4] However, a recent study presented evidence for urothelial origin in most clear cell carcinomas.[8] Few authors believe CCA as a morphologic expression of urothelial carcinoma with glandular differentiation.[2] In a study conducted by Oliva *et al*., nine of 13 CCA tumors either had minor foci of conventional urothelial carcinoma or foci resembling neoplastic urothelial cells.[2] The urothelial carcinoma *in situ* was present in our case. The tumor was seen arising from it. Intestinal metaplasia or Mullerian components were not seen. Our case supports the urothelial origin of CCA. Once diagnosis is established, radical surgery is recommended. The role of radiotherapy and chemotherapy is also documented in literature.

Conclusion

CCA of the urinary bladder is rare. The diagnosis is based on characteristic histological and immunohistochemical features. A thorough radiological assessment is required to exclude primary tumor elsewhere.

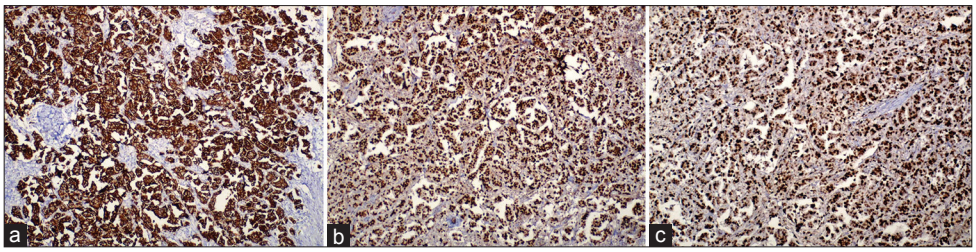

Figure 2: (a) Photomicrograph showing CK7 immunoreactivity (×100), (b) photomicrograph showing Ki67 expression (×100), (c) photomicrograph showing p53 immunoreactivity (×100)

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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