

## CASE REPORT

# Orthotopic neobladder in patient with locally advanced small cell carcinoma of the bladder: a case report and review of the literature

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## Abstract

Small cell carcinoma of the urinary bladder (SCCUB) is a rare, aggressive variant of neuroendocrine nonepithelial tumor. The best treatment results are achieved by combined cystectomy and chemotherapy. Same as in urothelial bladder cancer, a question remains about the urinary diversion in locally advanced disease. Studies on surgical treatment of patients with SCCUB most often do not clearly specify the type of urinary diversion performed, and we could not find information that orthotopic urinary diversion was performed in those patients. We present a 58-year-old patient with locally advanced SCCUB, treated by cystectomy and orthotopic urinary diversion (ileal neobladder-Hautmann) followed by six-cycle adjuvant chemotherapy. After 50-month follow-up, the patient showed no signs of relapse and the new bladder functioned perfectly well.

## INTRODUCTION

Small cell carcinoma of the urinary bladder (SCCUB) is a rare variant of neuroendocrine nonepithelial tumor characterized by aggressive behavior. Cramer was the first to publish a case report with this disease in 1981 [1]. Its incidence accounts for 0.5–0.7% of all urinary bladder carcinomas. Due to its low incidence, not many cases have been presented, and those have mostly been individual case reports. To date, the reports have tried to determine the optimum choice of therapy for those patients, while urinary diversion has been less explored. Better survival achieved by combination therapy also opens a question of orthotopic diversion for selected patients with SCCUB.

## CASE REPORT

A 58-year-old patient presented with intermittent hematuria. Urine cytology revealed carcinoma; ultrasound and cystoscopy

showed 7 × 4 cm tumor of the left side of the urinary bladder with infiltration to the left ureterovesical junction and Grade II left hydronephrosis. Computed tomography (CT) of the abdomen and pelvis detected 7 × 4 cm tumor of the left side of the urinary bladder with infiltration to the perivesical adipose tissue, enlarged lymph nodes along the left external iliac artery up to 23 mm, and Grade II left hydronephrosis. Transurethral resection of the bladder tumor (TURBT) was performed in an external institution, with histopathology showing small cell bladder carcinoma with infiltration to the muscle wall, a nest-formed accumulation of atypical mitotically active cells (up to 10 mitoses per 1 HPF) of scarce cytoplasm and oval nucleus with dispersed chromatin. Immunohistochemistry was positive for neuron-specific enolase, chromogranin A and synaptophysin, while proliferation activity as measured by Ki-67 was 70%. One month later, we performed radical cystoprostatectomy, lymphadenectomy and orthotopic urinary diversion (ileal

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neobladder-Hautmann). Histopathology showed small cell bladder carcinoma: T3a, N2 and M0. Adjuvant chemotherapy by PE protocol (cisplatin + etoposide) was started 1 month after the radical procedure. A total of six cycles of chemotherapy were given (cisplatin 120 mg, etoposide 200 mg). After a 50-month follow-up, laboratory tests and radiology exams were clear. Follow-up imaging procedures included 4-month CT scans during the first year, 6-month until the third year and annual imaging thereafter. The patient showed no signs of relapse with very good quality of life maintained.

## DISCUSSION

SCCUB is an extremely rare form of malignant tumor of the urinary bladder. It is more common in the male population and occurs mostly in the 70s and 80s. The most common symptom is macrohematuria. Despite poor knowledge of the biology of this tumor, we do know that it is an extremely aggressive tumor. At the time of diagnosis, we often find locally advanced or metastatic form of the disease. Metastasis commonly involves the liver, brain, lung, bone and lymph nodes. SCCUB is staged according to TNM classification or, depending on resectability of the primary tumor, divided into limited disease (LD) and extensive disease (ED), similar to classification with small cell lung cancer (SCLC). Considering a low number of patients with SCCUB and lack of high-quality prospective studies in the field, a standard therapy for patients with SCCUB has not yet been defined. Most frequently the treatment involves: independent chemotherapy, combination chemotherapy and cystectomy, cystectomy, transurethral electroresection of the tumor, radiotherapy, and combination radiotherapy and chemotherapy. There are no guidelines of urological associations that would include the treatment of SCCUB. Recent publications include guidelines of only two associations. The National Comprehensive Cancer Network guidelines from 2011 recommend combined chemotherapy and cystectomy for LD and chemotherapy with cisplatin or carboplatin combined with etoposide for ED [2]. The Canadian Association of Genitourinary Medical Oncologists guidelines from 2013 do not provide clear recommendations for treatment but do mention combined cystectomy and chemotherapy or combination radiotherapy and chemotherapy as options for LD (evidence-based Level 3, Grade C), whereas the bladder preserving method (TURBT) as an independent treatment is not recommended due to poor outcomes (evidence-based Level 4, Grade C). For ED, the recommendation is 4–6 cycles of platinum-based chemotherapy (evidence-based Level 4, Grade C) [3].

Prognosis depends on the spread of the disease and treatment method. Most studies have reported median survival of 9.3 months, but only 5 months for metastatic type [4–6]. There are no clear recommendations about which approach is better: neoadjuvant chemotherapy + cystectomy or cystectomy + adjuvant chemotherapy. Recent retrospective study from MD Anderson Cancer Center suggests neoadjuvant chemotherapy + cystectomy as a better approach with expected median overall survival of 159.5 months [7].

For patients with SCCUB undergoing cystectomy, the type of urinary diversion is determined based on the spread of the malignancy, age and comorbidities. For patients with infiltrative urothelial cell carcinoma of the urinary bladder (UCCUB), clear treatment guidelines have been developed due to known biology of the tumor and a much greater number of affected patients. Locally advanced and/or node-positive UCCUB have long been considered an absolute contraindication for orthotopic urinary diversion. Difficult treatment of potential local relapse and administration of chemotherapy for

patients with the neobladder have been considered as potential problems to be encountered. A recent review article by world renowned authorities in the field recommends reconstruction of neobladder in selected patients with locally advanced and/or node-positive UCCUB [8]. They showed no problems with local relapse in those patients and that potential toxicity of chemotherapy due to reservoir resorption may be prevented by enhanced hydration and insertion of urethral catheter during the therapy. Orthotopic diversion at this stage of the disease has been suggested by a growing number of recent studies [9, 10].

## CONCLUSION

Studies on surgical treatment of patients with SCCUB most often do not clearly specify the type of urinary diversion performed, and we could not find information that orthotopic urinary diversion was performed in those patients. The 58-year-old patient from this case report had good performance status and resectable locally advanced disease. In line with the previous approaches, we decided to perform orthotopic urinary diversion (ileal neobladder-Hautmann) after radical cystectomy. Fifty months after successful chemotherapy, the patient had no signs of relapse, a well functioning neobladder and very good quality of life maintained.

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