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Small-cell neuroendocrine tumor of the bladder: A rare disease in a low-risk woman

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ABSTRACT

Bladder cancer is the fourth most common malignancy in men and ninth most in woman. Most bladder cancers are urothelial, and the neuroendocrine sub-types make up 0.5–1.0% of cases. Here we present a 70-year-old female with poorly differentiated small cell carcinoma of the bladder who complains of an extensive history of gross hematuria. She was started on a neoadjuvant chemotherapy regimen of 21-day Etoposide with Carboplatin and radical cystectomy. More work needs to be done when it comes to the best treatment method for this rare cohort of patients.

1. Introduction

Bladder cancer is the fourth most common malignancy in men and ninth most in woman.[1] Most bladder cancers are urothelial and the neuroendocrine sub-types make up 0.5–1.0% of cases.[1] Neuroendocrine tumors are divided into small cell carcinoma (SCC) and large cell neuroendocrine carcinoma.[1] Most neuroendocrine tumors of the bladder are mixed with other subtypes.[1] Due to several factors, SCC often presents more aggressively and carries a worse prognosis for patients.[2]

Here we present a 70-year-old female with poorly differentiated SCC of the bladder who complains of an extensive history of gross hematuria.

2. Case presentation

A 70-year-old female presented to the urology clinic complaining of 6–12 months of hematuria. She has a past medical history of a thyroid nodule, hypothyroidism, fibrocystic breast disease, hypertension, and stage IIIa chronic kidney disease. She admits to a family history of pancreatic, breast, and kidney cancer. She has never undergone surgical evaluation for any genitourinary cancers. She denies any current or previous smoking or alcohol use. Today the patient only complains of continual hematuria, denying all other symptoms. Initial laboratory examination showed a complete blood count within normal limits. Metabolic examination showed an elevated creatine of 1.30, Alkaline phosphatase of 96, and mildly elevated liver enzymes (AST 40, ALT 42). Urine cytology was obtained and showed atypical urothelial cells, inconclusive for malignancy. Follow-up CT scan was obtained, reading a 4.4 × 1.6 cm lobulated mass involving the dome of the urinary bladder. No obstructive uropathy was noted. Small lymph nodes were noted along the lilac chain measuring 1 cm in the left external iliac chain. She then consented and was taken to the operating room for a transurethral resection of the bladder tumor (TURBT).

She presented to the operating room for cystoscopy and TURBT. On examination, there was a substantial amount of necrotic tissue present on the dome of the bladder. A biopsy of the area was taken and sent for pathology (Figs. 1 and 2). At first, this tissue was thought to be necrosis due to the patient's history of laser therapy treatment for incontinence. Pathology revealed small cell neuroendocrine carcinoma and invasive high-grade carcinoma (Fig. 3)[3] with squamous differentiation. The viable TURBT specimen was approximately 80% small cell carcinoma in etiology. She was sent referral for medical oncology. PET CT per medical oncology revealed a bladder tumor with SUV 17.4, left common iliac lymph node measuring SUV 15.6, and adjacent left external iliac lymph node measuring 4.1 × 2.5 cm with SUV 20.1. She will proceed for neoadjuvant chemotherapy with a 21-day Etoposide with Carboplatin. After completion of chemotherapy, she will likely undergo local treatment with radical cystectomy. The patient was consented for cystectomy and underwent the procedure. Negative margins were confirmed and she recovered from the procedure well without complications to date.

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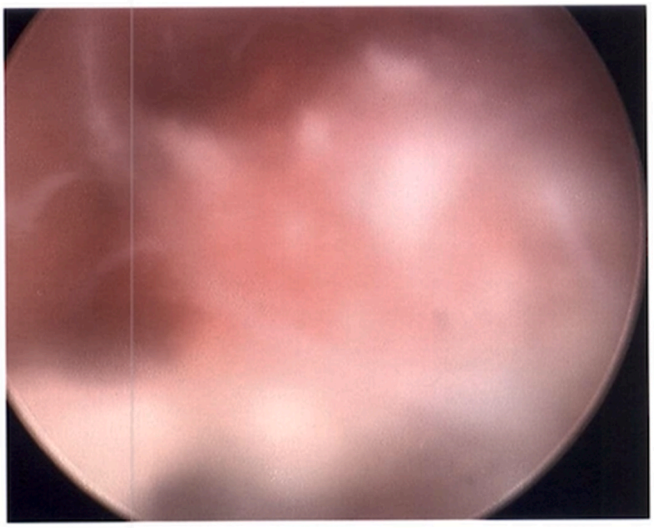

Fig. 1. Cystoscopic view of the dome of the bladder where a biopsy was taken.

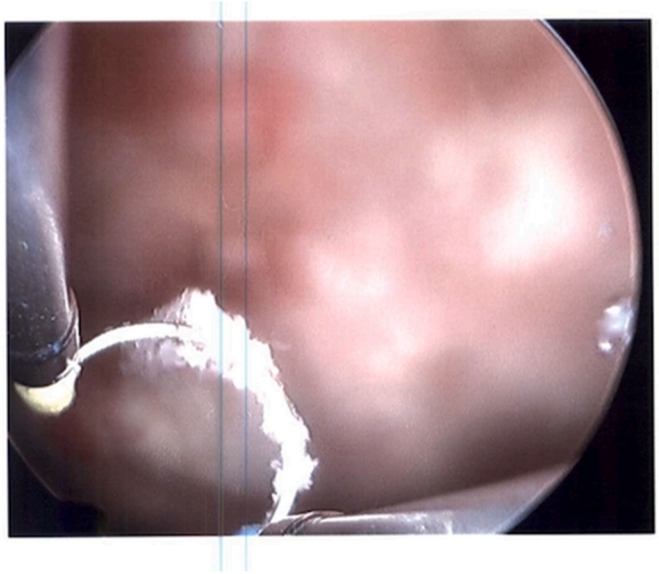

Fig. 2. Positioning of the resectoscope around the necrotic, pathologic tissue.

3. Discussion

SCC of the bladder is a rare disease with little clinical evidence on effective treatment.[4] For this reason, careful patient work-up and treatment should be considered. Similar to urothelial cancer, patients with SCC will likely present with painless hematuria.[4] A proper history and physical exam can guide clinical suspicion for this cancer. Smoking history is important to note, as this has been a well-described risk factor for all types of bladder malignancy.[1] Cystoscopy is done to visually assess the tumor burden.[1] Biopsy of the tissue via TURBT is needed to distinguish this rare tumor sub-type from other types of bladder malignancies.[1] Upon histologic examination, the tissue will stain with keratin, synaptophysin, and chromogranin to distinguish the cancer as SCC.[2]

Treatment regimens for local disease can range from TURBT, partial cystectomy, and radical cystectomy depending on tumor grade and stage.[4] TURBT alone was found to be inadequate for tumor burden for these patients.[4] This leaves radical cystectomy as the preferred option

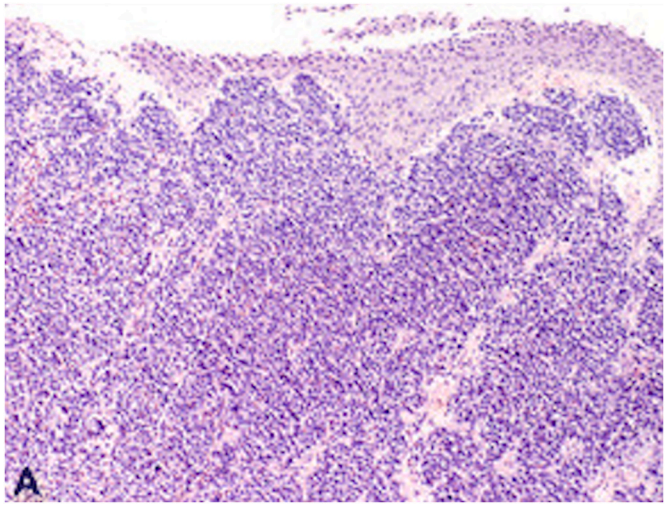

Fig. 3. An example pathology slide showing small cell neuroendocrine carcinoma of the bladder.

for treatment.[4] Unfortunately, these tumors tend to be aggressive and may present with locally advanced disease in at least 70% of cases.[2] For this reason, neoadjuvant or adjuvant chemotherapy options have been explored.[4] This decision may be dependent on the histological type of SCC.[4] Mixed SCC can respond better to MVAC (methotrexate, vinblastine, adriamycin, cisplatin) therapy.[4] Pure SCC will likely respond better to a cisplatin/carboplatin and etoposide therapy.[4] Radiation therapy may play a role for patients with local disease without progression.[4] Overall, most patients seem to benefit from neoadjuvant chemotherapy with radical cystectomy.[2] A retrospective study by Quek et al. supported this by concluding that neoadjuvant chemotherapy followed by radical cystectomy showed a better 5-year overall survival for patients compared to radical cystectomy alone.[5]

Our patient presented with concern for metastatic disease to local lymph nodes. Medical oncology started her on a neoadjuvant chemotherapy regimen of 21-day Etoposide with Carboplatin. Radical cystectomy will be undergone after this chemotherapy is complete. Follow-up will be routine with CT scans to assess for any further progression or recurrence of disease.

This case was a unique example exploring the presentation of a rare subtype of bladder cancer in a female. Although few case reports exist, it is important to inform the provider of this potential diagnosis. For this to present in a female who does not smoke emphasizes the importance to keep a broad differential and aggressively treat this rare cancer.

4. Conclusion

Bladder cancer remains a prevalent disease in men and women world-wide. The workup and treatment of this disease is guided by tumor grade and stage. A small, unique sub-set of patients will present with the more aggressive neuroendocrine sub-type. In this rare population, proper treatment is especially important due to its likelihood of advanced disease at presentation. This case was a unique presentation of a woman with no smoking history who presented with small cell neuroendocrine carcinoma and invasive high-grade carcinoma with squamous differentiation. Her treatment consisted of neoadjuvant chemotherapy with radical cystectomy. Overall, this case emphasizes the importance for providers to keep these bladder tumor variations in mind. More work needs to be done when it comes to the best treatment method for this rare cohort of patients.

Declaration of competing interest

None of the authors has a conflict of interest to report, real or

perceived, that would influence the results of this study. All authors contributed to a significant portion of this manuscript.

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