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Case Report

Primary Small Cell Neuroendocrine Carcinoma of Bladder – A Rare Diagnostic Entity

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Abstract

Primary small cell carcinoma of the bladder is very rare pathological entity, follows an aggressive course and carries poor prognosis. The literature carrying these articles are scarce and due to which it poses a diagnostic challenge to the radiologist and urologists. Herein, we present a case of small cell carcinoma of urinary bladder in a 75 year old male patient initially reported as poorly differentiated urothelial carcinoma on transurethral resection of bladder tumor specimen to emphasize its rarity as well as the role of immunohistochemistry to differentiate between the two.

Key words: small cell carcinoma; bladder; immunohistochemistry

Introduction

Primary small cell neuroendocrine carcinoma of the urinary bladder is a rare histological type shows poor differentiation and behaves in a highly aggressive manner. It accounts to 0.3- 0.7% of all bladder tumors. [1, 2] Neuroendocrine carcinomas predominantly occur in respiratory and gastrointestinal tract and very rarely in the urinary bladder.

Due to rarity of the tumor, its pathogenesis is unknown. Urothelial cell origin, stem cell theory and malignant transformation of neuroendocrine cell of urinary bladder lay the hypothesis of its pathogenesis. [1]

We hereby report a case of small cell carcinoma of urinary bladder in a 75 year old male patient initially reported as poorly differentiated urothelial carcinoma on transurethral resection of bladder tumor specimen to emphasize its rarity as well as the role of immunohistochemistry to differentiate between the two.

Case History

A 75year old male patient presented with gross haematuria and pelvic pain since a month. He is a chronic smoker with 40-pack year index. His family history is insignificant. Ultrasonography showed 2x2 cm broad based solid heteroechoic mass along the left lateral wall of urinary bladder.

His urine examination revealed presence of occult blood with microscopic examination of 3-4 RBC/ HPF. Other laboratory parameters were within normal limits. Following which he underwent transurethral resection of the bladder tumour. Grossly, we received multiple grey white to grey brown soft tissue pieces measuring 2x1.5x1.0 cm. entirely processed in one block. On pathological examination with haematoxylin and eosin staining demonstrated sheets and nests of loosely cohesive small round to oval cells with hyperchromatic coarsely granular nuclear chromatin and scanty cytoplasm invading lamina propria without muscle invasion. Occasional mitotic activity is seen and was reported as High grade poorly differentiated carcinoma with small cell features. [figure 1A-B] Additional pathological findings were marked chronic cystitis with cystitis et glandularis with urothelial carcinoma in situ features. On immunohistochemistry panel, the tumour cells were immunoreactive for CK7, synaptophysin, CD56, Chromogranin and Ki67 and non-immunoreactive for CK20, HMWCK, uroplakin and GATA-3. Morphologic and immunohistochemistry features were consistent with small cell neuroendocrine carcinoma with >95% of neuroendocrine component. The patient was planned for radical cystectomy, for which he refused after being informed on the associated morbidity risk and eventually succumbed to the disease 2 months after the diagnosis.

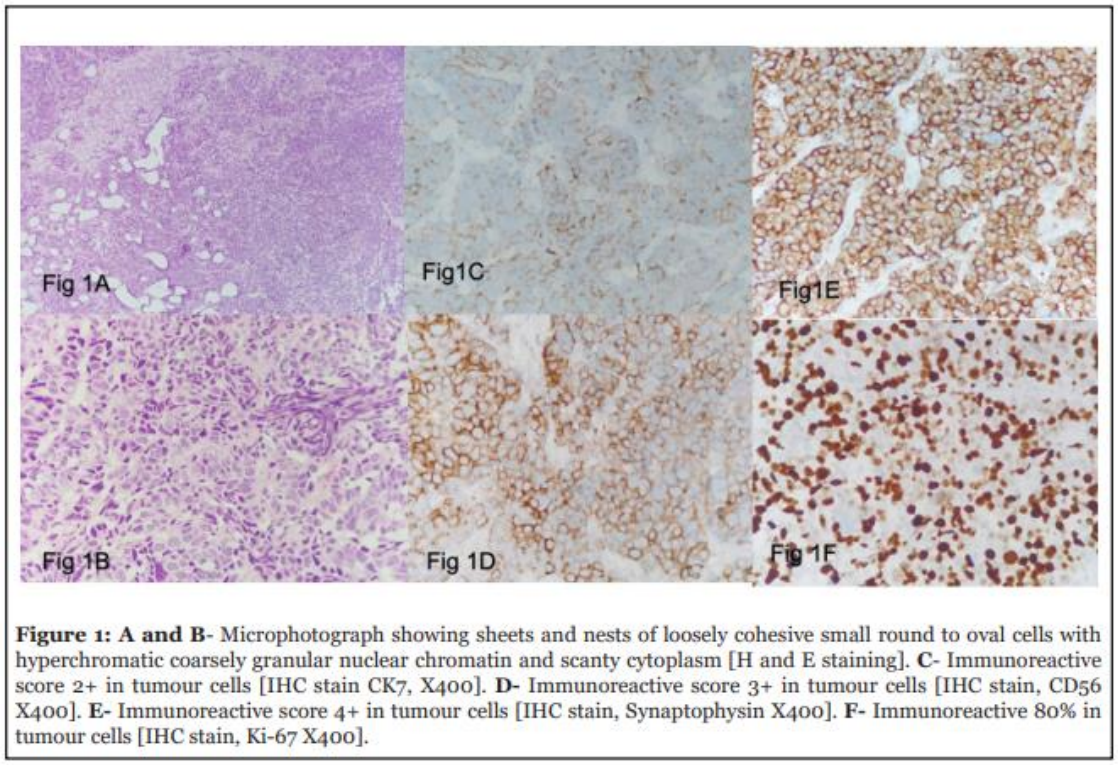

Figure 1: A and B- Microphotograph showing sheets and nests of loosely cohesive small round to oval cells with hyperchromatic coarsely granular nuclear chromatin and scanty cytoplasm [H and E staining]. **C**- Immunoreactive score 2+ in tumour cells [IHC stain CK7, X400]. **D**- Immunoreactive score 3+ in tumour cells [IHC stain, CD56 X400]. **E**- Immunoreactive score 4+ in tumour cells [IHC stain, Synaptophysin X400]. **F**- Immunoreactive 80% in tumour cells [IHC stain, Ki-67 X400].

Figure 1A-B: Microphotograph showing sheets and nests of loosely cohesive small round to oval cells with hyperchromatic coarsely granular nuclear chromatin and scanty cytoplasm [H and E staining]
Figure 1C: Immunoreactive score 2+ in tumour cells [IHC stain CK7, X400]
Figure 1 D: Immunoreactive score 3+ in tumour cells [IHC stain, CD56 X400]
Figure 1 E: Immunoreactive score 4+ in tumour cells [IHC stain, Synaptophysin X400]
Figure 1 F: Immunoreactive 80% in tumour cells [IHC stain, Ki-67 X400

Discussion

Neuroendocrine carcinoma presumably arises from the epithelium lined organs like respiratory tract and gastrointestinal organs, urinary bladder being the rarest site of it.

Most common symptom of presentation is haematuria in 88 % of cases. Other symptoms include local irritation, pelvic pain and urinary obstruction. These patients rarely have distant metastasis or paraneoplastic syndrome. [3]

Usually small cell carcinoma of the urinary bladder is admixed with the urothelial carcinoma in 68% of the cases, but in our present case there was no evidence of urothelial carcinoma and it was purely small cell neuroendocrine 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, lymphoepithelial-like carcinoma from lung. [4]

Chromogranin A, synaptophysin, CD56, and neuronal-specific enolase, are often immunoreactive for neuroendocrine tumors.

The typical microscopic features are hypercellularity, necrosis, nuclear chromatin crush artefact and mitoses. The present case had typical microscopic and immunohistochemical features appreciated on TURBT. Thus, a definitive diagnosis was rendered considering both the microscopic as well as immunohistochemical features. [3]

the optimal management of NEC is not well defined. Therapeutic modalities vary and include transurethral resection, cystectomy, radiation therapy and systemic chemotherapy. 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. [5]

Conclusion

The unknown etiology and natural history of small cell carcinoma of the urinary bladder represent a challenge both to the pathologist and urologists for its diagnosis and treatment respectively. The diagnosis of this malignancy mainly depends on histopathology, immunohistochemistry and cytomorphological characteristics. Multimodal approach to treatment is recommended, although the prognosis is poor. Long-term follow-up is warranted due to the risk of local recurrence and distant metastasis.

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