



### Small Cell Carcinoma of the Bladder

#### Mesane Küçük Hücreli Karsinomu

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#### ABSTRACT

Small Cell Carcinoma of the bladder accounts for less than 1% of all bladder tumors. Small Cell Carcinoma of the bladder has an aggressive behaviour and is usually metastatic at diagnosis. Due to its infrequent occurrence, the literature on this entity is limited; which unsurprisingly leads to an uncertainty in defining an ideal therapeutic approach. This report, overviews the literature while describing a 70- year- old female patient who is diagnosed with small cell carcinoma of the bladder arising in an unusual localization.

**Key words:** Bladder carcinoma, chemotherapy, small cell carcinoma.

#### ÖZET

Mesane küçük hücreli karsinomu, tüm mesane tümörleri içinde 1% den az sıklıkta izlenir. Agresif davranışından dolayı tanı konulduğunda sıklıkla metastaz yapmıştır. Nadir görülmesi nedeniyle az sayıda literatür bilgisi vardır. Bu durum ideal tedavide belirsizliğe neden olmaktadır. Bu olguda mesane tavanında yerleşim gösteren, mesane küçük hücreli karsinomu tanısı alan 70 yaşındaki kadın hasta literatür eşliğinde sunuldu.

**Anahtar kelimeler:** Mesane karsinomu, kemoterapi, küçük hücreli karsinom.

#### INTRODUCTION

Small Cell Carcinoma of the bladder (SCC<sub>b</sub>) is a neuroendocrine tumor. Small cell carcinomas usually arise in the lungs, salivary glands, larynx, oesophagus, stomach, colon, rectum and skin. The most common sites of involvement along the urinary tract are the urinary bladder, prostate and kidneys<sup>1</sup>. Involvement of urethra, testicles, ureters and adrenal glands is less common.

Here we report a case of SCC<sub>b</sub>, a rare non-urothelial tumor associated with a poor prognosis, arising in an unusual localization.

#### CASE REPORT

A 70-year-old female patient presented with gross haematuria and clots in the urine. The

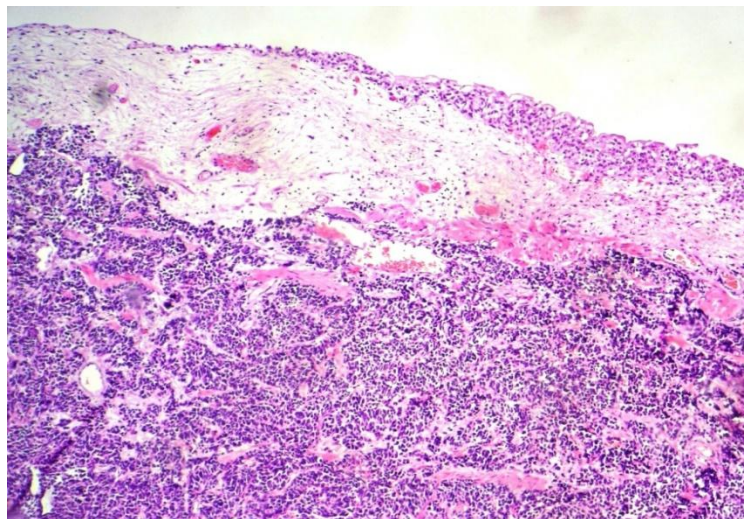
physical examination of the patient, who had a 35-year smoking history, was unremarkable. Following the urinalysis that confirmed hemoglobinuria, the patient was evaluated by urinary tract ultrasonography (USG). USG revealed a 50x40 mm mass in the bladder, prompting a contrast enhanced CT scan (Figure 1). The axial contrast enhanced CT imaging revealed prominent thickening and contrast enhancement of the anterior wall of the bladder. A transurethral cystoscopy confirmed a 50-mm solid mass originating from the bladder dome through the anterior wall.

The patient underwent transurethral resection of the bladder tumor (TUR BT, April 2013). During the operation it was noted that the tumor invaded muscularis propria and there was an

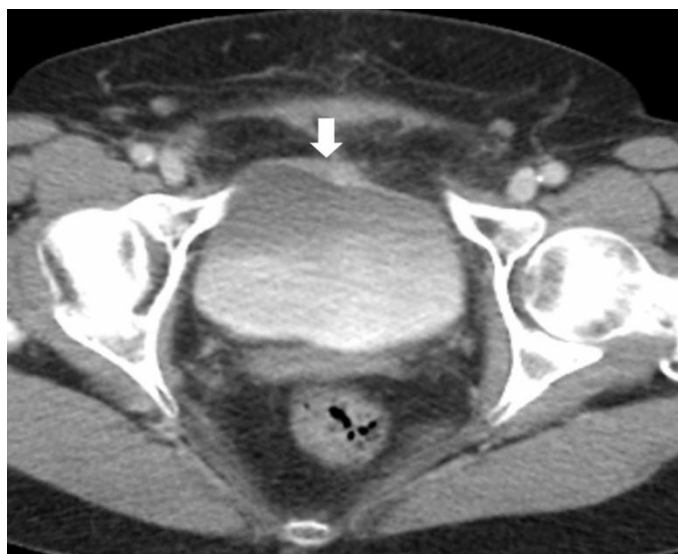
intraabdominal fluid collection. Due to suspected bladder perforation a decision was made to convert the operation to an open surgical operation. The urinary bladder was accessed via a midline suprapubic incision and a 1x1 cm perforated area was noted on the bladder dome. Thus, a wide partial cystectomy was performed around the perforation site. Following the closure of bladder wall, the peritoneum was accessed and the fluid collection was aspirated. After placing a perivesical drain, the surgery was terminated. The patient's postoperative course was uneventful and she was discharged with a urethral catheter on the postoperative third day.

The histopathologic evaluation of the resected specimen revealed a small cell carcinoma invading the bladder wall thoroughly and infiltrating the perivesical adipose tissue as well. In situ carcinoma was detected in the peritumoral bladder mucosa. Immunohistochemical analysis for further characterization of the tumor tissue revealed that the malignant cells were stained diffusely with

Synaptophysin and Thyroid Transcription Factor-1 (TTF1) and focal expression of Epithelial Membrane Antigen (EMA), pancytokeratin (PanCK) and Chromogranin. No staining with p63, CD56, PGP 9.5, or 34BE12 was detected in malignant cells. Hence, the tumor was diagnosed as SCC of the bladder (Figure 2). Abdominal and thoracic computed tomography (CT) scans performed for staging demonstrated no clinically relevant pathologic findings. The tumor stage was determined T2 (TNM staging system) and the patient was offered various treatment modalities including radical cystectomy. However she refused any surgical treatment or further examination, so was referred to medical oncology for chemotherapeutic intervention. She received 4 cycles of Cisplatin plus Etoposide based chemotherapy. Further surgical treatment was suggested again but the patient did not accept. So, pelvic radiotherapy (180Gy in 28 fractions and 200Gy in 5 fractions) was administered. After a year of follow up the patients is still alive.



**Figure 1.** Axial contrast enhanced CT imaging shows prominent thickening and contrast enhancement of the anterior wall of the bladder (white arrow).



**Figure 2.** Small cell carcinoma of the bladder. Sheets and aggregates of loosely cohesive cells with hyperchromatic small nuclei and scant cytoplasm (HE $\times$ 40).

## DISCUSSION

SCC<sub>b</sub> accounts for less than 1% of all bladder tumors<sup>2</sup>. As the rest of the bladder carcinomas, the most common symptom at presentation is hematuria. Half of the affected patients have a smoking history<sup>2</sup>. SCC of the bladder commonly occurs (15.7%) in the lateral walls of the bladder, but can rarely (2%) arise in the dome, as in our patient<sup>3</sup>.

The etiopathogenesis of SCC<sub>b</sub> is not yet clear. However, the malignant transformation of pluripotent stem cell-derived cells is one of the most credited theories<sup>4</sup>.

SCC<sub>b</sub> shares similar histological characteristics with its counterpart arising in lung. Therefore, the differential diagnosis should include metastasis of small cell carcinoma of lung, along with other malignancies such as the bladder invasion of prostatic small cell carcinoma (SCC<sub>p</sub>) and lymphoma. Differential diagnosis of SCC<sub>p</sub> and

lymphoma requires performance of detailed histopathological and immunohistochemical methods. Both SCC<sub>p</sub> and SCC<sub>b</sub> express neuroendocrine markers, while Prostate-Specific Antigen (PSA) and prostatic acid phosphatase (PSAP) are expressed only by SCC<sub>p</sub><sup>5</sup>. Lymphomas express Leucocyte Common Antigen (LCA) and are negative for neuroendocrine markers or Cytokeratin<sup>6</sup>. SCC<sub>b</sub> mainly (61.4%) occurs in pure form, but concomitant areas of adenocarcinoma and transitional cell carcinoma are not uncommon (38.6%)<sup>7</sup>. Fifty-two percent of SCC<sub>b</sub> is metastatic at diagnosis<sup>8</sup>. The common sites of metastasis of this highly aggressive tumor are pelvic and extrapelvic lymph nodes, lungs, liver, mediastinum, adrenal glands, bowels, and brain<sup>8</sup>. The ultimate diagnosis is based on the histopathologic evaluation of the resected tissues. Two staging systems can be used to evaluate the extent of the disease; the TNM staging system is used by urologists in most studies while the clinical stage also implies if the disease is localized or extensive.

Contrast enhanced CT scans including abdomen, thorax, cranium and pelvis should be preferred for the evaluation of disease stage. Owing to its high sensitivity, magnetic resonance imaging can be the first choice in detecting the extravesical and adjacent organ involvement in patients who are planned to undergo radical surgery. Although multimodal combined therapies such as radical surgery, radiotherapy, and chemotherapy are suggested for management of these patients, no consensus has been reached yet<sup>7</sup>.

A Mayo Clinic series consisting of 44 patients showed that radical cystectomy alone could not achieve cure. Furthermore, there are no studies reporting advantages or disadvantages of cystectomy or radiotherapy over chemotherapy alone<sup>9</sup>. The aggressive behavior and unfavorable progression of the tumor could cause relapses. Radical surgery, partial cystectomy and TUR-bladder tumor procedures are not efficient even in regional disease<sup>4</sup>. Recent studies have shown that neoadjuvant chemotherapy (four cycle Etoposide plus Cisplatin or doxorubicin plus ifosfamide) performed in surgically resectable SCCb patients achieves downstaging of the tumor and prolongs survival<sup>10</sup>. The authors detected a disease-specific survival of 5 years in 79% of patients undergoing radical cystectomy following chemotherapy<sup>10</sup>. Thus, we offered the patient a combined therapy consisting of radical surgery and chemotherapy (neoadjuvant and adjuvant). However, she refused surgical treatment and was referred to medical oncology for chemotherapy. She received Cisplatin plus Etoposide based chemotherapy. Further surgical treatment was suggested again but the patient did not accept.

In conclusion, SCC of the bladder is a rare tumor with a poor prognosis. It may develop in unusual localizations. There is no well-established treatment strategy for management of these patients. The patient should be informed thoroughly about the treatment options. This

disease requires a multidisciplinary treatment approach.

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## REFERENCES

1. Carranza OE, Castañón E, Abella LE, Zudaire ME, Castillo A, Arevalo E, et al. Clinical management of small-cell carcinoma of the urinary tract: A 10-year single-center's experience. *Clin Genitourin Cancer*. 2013;11:168-74.
2. Mukesh M, Cook N, Hollingdale AE, Ainsworth NL, Russell SG. Small cell carcinoma of the urinary bladder: a 15-year retrospective review of the treatment and survival in the Anglian Cancer Network. *BJU Int*. 2009;103:747-52.
3. Dong XU, Ping YX, Liang WC, Jian LZ, Lin ZJ. Small cell carcinoma of the urinary bladder diverticulum: A case report and review of the literature. *J Cancer Res Ther*. 2013;9:151-53.
4. Blomjous CE, Vos W, De Voogt HJ, Van der Valk P, Meijer CJ. Small cell carcinoma of the urinary bladder. A clinicopathologic, morphologic, immunohistochemical and ultrastructural study of 18 cases. *Cancer*. 1989;64:1347-57.
5. Ro JY, Têtu B, Ayala AG, Ordóñez NG. Small cell carcinoma of the prostate. II. Immunohistochemical and electron microscopic studies of 18 cases. *Cancer*. 1987;59:977-982.
6. Grignon DJ, Ro JY, Ayala AG, Shum DT, Ordóñez NG, Logothetis CJ, et al. Small cell carcinoma of the urinary bladder. A clinicopathologic analysis of 22 cases. *Cancer*. 1992;69:527-36.
7. Choong NW, Quevedo JF, Kaur JS. Small cell carcinoma of the urinary bladder. The Mayo Clinic experience. *Cancer*. 2005;103:1172-8.
8. Karpman E, Goldberg Z, Saffarian A, Gandour-Edwards R, Ellison LM, deVere White RW. Analysis of treatment for small cell cancer of the bladder and report of three cases. *Urology*. 2004;64:494-8.

9. Pons DF, Orsola A, Morte J, Bellmunt J. Variants Forms of Bladder cancer: Basic Considerations on Treatment Approaches. Curr Oncol Rep. 2011;13:216-21.
10. Lynch SP, Shen Y, Kamat A, Grossman HB, Shah JB, Millikan RE, et al. Neoadjuvant chemotherapy in small cell urothelial cancer improves pathologic downstaging and long-term outcomes: results from a retrospective study at the MD Anderson Cancer. Eur Urol. 2013;64:307-13.

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