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Case Report

Primary Small Cell Neuroendocrine Carcinoma of the Urinary Bladder: A Report of a Rare Case

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Abstract

Primary Small cell neuroendocrine carcinoma of the urinary bladder (SCNEC) is an uncommon and highly aggressive malignancy, accounting for less than 1% of bladder tumors. It is often diagnosed at an advanced disease stage. We report a case of a 58-year-old male presenting with painless hematuria, subsequently diagnosed as primary small cell neuroendocrine carcinoma of the urinary bladder on histopathology and immunohistochemistry. The patient was managed with TURBT, combination chemotherapy and concurrent radiotherapy. This case highlights the importance of considering neuroendocrine carcinoma in the differential diagnosis of bladder tumors due to its distinct clinical behavior and therapeutic implications.

Keywords: *Small cell neuroendocrine carcinoma, urinary bladder, rare tumour.*

Introduction

Primary small cell neuroendocrine carcinoma of the urinary bladder (SCNEC) is a rare and highly aggressive malignancy, first described by Cramer et al in 1981(1). A total of only about 150 cases has been reported in medical literature till date reiterating the rarity of this disease entity (1-3). The lateral and posterior wall of the bladder is commonly involved followed by the trigone, anterior wall and dome of the wall in that order. Smoking, chronic cystitis and bladder calculi are considered to be the common etiological factors.(3). The pathophysiological mechanisms suggested include dedifferentiation or trans differentiation from urothelial carcinoma with pluripotent urothelial stem cells as the possible cell of origin (4). Painless gross or microscopic hematuria is the common clinical presentation. The occurrence of concurrent urothelial carcinoma with small cell carcinoma of urinary bladder has been reported (1,2). The prognosis is comparable to stage matched urothelial carcinoma unless metastases are present, in which case the prognosis of small cell neuroendocrine carcinoma is significantly worse. ~90% of bladder small cell neuroendocrine carcinomas have at least invasion of muscularis propria at diagnosis, with most cases presenting with regional lymph nodal and distant metastases at presentation. (3).

Recurrence rates are high compared to urothelial carcinoma. According to various studies, the median survival rate ranges from 11.8 to 15.9 months. This highlights the importance of considering neuroendocrine carcinoma in the differential diagnosis of bladder tumors due to its distinct aggressive clinical behavior.

Case Presentation

A 58-year-old male presented with the complaints of painless gross hematuria and dysuria for a period of 3 months. There was no history of smoking, occupational exposure or prior pelvic irradiation. Clinical examination was unremarkable except for anemia.

Ultrasound abdomen and pelvis revealed a polypoid mass in the urinary bladder.

CT scan confirmed a 3.2 × 2.5 cm enhancing lesion on the lateral bladder wall. A PET CT scan revealed FDG active liver lesions suggestive of metastatic disease.

Cystoscopy was performed which showed a polypoidal lesion arising from the lateral wall of the bladder.

Management:

The patient underwent transurethral resection of bladder tumor (TURBT). Histopathology showed sheets of small round cells with hyperchromatic nuclei, scant cytoplasm, and high mitotic activity. Stippled chromatin was seen focally. Large areas of necrosis were noted. (Figure 1). The H and E diagnosis was rendered as small cell neuroendocrine carcinoma of the bladder. A differential diagnosis of Non Hodgkin's Lymphoma was also considered due to the diffuse sheet like cellular arrangement.

Immunohistochemistry (IHC): Tumour cells were positive for cytokeratin, NSE, synaptophysin, CD56, and negative for LCA, CD 20, CD 3, GATA 3, chromogranin, NKX3.1. (Figure 2,3). The Ki 67 was 80 % confirming the diagnosis of high-grade small cell neuroendocrine carcinoma of the bladder.

Treatment & Outcome:

The patient received systemic chemotherapy with cisplatin + etoposide and adjuvant radiotherapy. The patient is on follow up. At the end of six months follow up, the patient is recurrence free.

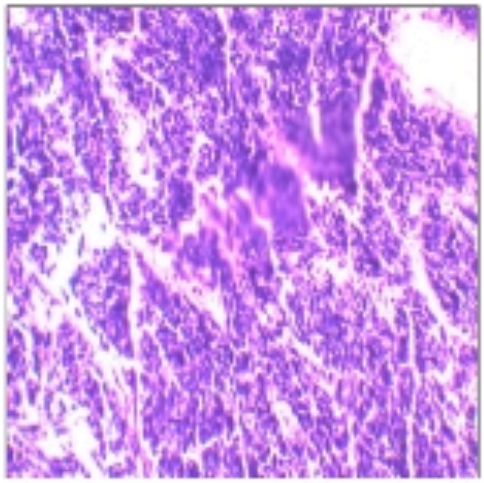

Figure 1: H and E Image showing diffuse sheets of small cells

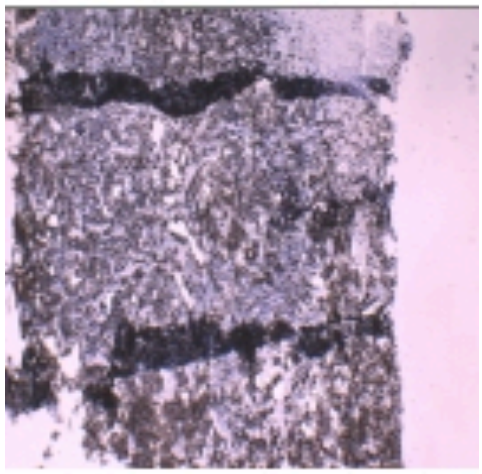

Figure 2: Ki-67 showing high proliferative index.

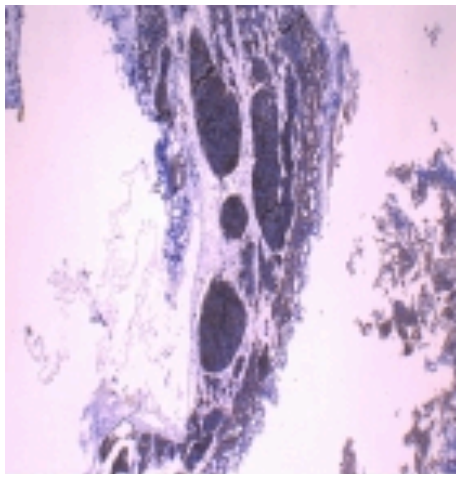

Figure 3: Synaptophysin showing positive staining in tumour cells.

Discussion

Primary neuroendocrine carcinoma of the bladder is rare, with fewer than 200 cases reported worldwide. (1) The most common type of neuroendocrine carcinoma of the bladder is small cell type. Bladder neuroendocrine carcinoma can occur as a primary tumour or as a concurrent tumour with urothelial carcinoma or squamous cell carcinoma of the bladder. Risk factors include smoking and chronic cystitis [1-6].

Our patient was a non smoker. The clinical behavior, morphology and immunohistochemical profile is similar to that of pulmonary small cell neuroendocrine carcinoma.[6] There is a propensity for early metastasis. The disease is more common in males according to various previous studies, similar to our case. Age at presentation is a crucial risk factor for disease progression and death with increasing risk with age. [7] Lymph nodal metastasis and distant metastasis at presentation correlated with overall poor survival according to various previous studies.[7] Our patient had liver metastasis at presentation.

Diagnosis requires histology and IHC to differentiate from poorly differentiated urothelial carcinoma, lymphoma, or metastatic small-cell carcinoma. Positive neuroendocrine markers (chromogranin, synaptophysin, CD56) and absence of urothelial markers aid confirmation.[5-7] Ki 67 plays an important role in ascertaining the grade and clinical behavior of the tumour. The Ki 67 index varied from 20 to 90 % in various previous case reports [7]. In our case the Ki 67 index was 80 % indicating an aggressive tumour.

Optimal treatment is not standardized due to rarity. Most authors recommend multimodal therapy—TURBT combined with platinum-based chemotherapy and/or radiotherapy. Our patient received all three modalities and is alive at 6 months follow up. Prognosis remains poor, with median survival ranging between 9–24 months, depending on stage and treatment.[3]

Conclusion

Primary neuroendocrine carcinoma of the bladder is a rare, aggressive malignancy that should be considered in cases of bladder tumors with unusual histology. The tumour is a distinct entity which require therapeutic strategies different from urothelial carcinoma. Hence early recognition with IHC confirmation is crucial, and a multimodal treatment approach may improve survival outcomes.

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