CASE REPORT:

A Rare Case of the Small Cell Neuroendocrine Carcinoma of Urinary Bladder

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ABSTRACT:

Small cell neuroendocrine carcinoma of urinary bladder (SCCB) is a rare, prevalent in males, highly aggressive carcinoma being diagnosed usually at advanced stages. The origin of the disease is unknown; however the multipotent stem cell theory applies best to this case. Histology and immune histochemistry shows a tumor which is indistinguishable from small cell lung carcinoma (SCLC). We report a case of SCCB in a 70 year old female who presented with history of recurrent urinary tract infections and hematuria for six months. CT scan showed a large mass in bladder, infiltrating muscle along the left lateral wall with no extra-vesical extension. Cystoscopy revealed a muscle invasive mass protruding into the bladder lumen, extending from 3-5 o`clock. Initial histopathology showed poorly differentiated urothelial neoplasm. She underwent an uneventful radical cystectomy with urinary diversion to ileal conduit. Final histopathology revealed SCCB. Patient is followed up in the oncology department.

Keywords: Urinary Bladder, Neuroendocrine Carcinoma, Small Cell Neuroendocrine Carcinoma.

INTRODUCTION:

Small cell carcinoma of the bladder (SCCB) is a rare, poorly differentiated neuroendocrine epithelial tumor associated with a more aggressive behavior and poorer outcome than bladder transitional cell carcinoma (TCC). It is mostly diagnosed at advanced stage and generally believed to have a high metastatic potential. Current knowledge of this disease is limited and was based mainly on retrospective investigations. The disease was initially described in 1981by Cramer. Bladder small cell carcinoma (SCC) is frequently found combined with other histological forms of bladder cancer: TCC, adenocarcinoma and squamous cell carcinoma. The pathogenesis of primary SCCB is unknown. However, several hypotheses were proposed to explain the origin of SCC in the bladder.[1] Primary neuroendocrine carcinomas of Urinary Bladder account for <1% of bladder malignancies. Neuroendocrine tumors of urinary bladder comprise of carcinoid tumors, large cell neuroendocrine carcinomas, and small cell carcinomas. They are usually more prevalent in male patients in the ratio of 2:1-10:1.'However, this case report presents a case of small cell neuroendocrine carcinoma of the urinary bladder in a female.

CASE REPORT:

A seventy year old female presented with a history of recurrent urinary tract infections and hematuria for last six months. The general physical examination was unremarkable except for mild pallor. The systemic examination revealed a third degree utero-vaginal prolapse. She was a known case of diabetes mellitus and was on oral hypoglycemic (Biguanide). The investigations revealed that her hemoglobin was 10 gm. /dl and she had good glycemic control. Her renal profile and serum electrolytes were normal. Ultrasound scan revealed a mass inthe urinary bladder along the left lateral wall. CT scan showed a large lobulated mass in bladder measuring 6.0 x 5.0 x 7.6 cm (AP x TS x CC) along the left lateral wall, infiltrating the muscles with no extra-vesical extension (Figure 1)

Figure 1
CT-scan showing mass in the bladder

On Cystoscopy, a muscle invasive mass was found protruding into the bladder lumen, extending from 3-5 o'clock, just above the bladder neck. As complete resection was not possible, multiple biopsies were obtained with a resectoscope. The Histopathology showed poorly differentiated urothelial neoplasm. She underwent an uneventful radical cystectomy with urinary diversion to ileal conduit. Final histopathology revealed small cell neuroendocrine tumor of urinary bladder with sensitivity to synaptophysin, chromogranin, (Figures 2 and 3) thyroid transcription factor-i (TTF-1) and CD 56. On microscopic examination it was revealed that the tumor had poorly differentiated papillary and nodular growth pattern. Her chemotherapy was planned.

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Figure 2a
Histopathology of specimen shows sensitivity to Chromogranin

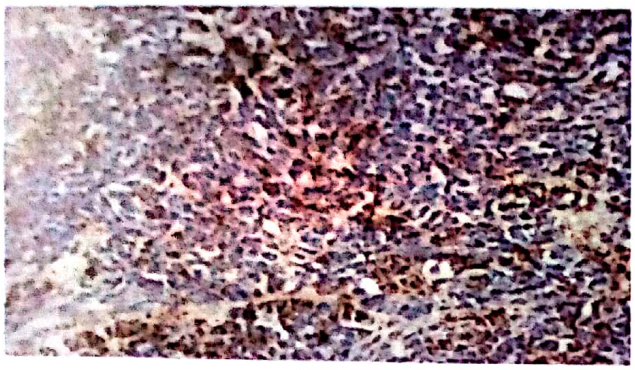
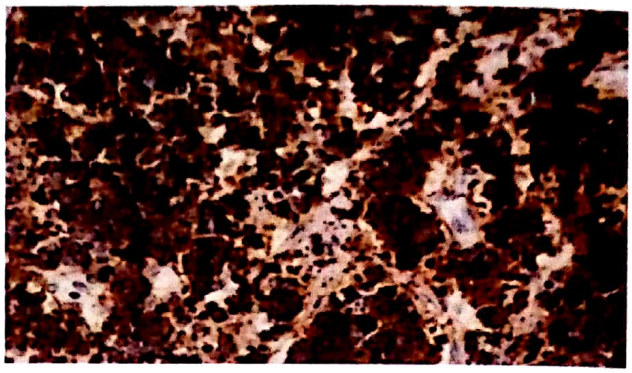


Figure 2b
Histopathology of specimen shows sensitivity to Synaptophsin



DISCUSSION:

Neuroendocrine tumors occur in the epithelium lined organs, especially of the gastro-intestinal and respiratory tracts. They can arise in the urinary bladder as well, but very rarely. They are classified as "Small Cell Carcinomas" (the most common, with over 100 cases reported), atypical and typical Carcinoid"(less common) and large cell neuroendocrine carcinomas" (very rare).[2,3] Small cell cancer of the urinary bladder is documented to have a mean frequency of 0.7% and a range between 0.35% and 1.8% . Searching done up till 2011 showed that the reported incidence is less than 1-9/1,000,000 habitant. Since 1980, less than 1000 cases of SCCB have been diagnosed and reported in the literature up to July 2011. The demographic characteristics of SCCB are similar to those seen in patients with transitional cell carcinoma (TCC). The majority of patients are male, with a mean sex ratio of 5:1, and a range between 1:1 tol6:1. Most patients are in the sixth to seventh decade. Mean age at the time of first diagnosis is 67 years; ranging between 32 to 91 years Like TCC, SCCB is often associated with a smoking history (in 65 to 79% of the cases) . White patients represent the vast majority of cases (74% to 97%).

The first small cell carcinoma of neuroendocrine origin was reported by Cramer in 1981 .[4]Pure small cell neuroendocrine tumor of the bladder is infrequent and is usually mixed with another histological subtype most commonly urothelial carcinoma. The tumor presents late, behaves more aggressively than urothelial carcinoma and carries a poor prognosis.[5]

Pathogenesis of SCCB is not well defined. However, several hypotheses were proposed to explain the origin of SCC in the bladder. Researchers have postulated the origin of this unique and rare neoplasm to be differentiation of the multi-potent stem cells, or sub-mucous neuroendocrinecells.[6]One hypothesis states urachal epithelium, a remnant of the fetal excretory canal: allantoismay be its origin.[7] It usually presents as an advanced cancer (70% in T3 and 16.3 % in T4 stage) at the time of diagnosis.[8]The 5-year survival rate has been reported to be 8. 1-19%, yielding a poor prognosis.[9] Diagnosis is made ontrans-urethralresection for tissue sampling. Neuroendocrine tumors are sensitive to Neuron-Specific Enolase (NSE), Keratin Cam 5.2, Synaptophysin, Chromogranin Q, Positive in one half of small cell and 5% of urothelial carcinoma), Polypeptide Glycoprotein 9.5, Thyroid Transcription factor-i (positive in 40%), p53 and Ki67.[10]

There is no established protocol to treat the disorder as yet. A combination of therapies:surgical, adjuvant/neo-adjuvant chemotherapy and radiation are being used depending upon patient's state of health and the stage of tumor at the time of presentation. There is a consensus that TURBT (Transurethral Resection of Bladder Tumor) may have better prognosis than chemotherapy. Thus primary SCCB is a rare and aggressive tumor. In more than 50% of the cases, the diagnosis is performed at advanced stages III/IV. Demographic and clinical features are comparable to those of bladder TCC. The origin of disease is not clearly defined; but the multi potent theory is the most accepted. Criteria of pathological diagnosis and

logical work-up are similar to those of SCLC. xistence of SCCB with other types of carcinoma ommon. Immunochemistry plays a major role e diagnosis using the markers of neuroendocrine ors. The staging system mostly used is the M-staging system of bladder TCC. The best eatment for this tumor is not established for certain; nly one prospective study has been published up ll now. The strategy of therapy was extrapolated from SCLC. In surgically resectable disease, the management should include multimodal therapy with chemotherapy first followed by radical resection or radical radiotherapy. In advanced disease, chemotherapy using platinum agent (cisplatin in fit patients) is the mainstay treatment. The prognosis of SCCB is poor. Pure small cell histology have worse prognosis than the mixed small cell histology. Further investigations are needed to improve our knowledge in the diagnosis and treatment of this rare disease.

CONCLUSION:

The reported patient is alive and is being followed up in the oncology department. Small cell carcinoma of the bladder (SCCB) is a rare, poorly differentiated neuroendocrine epithelial tumor associated with a more aggressive behavior and poor outcome. It is mostly diagnosed at advanced stage and generally believed to have a high metastatic potential. Current knowledge of this disease is limited and is based mainly on retrospective investigations.

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