Journal of Pathology of Nepal (2015) Vol. **5**, 869 - 871

Journal of
PATHOLOGY
of Nepal

www.acpnepal.com

Case Report

Primary small cell carcinoma of urinary bladder

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Keywords:

Small cell carcinoma;
Urinary bladder;
Urothelial carcinoma.

ABSTRACT

Primary pure small cell carcinoma of the urinary bladder is an extremely rare and highly aggressive tumor with an average five-year survival rate of less than 10% as cited by multiple case reports. It accounts for about 0.5-1% of all bladder tumors. We present the case of an 87-years-old man; smoker hospitalized in the Department of Urology, from the Institute of Medicine, Kathmandu for intermittent painless hematuria. Ultrasonography showed a sessile tumoral growth. Transurethral resection of the tumor mass was performed and tissue fragments were sent to the pathologic lab to establish the histologic type, the degree of differentiation and invasion. Fragments of the tumor were fixed in 10% formaldehyde, paraffin embedded and processed as standard technique; the sections were stained with H and E and immunohistochemically with NSE and Cytokeratin. A diagnosis of small cell carcinoma was established. Because of aggressive behavior and distinct treatment, the pathologist should watch out for the presence of small cell carcinoma component.

INTRODUCTION

Primary small cell carcinoma of the bladder is a rare entity accounting for less than 1% of all bladder tumors.[1] The first case was described in 1981 by Cramer et al.[2] Small cell carcinomas of the urinary bladder are frequently found combined with other histological forms of bladder cancer such asurothelial, adenocarcinoma and squamous cell carcinoma.The pathogenesis of primary small cell carcinoma of bladder (SCCB) is unknown. However, several hypotheses were proposed to explain the origin of small cell carcinoma (SCC) in the bladder. The most important hypothesis was: the origin of SCCB may be a multipotential common stem cell.[3] Because of the rarity of small cell carcinoma, there is no standard treatment of the disease. We hereby report a case of primary small cell carcinoma of urinary bladder who presented with intermittent painless hematuria.

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Case Report

An 87-year-old smoker man was admitted to TUTH with a 3-month history of intermittent painless hematuria. There was no mass palpable in the pelvic area. An ultrasonography of the pelvis showed sessile tumoral growth in the urinary bladder along with bilateral hydronephrosis. The patient's urine showed plenty of RBCs on cytology and negative growth on culture.The transurethral resection of the bladder tumor (TURBT) removed small bits of the tumor tissue. Tissue fragments were sent for histopathological examination to establish the histologic type, the degree of differentiation and invasion. Fragments of the tumor were fixed in 10% formaldehyde, paraffin embedded and

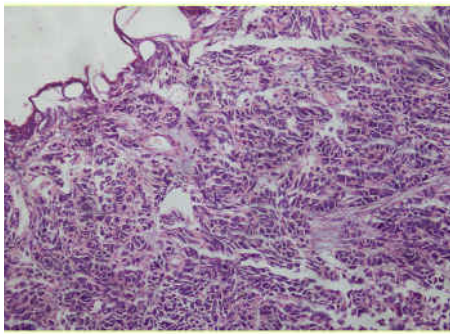

Figure 1: *Tumor cells in sheets and nests invading the lamina propria (HE stain; X100).*

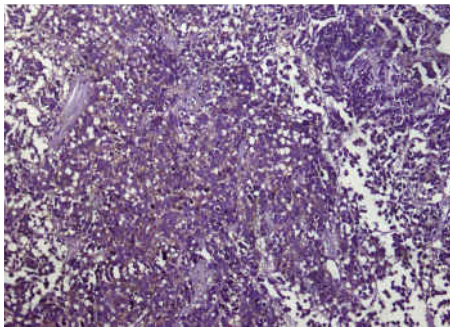

Figure 3: *Tumors cells are positive for NSE. (HE stain; X40).*

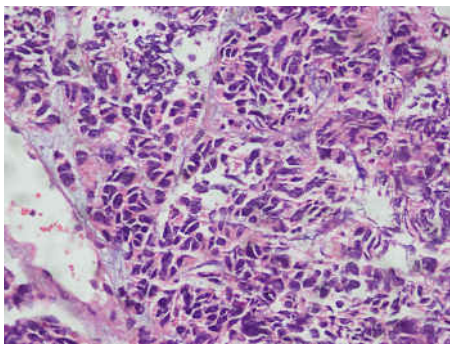

Figure 2: *Mild to moderately pleomorphic tumor cells with scant cytoplasm, round to oval nuclei with stippled chromatin and inconspicuous nucleoli (HE stain; X400)..*

processed as standard technique; the sections were stained with H and E and immunohistochemically with NSE and Cytokeratin. Hematoxylin and eosin slides were examined under light microscopy which revealedtumor cells in sheets and nests invading the lamina propria (fig.1). These tumor cells showed mild to moderate pleomorphism with scant amount of cytoplasm. Nuclei were round to oval with stippled chromatin and inconspicuous nucleoli (fig.2). Few mitotic figures were seen. Immunohistochemistry was performed which was positive for neuron specific enolase (NSE) (fig. 3) and negative for pancytokeratin.

Based on these features a diagnosis of Small cell carcinoma of the urinary bladder was given. Complete metastatic workup of the patient was performed. X-ray and CT scan of the lung was normal.

DISCUSSION

Neuroendocrine tumors can arise in almost all epithelium-containing organs and are commonly encountered in the respiratory and gastrointestinal tract while involvement of the urinary bladder is very rare. Small cell carcinoma of the bladder is similar to small cell carcinoma of the lung in clinical behavior, with wide age range (20-91 years) and 3-5:1 male female ratio. Cigarette smoking, bladder calculi and long-term cystitis are thought to be the etiological factors involved in its pathogenesis.[4] Patients typically present with hematuria in 88% and history of smoking cigarettes in 65% cases. Tumors are usually large and polypoid or nodular and may have an ulcerated surface. Other symptoms such as local irritation, pelvic pain and urinary obstruction are also reported in the literature. Rarely, patients can develop distant metastases or paraneoplastic syndromes.[5] The present patient was also a known chronic smoker and presented with hematuria only. No evidence of distant metastasis, paraneoplastic syndrome or primary neuroendocrine tumor of other organ was detected.Small cell carcinomas of the urinary bladder are mixed with classic urothelial carcinomas or adenocarcinomas of the bladder in 68% cases but the present case did not reveal evidence of urothelial carcinoma. Sometimes, features of metastatic small cell carcinoma of lung origin are indistinguishable from small cell carcinoma urinary bladder on the basis of histology alone. Immunohistochemistry helps to differentiate between them and other vast differential diagnosis such as high-grade urothelial carcinoma, lymphoma, carcinoid and lymphoepithelial-like carcinoma from lung.[4]

Neuroendocrine markers, such as chromogranin A, synaptophysin, CD56, and neuron-specific enolase, are often focal or diffusely positive for these tumors by immunohistochemical method. A cocktail of cytokeratin markers is often nonreactive, but low molecular cytokeratin, CAM5.2, and epithelial membrane antigen are mostly positive. The present case was also positive for NSE and negative for cytokeratin cocktail.

Because of the rarity of small cell carcinoma bladder, there is no standard treatment of the disease.Therapeutic modalities vary and include transurethral resection, cystectomy, radiation therapy and systemic chemotherapy.[6] Surgical resection (radical cystectomy and extended pelvic lymphadenectomy) alone is unlikely to be curative, unless the tumor is confined to the bladder. Combination therapy with adjuvant or neoadjuvant chemotherapy appears beneficial.[7] The prognosis of SCCB is poor. The overall 5-year survival rate in all stages is 19%.[8] Lymph node metastases occur in 66% of cases, with distant metastases occurring in the liver, bone and lung.[4] The pure small cell histology has poorer outcome than the mixed small cell histology.

CONCLUSION

Though rare, primary small cell carcinoma bladder should be considered as one of the differential diagnosis of urinary bladder tumor.Because of aggressive behavior and distinct treatment, the pathologist should watch out for the presence of small cell carcinoma component.

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