

Small Cell Carcinoma of the Bladder-A Case Report and Literature Review

Arun Lakshmpathy, MD;¹ Istvan Wollak, MD;¹ William R. Friedenber, MD²

Abstract

Primary small cell carcinoma of the bladder is rare. The incidence varies between 0.5-1% of all primary bladder tumors. Fifty percent of small cell carcinomas of the bladder are mixed with other tumors of the bladder. Identifying small cell carcinoma of the bladder has both therapeutic and prognostic implications. They are much more aggressive than transitional cell carcinoma of the bladder and are biologically similar to small cell carcinoma of the lung.

Case Report

A sixty year old man with a history of heavy smoking (60 pack years) and significant alcohol use (admitted 40-50 cans of beer/week) presented to the emergency room with gross hematuria and severe anemia. He had noticed intermittent hematuria with occasional clots and cramping for two months before presenting to the hospital. His past medical history was significant for chronic alcoholism, tobacco abuse, hypertension, seizures, cerebral and cerebellar infarcts. He had a family history positive for lymphoma in his father. He had been hospitalized a month earlier and was treated for left lower lobe lung abscess which had completely resolved on subsequent radiographs. During that hospitalization he had an extensive work up including CT of the chest and bronchoscopy which were negative for malignancy but his urinalysis, performed in the ER after insertion of a foley catheter, and which showed 25-50 RBC/HPF, was not further evaluated on that admission.

Physical exam was unremarkable except for soft systolic cardiac murmur and lower extremity edema. His hemoglobin was 4.1 g/dl. Urine analysis confirmed hematuria. A CT of the abdomen and pelvis showed an extensive (7 x 3 x 7.5 cm) heterogenous mass in the bladder along the left lateral wall. (Figure 1) No hydronephrosis or significant lymphadenopathy was noted. CT of the chest showed further resolution of the previously mentioned lung abscess and there was no evidence of malignancy or lymphadenopathy. After bladder irrigation and correcting the anemia the patient was discharged with a follow-up visit

scheduled for cystoscopy. A few days later the patient was readmitted with recurrent hematuria and cystoscopy at that time showed large sessile, friable, and highly vascular mass on the left lateral wall of the bladder just lateral to the left ureteral orifice. Biopsy was not performed, as the mass was highly vascular with significant risk for bleeding. Due to the size and vascularity of the tumor the urologist felt that transurethral removal of the mass was not feasible. Subsequently the patient underwent a cystoprostatectomy with ileal conduit. A large bladder tumor was found in the lateral wall of the bladder with no gross lymph node involvement. Intra-abdominal exploration did not reveal any obvious metastasis.

Histopathology showed grade III/III (small cell and transitional cell) carcinoma with the majority being small cell carcinoma. (Figure 2) Immunoreaction was positive for chromogranin and synaptophysin.

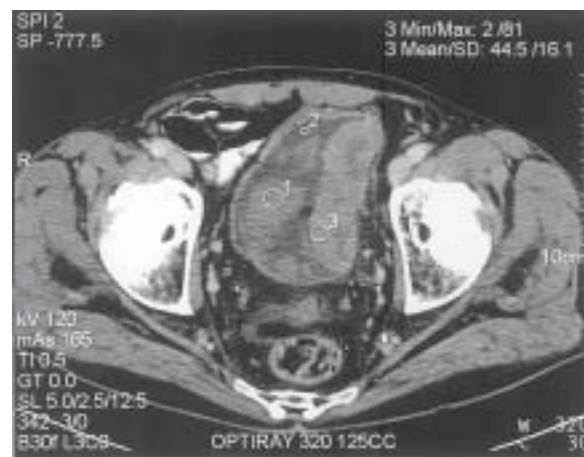


Figure 1.
Computed tomography of abdomen and pelvis showing extensive heterogeneous mass in bladder.

¹ Resident, Internal Medicine, Robert Packer Hospital, Sayre PA 18840

² Chief, hematology/Oncology, Robert Packer hospital and Guthrie Clinic, Sayre PA 18840

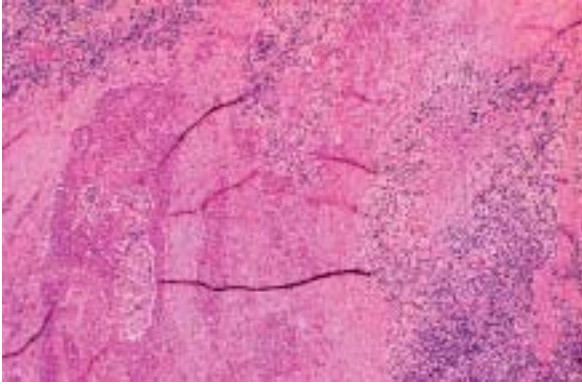


Figure 2.
H and E stain showing Urothelial carcinoma on left
and small-cell carcinoma on right (X100).

There were also areas of transitional cell carcinoma which were multifocal. The majority of the specimen showed small cell carcinoma. Interestingly no classic papillary carcinoma was seen. The tumor was deeply invasive (0.3mm) with perineural and vascular invasion. The prostate showed evidence of adenocarcinoma in both the lobes. No tumor was noted in the pelvic lymph nodes.

Discussion

Transitional cell carcinoma, squamous cell carcinoma and adenocarcinoma are the three most common primary bladder tumors. Urachal and metastatic adenocarcinoma are less common. Small cell carcinoma and mixed small cell carcinoma (small cell carcinoma can occur with transitional cell carcinoma, squamous cell carcinoma or adenocarcinoma, spindle cell carcinoma, and atypical carcinoid tumor) account for around 0.48-1% of all bladder cancers.^{1,2,3,4} Primary small cell carcinoma has to be excluded as it can rarely metastasize to the bladder. Patients usually present with gross hematuria. Clinical suspicion of small cell histology should be high when the tumor is very aggressive and has early metastasis.

Some patients have positive urine cytology with small round cells with naked hyperchromatic nuclei and fine granular chromatin.⁵ Diagnosis is established when the histopathology specimen shows small round cells with hyperchromatic nuclei and the immunoreaction confirms the diagnosis. The stains used are chromogranin and

synaptophysin, which are specific for cells of neuroendocrine origin. The other immunoreaction tests done are CD44V6, cytokeratin, neuron specific enolase, Leu 7, VIP, bombesin and serotonin.^{1,6,7,8} Electron microscopy will show dense core membrane bound intracytoplasmic granules, but it usually is not necessary for diagnosis.

Chromosomal imbalances noted are deletion at 10q, 4q, 5q, 13q, gains of DNA sequences at 8q, 5p, 6p, 20q and high level amplifications 1p22-32, 3q26.3, 8q24 and 12q14-21. The analysis of these findings suggests that small cell carcinoma can develop from transitional cell carcinoma by acquiring additional genetic alterations.⁹

Treatment of small cell carcinoma is different from transitional cell carcinoma as the tumor itself is much more aggressive. Most patients reported so far have undergone radical cystectomy except certain patients with early stage cancer.¹⁰ Some small studies and case reports have suggested survival benefit with the use of combination chemotherapy, but larger studies are necessary to further evaluate their benefit.^{3,4,5,11} There was apparent benefit to the use of integrated chemoradiation in patients with limited stage small cell carcinoma of the bladder on long term outcome.³ The most commonly used regimens contain cisdiaminedichloroplatin (CDDP), etoposide, doxorubicin, vincristine, or vinblastine.^{3,4,12,13,14} There are case reports showing apparent cure of small cell carcinoma with combination chemotherapy with a 6 month follow up.^{14,15,16} Metastatic disease has poor outcome irrespective of the treatment protocol.¹⁷

Prognosis of small cell carcinoma of the bladder is worse than transitional cell carcinoma but better than small cell carcinoma of the lung.¹⁶ There are around 140 cases reported so far and a very few who presented at an early stage were cured with chemotherapy. Generally patients undergo radical cystectomy with adjuvant chemotherapy. In one study (18 patients), 78% of the patients died at a mean follow up period of 9.4 months and only one patient survived at the end of 5 years.¹ But integrated chemoradiation in patients with limited stage disease have shown much better survival. The five-year survival reported varies from less than 10% to around 44%.¹⁶

Conclusion

Small cell carcinoma of the bladder is rare but important to identify as chemotherapy is indicated in most of these patients and there is a significant prognostic difference compared to transitional cell carcinoma. Chemotherapy may cure the cancer in early stages. Radical cystectomy along with chemoradiation may prolong survival compared to just cystectomy. Prognosis is worse compared to transitional cell carcinoma but better than small cell carcinoma of the lung. Primary small cell carcinoma of the lung has to be ruled in these patients.

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