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A patient with neuroendocrine carcinoma of the urinary bladder and paraneoplastic degenerative parencephalitis: A case report and review of the literature ☆

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Abstract
Neuroendocrine carcinomas of the bladder (small cell, large cell, typical and atypical carcinoids) are rare and usually co exist with urothelial carcinoma. As in small cell carcinoma of the lung, various paraneoplastic neurologic disorders can occur although they are even less frequent. Here we report the case of a 63 year old man with small cell carcinoma of the urinary bladder and with a paraneoplastic neurologic disorder.

1. Introduction

Neuroendocrine carcinomas can arise in almost all epithelium-containing organs, most commonly encountered in the respiratory and gastrointestinal tract. Among the histological patterns of urinary bladder tumors, neuroendocrine tumors can also be found. Although rare, they can be distinguished and differentiated as small cell carcinomas (SCUC), large cell neuroendocrine carcinomas (LCNEC), typical and atypical carcinoids. Since the first report of a case of SCUC by Cramer [1], the cumulative number reported has risen significantly. The estimated incidence is roughly 500 new cases annually [2].

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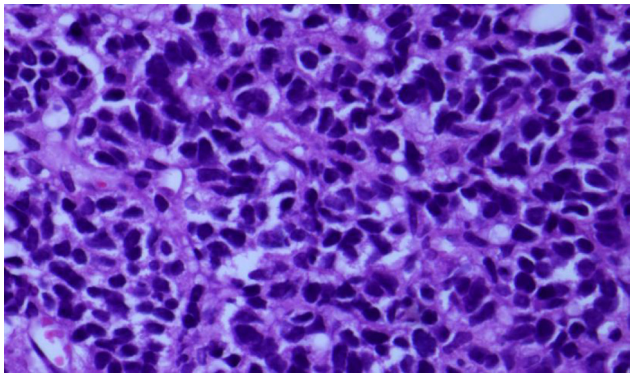

Figure 1 Small cell tumor with patterneless pattern.

What is even rarer is the co-existence of a paraneoplastic neurologic disorder (PND) in this setting. We know that the most common PND encountered in SCLC is the Lambert-Eaton myasthenic syndrome which affects 3% of patients. For other solid tumors the incidence of PND is less than 1% [3].

The purpose of this review is to present a case of SCUC with a PND.

2. Case report

A 63 year old man was referred to our institution with recurrent episodes of painless haematuria over an one month period. The patient had a history of diabetes mellitus, hypertension and hyperthyroidism. He reported moderate alcohol consumption and was a smoker of 80 pack years.

A cystoscopy revealed a bladder tumor and a biopsy specimen was obtained. Subsequently staging was performed with contrast enhanced total body computed tomography. No evidence of metastatic disease was found except an enlargement of an adjacent lymph node to the bladder. A radical cystoprostatectomy was performed which revealed a 4×3 cm mass that invaded the entire bladder wall, pericystic fat and blood vessels as well as an adjacent lymph node (T4N1M0).

The mass cytomorphologic features demonstrated small cells, hypercellularity, necrosis, atypical nuclear hyperchromatism and minimal cytoplasma (Figure 1). Immunohistochemical staining was positive for CK 20, CD 56, CK 7, CK 8/18, CEA, TTF-1, S-100, synaptophysin, chromogranin and negative for PSA (Figures 2 and 3). Ki-67 was positive in 60% of the neoplastic cells. It was defined as a small cell carcinoma of the urinary bladder, high grade, with neuroendocrine differentiaton. In light of these findings, the patient underwent a bronchoscopy which revealed macroscopically normal mucosa. Brushing and washing cytology samples were analyzed with no signs of malignancy. An octeotide scintigraphy did not identify any systemic lesions.

One month after surgery the patient was admitted to hospital due to dysarthria, ataxia, opsoclonus, instability and muscle weakness. On physical examination he had positive Romberg sign, nystagmus in all directions, positive Barre sign on his left upper extremity (LUE), decreased muscle strength (2/5) on his right lower extremity (RLE) and a negative Babinski sign. He was alert and orientated and had no fever. Review of the other systems revealed no abnormality. The patient's lab work (complete blood count, liver function tests, electolytes, C-reactive protein, D-Dimers, partial thrombin,

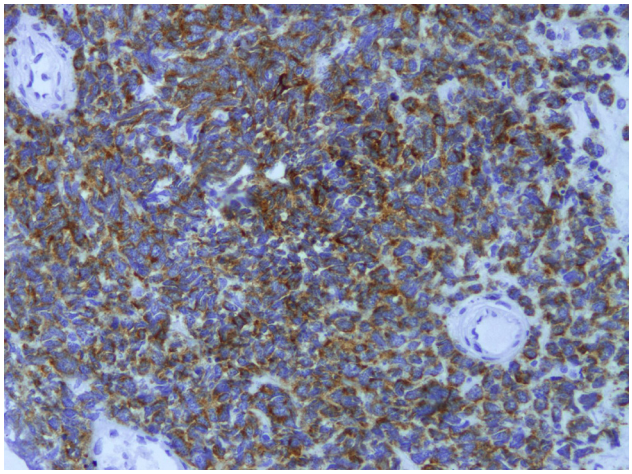

Figure 2 Tumor cells positive for synaptophysin.

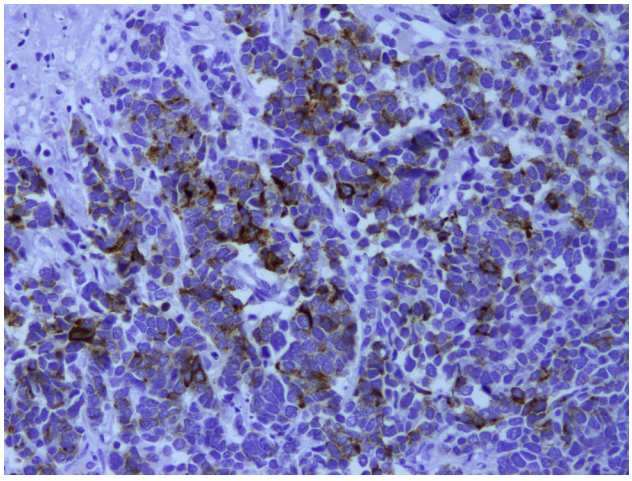

Figure 3 Tumor cells positive for chromogranin.

partial thromboplastin time, international normalized ratio) were unremarkable. A brain MRI revealed chronic ischemic changes. He underwent a diagnostic lumbar puncture and cerebrospinal fluid (CSF) was sent for analysis. There was mild leukocytosis, PCR for HSV being negative. CSF cytology was negative for malignant cells. The autoantibodies Anti-Yo and Anti-Hu were detected in the CSF. Based on the presenting symptoms, the work up and the findings, a neurological consultation was ordered and a diagnosis of paraneoplastic degenerative parencephalitis was deduced.

One month later, it was decided to administer 6 courses of «adjuvant-like» chemotherapy with carboplatin AUC 5 day 1 and etoposide 100 mg/m^2/day Days 1-3 q 21 days. Upon completion of cycle 3 there was a significant improvement in his neurological symptoms with only a persistent muscle weakness on his RLE (2/5) and opsoclonus. Restaging performed with total body contrast enhanced computer tomography revealed no signs of reccurence. An additional three courses of carboplatin and etoposide were administered uneventfully (Table 1).

One month after completion of his therapy the patient is still alive with no sign of reccurence, apart from a mild muscle weakness on his RLE (4/5).