Central European Journal of Urology

CASE REPORT

UROLOGICAL ONCOLOGY

Partial cystectomy in a 76 year old patient suffering from small cell carcinoma of the urinary bladder

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Article history
Submitted: Nov. 7, 2012
Accepted: Feb. 5, 2013

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Small cell carcinomas of the urinary bladder originating from the neuroendocrine cells are extremely rare. We present a case of a 76–year–old patient with small cell carcinoma of the urinary bladder. The patient had hematuria and cystoscopy revealed a tumor located in a urinary bladder diverticulum. Partial resection of the bladder wall with diverticulectomy was performed. Microscopic examination established the diagnosis of neuroendocrine carcinoma, which was confirmed by immunohistochemistry. Three–month follow–up showed no recurrent disease. Patient refused further chemotherapy and radiotherapy.

Key Words: small cell carcinoma ‹› urinary bladder

INTRODUCTION

Tumors of the urinary bladder originating from the neuroendocrine cells are extremely rare. Small cell carcinomas (SCC) are the most frequent subtype among them and account for approximately 0.5–1% of all primary neoplasms of the urinary bladder [1]. Pure SCC of the bladder is known to be of high metastatic potential with lymph nodes, viscera, and vertebral bones being the most common sites of secondary deposits [1]. Painless gross hematuria is the most common clinical manifestation of the tumor. Diagnosis of the disease in most cases is based on transurethral resection of the bladder tumor (TURBT). Prognosis of the disease remains poor as the majority of cases present with advanced disease. The overall survival rate at five years in advanced stages does not exceed 8%. SCC of the urinary bladder can be treated with local resection of the tumor or radical cystectomy with neoadjuvant or adjuvant chemotherapy [2]. Radiation therapy is used as an alternative to radical cystectomy or as a palliative measure.

CASE REPORT

A 76–year–old male was admitted to Department of Urology and Urological Oncology of Medical University of Lublin in September 2010. He presented to the Department of Urology two weeks earlier with gross hematuria and lower abdominal pain. He had a history of Å tumor of the urinary bladder in August 2010, which was removed by transurethral electroresection. Microscopic examination diagnosed the tumor as moderately differentiated transitional cell carcinoma (no written data available). Cystoscopy done at the time of admission showed a diverticulum and a papillary tumor, both located within the posterior wall. The tumor was biopsied. CT scan was performed and did not show any other lesion within the patient's chest, abdomen, or pelvis. Blood and biochemical tests were unremarkable. As the patient

DOI: 10.5173/ceju.2013.02.art12

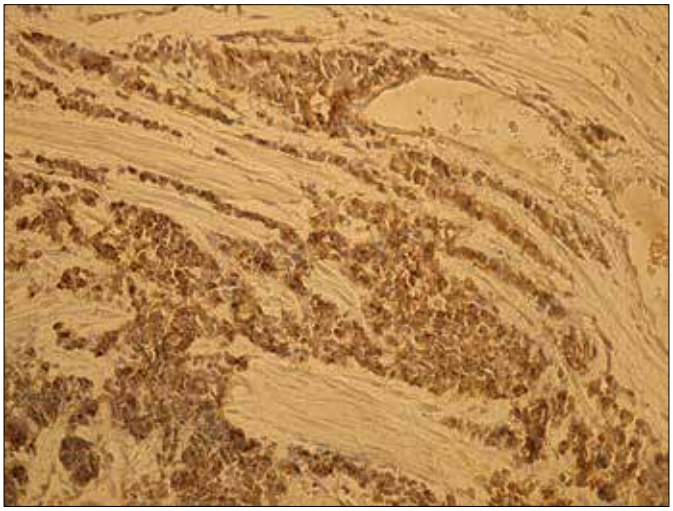

Figure 1. *Immunohistochemical expression of chromogranin in tumor cells (magnification 200x).*

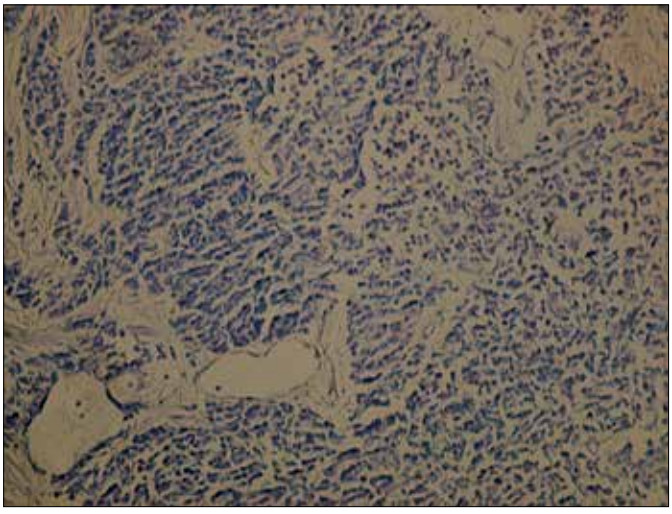

Figure 2. *Negative immunostaining for cytokeratin in tumor cells (magnification 200x).*

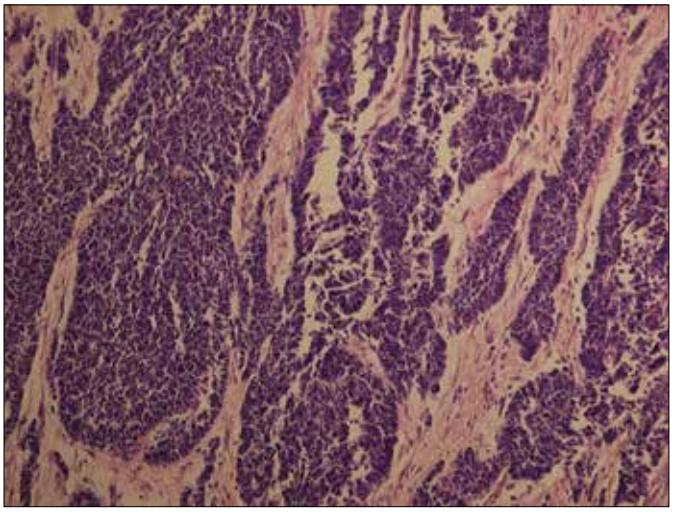

Figure 3. *Nests of small cell carcinoma infiltrating the bladder wall (H+E staining, magnification 200x).*

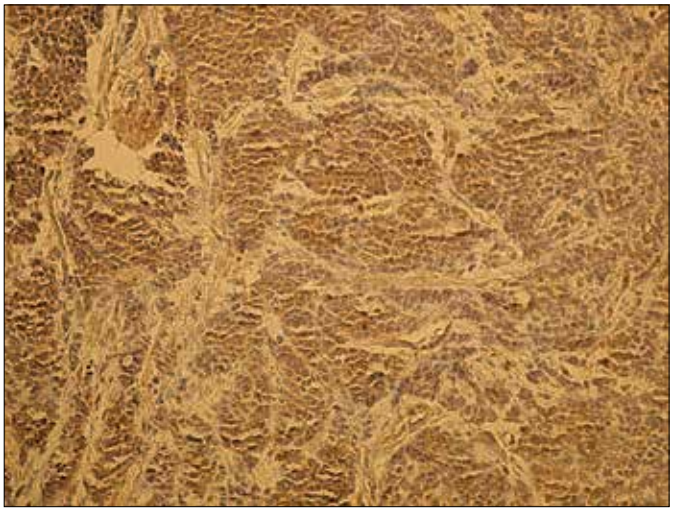

Figure 4. *Immunohistochemical expression of neuron specific enolase (NSE) in tumor cells (magnification 200x).*

did not agree for total cystectomy, we performed a partial resection of the bladder wall with removal of the tumor and diverticulum. The surgical specimen was fixed in 10% buffered formalin and sent to the Department of Clinical Pathomorphology for microscopic examination. Microscopy showed an ulcerated tumor composed of sheets and nests of mildly pleomorphic, small and mid–sized cells with scanty cytoplasm and dark hyperchromatic nuclei. Multifocal invasion of the bladder wall was observed with lymphovascular space involvement. Immunohistochemistry was performed and showed these neoplastic cells to be positive for cytokeratin, chromogranin, synaptophysin, and NSE and negative for vimentin. Scattered mitotic figures were observed and immunohistochemical staining for Ki 67, a marker of cell proliferation, was noticed to be positive in 33% of tumor cells. Microscopic appearance and immunoprofile were consistent with diagnosis of primary neuroendocrine SCC of the bladder. The patient was referred for further treatment in Department of Oncology. He did not agree to the suggested treatment in the form of adjuvant chemo– and radiotherapy. The cystoscopy carried out three months after surgery did not show any gross lesion within the bladder wall.

DISCUSSION

SCC of the urinary bladder is a rare tumor, but the bladder remains the most frequent location for non–pulmonary SCC of the urinary tract [3]. The clinical manifestation is very similar to other bladder

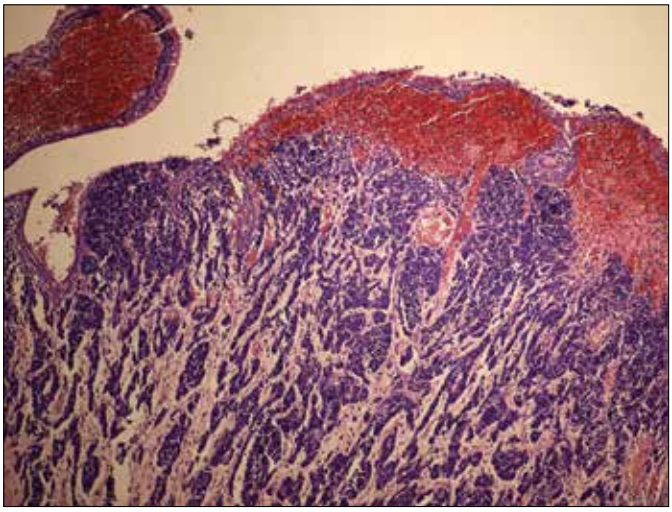

Figure 5. *Mucosa of the bladder infiltrated by nests of small cell carcinoma (H+E staining, magnification 100x).*

tumors with painless gross hematuria and dysuria being the most frequent signs of the disease. The tumor can also be found during abdominal ultrasound examination. The estimated incidence of SCC is 0.5–1% of all bladder tumors, with a male to female ratio of 6:1 [4, 5]. Macroscopically they are usually 4–10 cm in size and polyp–shaped with ulceration in some cases [5,6]. All these features were present in our case. Gross examination reveals a solid tumor mass that originates from the mucosa and often penetrates deeply into the bladder wall [1, 2, 7]. Histologically, in 68% of cases, SCC coexists with classic urothelial carcinomas or adenocarcinomas of the bladder. Microscopic examination reveals a tumor composed of sheets and nests of loosely cohesive, small, round, or oval cells with very scanty cytoplasm. The tumor cell nuclei are hyperchromatic with coarsely granular chromatin. Nuclear molding can be seen. Mitotic figures are present and may be frequent. Nucleoli are absent or small. Tumor necrosis is often present [1, 9]. Urinary cytology often shows single and loosely cohesive clusters of tumor cells with typical SCC morphology. Neuroendocrine markers, such as chromogranin A, synaptophysin, CD56, and neuron specific enolase (NSE), are often focally or diffusely positive for these tumors by immunohistochemical methods, and they are useful tools that aid in establishing the diagnosis [4, 7, 8]. A cocktail of cytokeratin (CK) markers is often nonreactive, but low molecular cytokeratin, CAM5–2, and epithelial membrane antigen (EMA) are mostly positive [4, 7, 8].

Prognosis of SCC remains poor due to very aggressive behavior with up to 25% of patients presenting metastatic disease at the time of diagnosis and absence of symptoms at the beginning of disease. The overall survival rate for all stages at five years is variable and ranges from 8% to 40% [10]. Treatment outcome of SCC of the urinary bladder is relatively better than for small cell lung carcinoma because the tumor volume at the time of diagnosis is smaller in urinary bladder than in lung [11]. Neoadjuvant chemotherapy followed by partial resection or radical cystectomy constitutes the main treatment option [12]. It is advised to use chemotherapy regimens active in small cell lung carcinoma, with the cisplatin–based regimen being the most important. It has been shown that patients who received preoperative chemotherapy in a regimen directed towards small cell carcinoma had significantly increased 5–year disease free survival, compared to patients receiving classical chemotherapy directed towards urothelial cancer (M–VAC regimen) [13]. Radiation therapy can be used as an alternative to radical cystectomy or as a palliative measure [14]. In our case we performed diverticulectomy to preserve the patient's urinary bladder since he refused to undergo radical cystectomy. Although the patient did not agree to be subjected to adjuvant chemotherapy or radiation therapy, a diagnostic cystoscopy performed three months postoperatively showed a normal mucosa without recurrence.

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