

# Primary Small Cell Carcinoma Of The Bladder: A Case Report And Review Of The Literature

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## Abstract

Primary small cell carcinoma of the bladder (SCCB) is a rare disease entity. Despite its aggressive course, there is not a consensus on the optimal therapy for this process. We present a case of locally advanced SCCB managed with chemoradiation and provide a review of the contemporary literature. A 90-year-old woman with gross hematuria was found to have a large, locally invasive bladder tumor on radiographic studies. SCCB was confirmed histologically from the transurethral resection specimen. The patient's comorbidities made her unfit for radical surgery along with intolerance to chemotherapy. The patient is pursuing palliative radiation for her symptom.

## INTRODUCTION

Small cell carcinoma (SCC) accounts for 20-30% of the diagnosis of lung cancer. This histology is not only limited to the lung; extrapulmonary sites such as gastrointestinal and genital urinary tracts are usually associated with an aggressive clinical course. Primary small cell carcinoma of the bladder (SCCB) is a rare entity accounting for less than 1% of all bladder tumors [1]. Since the first published case in 1981, this disease process is only described in small series and case reports [2]. Its origin is still unknown currently; several theories such as malignant transformation of neuroendocrine cells or metaplastic transformation of other high-grade malignancies are being debated [3]. Regardless of its unproven pathogenesis, extrapulmonary SCC is associated with an aggressive course with early metastasis and high disease-specific mortality. Due to its rarity, there is not a consensus on the optimal therapy for this aggressive disease. We report a case of invasive primary SCCB being managed with non-operative therapy.

## CASE REPORT

A 90-year-old woman with multiple comorbidities was admitted to our hospital for congestive heart failure exacerbation and gross hematuria. The patient's performance status was two to three. Radiographic workup with computed tomography (CT) and pelvic ultrasound showed a large tumor arising from the lateral wall of the bladder [Figure 1]. The mass appeared echogenic with increased vascularity. The largest diameter measured approximately

seven cm. The tumor appeared locally invasive without any evidence of hydronephrosis, lymphadenopathy or abdominal metastasis. Cystoscopic evaluation showed a large friable tumor on the left, superior bladder wall with active bleeding. Biopsy of the tumor was performed, and the bleeding was controlled. Pathological examination of the specimen revealed: atypical cells with irregular nuclei and high nuclei to cytoplasm ratio on medical cytology [Figure 2], malignant cells with epithelial origin on immunocytology [Figure 3], and morphologically small cells with minimal cytoplasm and hyperchromatic nuclei on hematoxylin and eosin staining [Figure 4]. The morphology and immunophenotype of the specimen are consistent with small cell carcinoma. A complete metastatic workup was performed: CT of the brain and chest were negative for additional disease. Due to her comorbidities and performance status, the patient was not an optimal candidate for radical cystectomy with pelvic exenteration. The patient was started on an abbreviated chemotherapy regimen consisted of oral etoposide at 50 mg once a day. After one week of therapy, etoposide was stopped due to a significant decrease of white blood cell count. Patient is alive with persistent gross hematuria, four months after diagnosis. We are pursuing palliation for her symptomatic disease.

Figure 1

Figure 1: Ultrasound of the bladder showed an irregular, echogenic mass with increased arterial and venous flow.

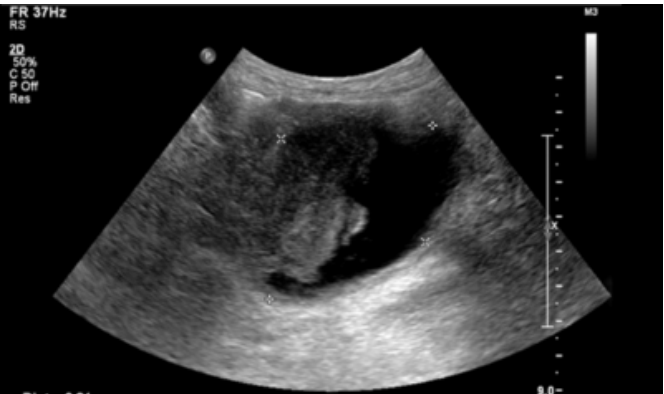


Figure 2

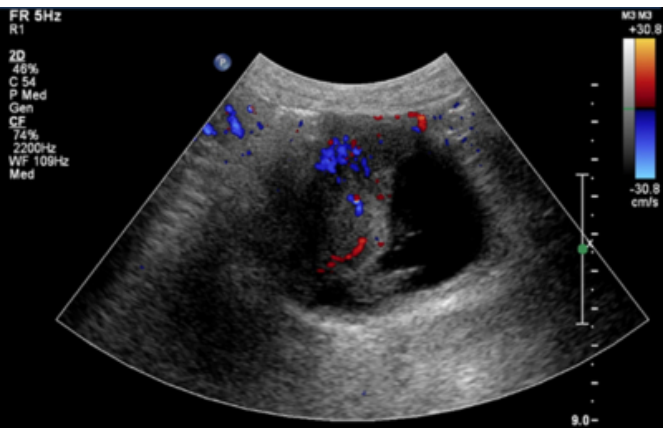
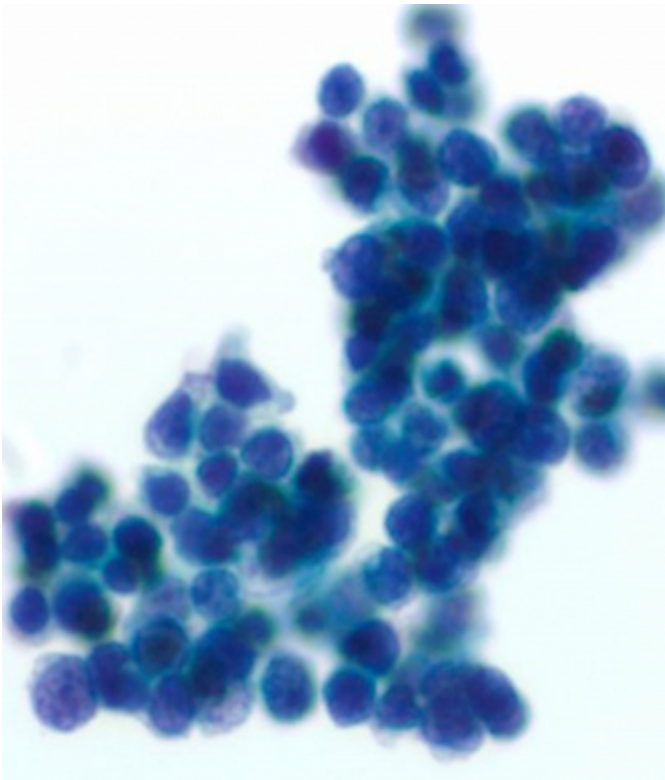


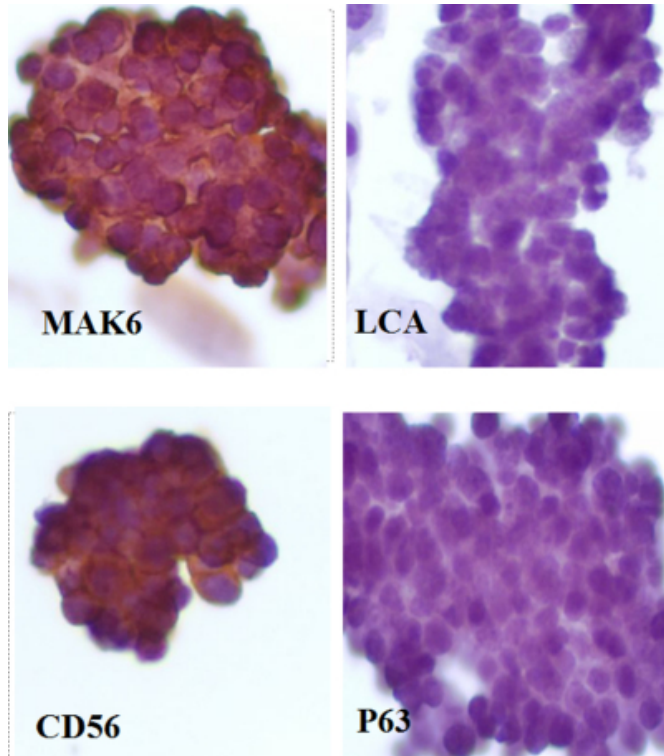
Figure 3

Figure 2: medical cytology showed groups of small atypical cells with irregular nuclei and high nuclei/cytoplasm ratio.



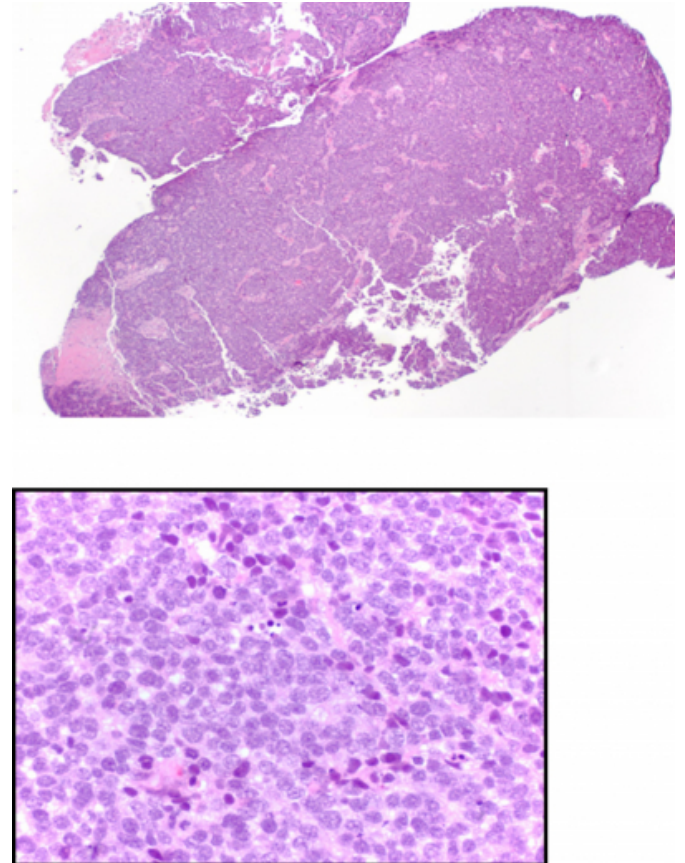
**Figure 4**

Figure 3: immunocytochemistry evaluation showed malignant cells with epithelial origin (MAK6 positive and LCA negative). With addition of CD56 positive and P63 negative tests, these results are consistent with small cell carcinoma.



**Figure 5**

Figure 4: Hematoxylin and eosin staining of the biopsy specimen showed tumor composed of small cells with minimal cytoplasm and hyperchromatic nuclei with crowding, molding and overlap. Morphologically consistent with small cell carcinoma.



## DISCUSSION

SCC of the genital urinary tract shares many similarities with its pulmonary counterpart. It is often a disease of the elderly men and associated with cigarette smoking. Patients with SCCB tend to have a better prognosis than SCC of the prostate, median survival 10 versus 19 months [4]. Primary SCCB is a rare disease that accounts for less than 1% of bladder cancers. Microscopic hematuria is the most common presentation. It behaves aggressively unlike urothelial carcinoma, with a 25% 2-year survival and 8% 5-year survival rate [5]. It is associated with high recurrence rate and early metastasis. Factors impacting survival of SCCB include: tumor stage, performance status, and metastatic disease [4-6].

Histologically, SCCB is indistinguishable from SCC of the lung. The diagnosis is based on the established classification system by the World Health Organization [7].

Microscopically, the specimen is composed of sheets of

small, round cells with overlapping and hyperchromatic nuclei. Advances in immunohistochemical staining contributed to the accurate differentiation of pure neuroendocrine tumor from the more common SCCB mixed with urothelial carcinoma. Patient's prognosis has been shown to be associated with the histology: pure SCCB appeared to have worse outcome than the mixed type [8]. Chemotherapy is often tailored based on the histologic analysis.

Because of the rarity of SCCB, treatment recommendations are based on case reports and small retrospective series. Current armamentarium for treating this disease includes surgery, radiation, chemotherapy or any combination of these strategies. Since most of these patients are elderly with reduced performance status, the available data analyzing each treatment option is often flawed with selection bias. For patients with metastatic disease, only chemotherapy, and not primary surgery, has been shown to improve survival [5,9-10].

Chemotherapy regimen for SCCB is based on our experience with SCC of the lung which center on cisplatin and etoposide [11]. Chemotherapy has been shown to prolong median survival of 33 months comparing to 3 months in patient who did not receive chemotherapy in a 15 year experience [5]. Despite the lack of standardized protocol, chemotherapy is consistently the treatment strategy improving outcome of SCCB patients in the literature [1,9-10]. A recently published phase-two trial demonstrated that four cycles of neoadjuvant chemotherapy was associated with a 78% downstaging of disease and improved long term disease control in patients with surgically resectable disease [6]. For the rare patients with limited disease on presentation, a bladder-sparing chemoradiation protocol was recently reported to show comparable outcome to surgery and adjuvant chemotherapy [12].

## CONCLUSION

We report a case of primary SCCB in an elderly female patient. Since the first description of this aggressive malignancy in 1981, there is still a lack of standardized treatment due to the rarity of the disease. In absence of

prospective randomized studies, platinum-based chemotherapy appears to be the most beneficial treatment option at this point. Unfortunately, most SCCB patients have comorbidities and poor performance status that precludes them from many treatment options which is exemplified in our case. Future research on a standardized treatment and the role of palliation is needed in a randomized, prospective setting.

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