



## Case Report

## Paraplegia due to medullary compression caused by a large cell neuroendocrine carcinoma of the urinary bladder: A case report

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## ABSTRACT

**Background:** Neuroendocrine carcinomas of the urinary bladder are rare tumors, estimated at less than 1% of urinary bladder malignancies. They are mainly represented by small cell neuroendocrine carcinoma, while large cell neuroendocrine carcinoma (LCNEC) is rarely reported.

**Case presentation:** We report a case of a 49-year-old man presenting paraplegia caused by a metastatic urinary bladder LCNEC, which was managed with palliative external beam radiotherapy (EBRT) associated with MVAC chemotherapy, including methotrexate, vinblastine sulfate, doxorubicin hydrochloride (Adriamycin), and cisplatin. At the last follow-up of one year after his admission, there was a symptomatic improvement in the pain intensity.

**Conclusion:** LCNEC of the bladder was first described in 1986, and, until now, less than 40 cases have been published in the literature. To the best of our knowledge, this is the first case of primary LCNEC of the urinary bladder presenting with paraplegia.

## 1. Introduction

Neuroendocrine carcinomas of the urinary bladder are rare tumors, estimated at less than 1% of urinary bladder malignancies [1,2]. They are mainly represented by small cell neuroendocrine carcinoma, while large cell neuroendocrine carcinoma (LCNEC) is rarely reported [1,3]. This manuscript, describes a large cell neuroendocrine carcinoma of the urinary bladder presenting with Paraplegia due to medullary compression caused by a metastasis. The work has been reported in line with the SCARE criteria [4].

## 2. Case report

A 49-year-old man presented with sudden onset of paraplegia and pain in the lower extremities for one day. He discloses that he has smoked one pack of cigarettes per day for 30 years. He was otherwise healthy, worked as a tradesman. There was no history of trauma or urinary symptoms. On physical examination, we identified weakness

and loss of sensation in both lower limbs up to the D4 level. The patient had muscle power of 2/5 and 5/5 in the lower and upper limbs, respectively. The whole spine Magnetic resonance imaging (MRI) showed multiple bone metastases in D4, D9, D11, and L4 vertebrae with extradural cord compression at D4 and L4 (Fig. 1). Abdominal contrast-enhanced computed tomography (CT scan) showed a large intraluminal lesion (7 × 5 cm) arising from the left lateral wall of the bladder with an irregular surface and spotted calcification (Fig. 2).

The option of surgical spinal decompression was declined due to the disseminated disease. Hence, he was started on palliative external beam radiotherapy (EBRT). The patient also underwent transurethral resection of the tumor. On microscopic examination, the tumor was composed of large pleomorphic cells with a moderate amount of cytoplasm and coarse nuclear chromatin, organized in trabecular and rosette-like patterns with a high mitotic rate with muscular invasion. On immunohistochemistry, the tumor cells were positively stained for the CD56, NSE, synaptophysin and focally positive for chromogranin. The proliferation index evaluated with Ki-67 was >95% (Fig. 3). Based on those anatomopathological findings, The patient was diagnosed with

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**Abreviation**

LCNEC	Pure large cell neuroendocrine carcinoma
MRI	Magnetic resonance imaging
MVAC	methotrexate, vinblastine sulfate, Adriamycin and cisplatin
NMIBC	non-muscle-invasive bladder cancer
CT scan	contrast enhanced computed tomography



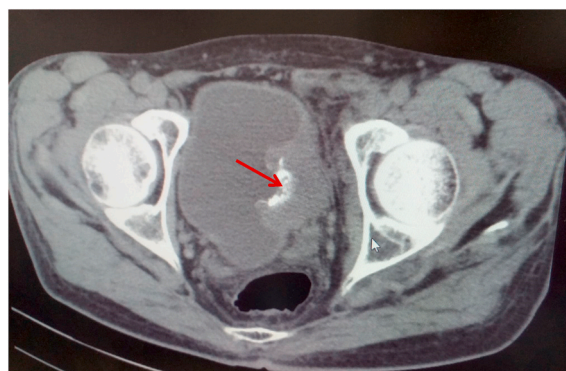
**Fig. 1.** Spine MRI suggestive of multiple bone metastases in D4, D9, D11, and L4 vertebrae with extradural cord compression at D4 and L4 (red arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

primary LCNEC of the urinary bladder.

A combination of four courses of MVAC chemotherapy, including methotrexate, vinblastine sulfate, doxorubicin hydrochloride (Adriamycin), and cisplatin and EBRT was scheduled. The tumor response was monitored by cystoscopy. A radical surgery, such as cystectomy was not considered because of non-resectable spine metastasis. At the last follow-up of one year after his admission, there was a symptomatic improvement in the pain intensity with the completion of EBRT. Whereas he had muscle power of 2/5 and 3/5 in the lower and upper limbs, respectively.

### 3. Discussion

Neuroendocrine tumors of the urinary bladder are in the majority represented by small cell neuroendocrine carcinoma, followed by carcinoid tumors,



**Fig. 2.** Abdominal CT scan showing large intraluminal mass lesion (7 × 5 cm) arising from the left lateral wall of the urinary bladder, the surface of the lesion is irregular, and associated to a spotted calcification (red arrow). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

while LCNEC tumors are sporadic, first described in 1986, with less than 20 cases reported in the literature [1,2]. The most common age of presentation is after the fifth and sixth decade, with nearly 80% of patients diagnosed after 50 years. Males are more commonly affected than females, with the male: female ratio of nearly 4:1 [3]. The typical symptom is hematuria, followed by lower urinary system symptoms [3,5]. Pusiol et al. reported that most patients diagnosed with LCNEC of the bladder presented hematuria (8/11 patients) [3]. This case is the first case of primary LCNEC of the urinary bladder presenting with paraplegia to the best of our knowledge. Many risk factors have been reported; smoking is the most critical risk factor [2,6].

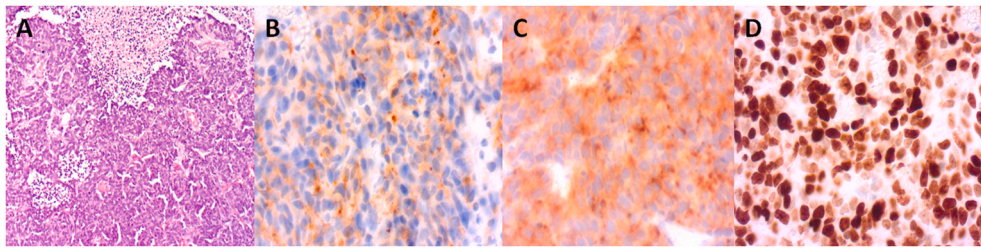
Many authors have studied tumor formation and reported several theories.

The most accepted is the multipotent stem cell theory. According to this theory, multicentric cancer cells develop with neuroendocrine differentiation during the carcinogenic process in the bladder [7,8].

Several studies have shown that the natural history of LCNEC of the bladder differs from that of urothelial carcinoma. Therefore the treatment strategy may be different from the urothelial carcinoma of the bladder [9].

Anastasios et al. reported that 75–85% of patients with bladder cancer present with non-muscle-invasive bladder cancer (NMIBC), a disease confined to the mucosa (stage Ta, carcinoma *in situ*) or submucosa (T1) [10]. However, in LCNEC of the urinary bladder, most of the patients presented an advanced tumor stage (pT3) with lymph node invasion, and 25% of patients presented distant metastases at the time of diagnosis. LCNEC tumors of the urinary bladder are often diagnosed at an advanced clinical stage, explicated by the aggressive nature of the disease and inconspicuous clinical manifestations [9].

Some authors reported the best overall survival for patients who received cystectomy, chemotherapy, and radiotherapy for neuroendocrine tumors of the bladder [8,9]. For Small-cell carcinoma of the urinary bladder, the treatment is mainly extrapolated from small cell carcinoma of the lung. The National Comprehensive Cancer Network's guidelines of 2015 recommended surgery and chemotherapy, with or without radiotherapy for non locally advanced tumor, however; chemotherapy alone is recommended for metastatic tumor [11]. In the case of LCNEC of the bladder, there is no standard treatment or guidelines because of the limited published cases. None of the published cases showed the benefit of surgery in the case of locally advanced and non-resectable metastatic tumors [9,11]. Therefore, we decided to treat this case of locally advanced and metastatic LCNEC of the bladder using chemotherapy and radiotherapy without surgery. Due to its aggressive nature, the 3-year overall survival of LCNEC of the bladder is lower than 25% [9].



**Fig. 3.** Microscopically, the tumor was composed of large pleomorphic cells with a moderate amount of cytoplasm and coarse nuclear chromatin, organized in trabecular and rosette-like patterns. (HEX200) (a), Immunohistochemical analysis demonstrated that tumor cells were diffusely positive for synaptophysin(b), chromogranin(c), and a proliferation index evaluated with Ki-67 up to 95%(d).

#### 4. Conclusion

LCNEC is an extremely rare and aggressive disease. The overall prognosis is poor, and most patients present with advanced tumor stage at diagnosis. Further investigations are needed in order to establish an optimal treatment for this tumor.

#### Provenance and peer review

Not commissioned, externally peer reviewed.

#### Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. approval references approved by Sahloul hospital ethic committee: U2341.

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#### Informed consent

The patient provided informed written consent prior to submission of this manuscript.

#### Article guarantor

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Wiem Majdoub– Editing of manuscript, data collection, Anatomopathology analysis.

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Sonia Dziri– Data collection, Editing of the manuscript.

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Mehdi jaidane– Editing of manuscript, data collection.

Rahul Gupta– Editing of manuscript, literature review, drafting the manuscript.

Najmeddine jalleli– manuscript correction, supervision of the manuscript.

Awatef Azzabi – Supervision of the manuscript, manuscript correction.

#### Registration of research studies

1. Name of the registry:
2. Unique Identifying number or registration ID:
3. Hyperlink to the registration (must be publicly accessible):  
This is not applicable, because this is a case report.

#### Declaration of competing interest

The authors declare no conflict of interest.

#### Acknowledgements

Not applicable.

#### Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.amsu.2021.102475>.

#### Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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