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A Rare Presentation of Primary Small-cell Carcinoma of Urinary Bladder

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Abstract Primary small cell carcinoma of urinary bladder is rare and aggressive neuroendocrine tumor. It is part of neuroendocrine tumor family that affects respiratory system, gastro intestinal tract and genitourinary system of male and female. We report a case of primary small cell carcinoma of urinary bladder treated with chemotherapy. Patient is 81 year old male who presented to emergency department with recurrent urinary retention associated with hematuria. Patient had cystoscopy and was diagnosed with small cell carcinoma of urinary bladder with no distant metastasis. Patient was treated with chemotherapy. Patient died with septic shock due to clostridium difficile colitis.

Keywords: *small cell, cystoscopy, clostridium difficile colitis*

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1. Introduction

Small cell carcinoma of urinary bladder is rare, poorly differentiated neuroendocrine tumor of urinary bladder. It is also called oat cell carcinoma. It has poor prognosis as compared to urothelial carcinoma of urinary bladder in spite of having same clinical presentation, demographics, risk factors and diagnostic approach. Small cell carcinoma of urinary bladder is extremely rare accounting for 0.5 -1% cases [1]. It is commonly seen in old population. Patient can present with painless hematuria or bladder irritation, abdominal pain and urinary obstruction. As it is rare, it is difficult to have case control study. Sometime, patient are misdiagnosed. It is important to collect data about small cell carcinoma of urinary bladder for better understanding of presentation, diagnostic plan, treatment and follow up.

2. Case Presentation

Patient is 81 year old male with history of atrial fibrillation, coronary artery disease, severe aortic stenosis, chronic diastolic congestive heart failure, congenital solitary kidney who presented to the emergency department with recurrent hematuria and urinary retention. In the emergency department, Foley catheter was placed. Patient was discharged home. Patient had urology follow up as outpatient. Patient had flexible cystoscopy that showed thrombus versus mass in urinary bladder. Later on, patient had rigid cystoscopy that showed bladder mass. Transurethral resection of urinary bladder tumor was performed. Histopathology report showed bladder high-grade carcinoma with neuroendocrine differentiation and necrosis admixed with blood clot, consistent with bladder Small Cell Carcinoma. Histochemical staining was positive for synaptophysin, chromogranin and p53 negative for CK 20 and p63. Patient had CT chest, CT abdomen and pelvis that was negative for any distant metastasis. Positron emission tomography scan was unremarkable. Patient was started on neoadjuvant chemotherapy including VP-16 and Carboplatin. Patient had two cycles of chemotherapy. Following his second cycle of chemotherapy patient developed clostridium difficile colitis. He was treated with oral vancomycin as well as intravenous metronidazole. Patient developed septic shock secondary to clostridium colitis, acute renal failure and died due to septic shock.

3. Discussion

Small cell carcinoma is poorly differential and aggressive neuroendocrine tumor. Most of the time small cell carcinoma of urinary bladder is mixed with other urothelial carcinoma, squamous cell carcinoma and adenocarcinoma of urinary bladder [2]. Our case had isolated small cell carcinoma of urinary bladder. In case of small cell carcinoma of urinary bladder, 5 year survival rate is less than 10 percent as reported in many case report [3]. Most common presenting symptoms are hematuria, ureteral obstruction, acute renal failure, increase urgency, frequency and recurrent urinary tract infection. It can present with carcinoid tumor, hypercalcemia and syndrome of inappropriate secretions. [4] Due to rarity of it, pathogenesis in not really understood. As patient does not has specific symptoms suggestive of small cell carcinoma of urinary bladder diagnosis is based on

histopathology and immunochemical assays. Typical microscopically features of SCC include small, round or oval-shaped tumor cells, a nest-like structure, little cytoplasm, hyperchromatic nuclei, a rough granular karyosome and frequently occurring massive mitotic figures, and extensive necrosis. The immunohistochemical assay is positive for CgA and CK, and negative for epithelial membrane antigen, leukocyte common antigen, synaptophysin and CD56 [5]. Due to poorly differentiation, it can metastasize to other tissue very easily.

Small cell carcinoma of urinary bladder diagnosis mainly depends on preoperative biopsy of lesion and postoperative histopathological examination, such as measurements by light microscopy cell morphology, cell ultrastructure electron microscope examination, and immunohistochemical examination. Preoperative examinations must include CT or MRI scan, urine cytology and cystoscopy. Cytology of small cell carcinoma of urinary bladder can be similar as poorly differentiated squamous cell carcinoma, adenocarcinoma, and transitional cell carcinoma, so diagnostic identification relies on electron microscopy or immunohistochemistry [6]. Small cell carcinoma of urinary bladder can be misdiagnosed transitional cell carcinoma, inverted papilloma, and glandular cystitis. Since there are clear distinctions in treatment programs between SCCB and other bladder tumors, we should raise awareness of the disease and carefully check the tissue samples in order to avoid misdiagnosis, missed diagnosis, and delay of treatment timing.

Due to rarity of disease having no randomized controlled study there is no defined treatment for small cell carcinoma of urinary bladder. According to the experience of the Mayo Clinic (Rochester, MN, USA), a radical cystectomy should be applied to all SCBC patients unless there is metastasis (M1). [7] In literature review, we found evidence that TURBT alone was an inadequate method of control of the disease due to its aggressive nature, even in limited disease. Lynch and colleagues discovered that in combined treatment modalities (neoadjuvant chemotherapy+cystectomy versus cystectomy + adjuvant chemotherapy), the median overall survival was 159.5 months in the first group and 18.3 months in the latter [8]. In review of case report, there is documentation of treatment with immunotherapy PD1 inhibitor pembrolizumab who has significant response in clinical as well as radiographically but this needs further investigation [9].

4. Conclusion

Primary SCCB is a very rare and aggressive tumor. Local disease can be treated with Neoadjuvant chemotherapy, radiation and surgery. For distant disease the chemotherapy using a platinum agent is the mainstay of treatment. Patient was on oral anticoagulation, always look for secondary reason of hematuria or bleeding. Effectiveness of Immunotherapy in treatment of small cell carcinoma of urinary bladder needs to be assessed.

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