African Urology 2023;3:50-52
https://doi.org/10.36303/AUJ.0048
Open Access article distributed under the terms of the
Creative Commons License [CC BY-NC 3.0]
http://creativecommons.org/licenses/by-nc/3.0

AFRICAN UROLOGY
ISSN 2710-2750 EISSN 2710-2750
© 2023 The Author(s)
CASE REPORT

Small cell neuroendocrine tumour of the bladder: a case report

S Chetty, K Makamba, LD Scheepers

Division of Urology, Port Elizabeth Provincial Hospital, South Africa

Corresponding author, email: chetty.srikesh@gmail.com

Neuroendocrine tumours of the bladder are rare, with an incidence reported at less than 1% of all bladder tumours. We report on a case of small cell neuroendocrine tumour in a 51-year-old male. The diagnosis was made after an initial resection of a bladder mass. He received four cycles of neoadjuvant chemotherapy resulting in a positive response initially, but was noted to have progression of disease prior to planed radical cystectomy.

Keywords: small, cell, neuroendocrine, bladder, tumour

Case report

A 51-year-old male from the western part of the Eastern Cape province of South Africa presented to the urology outpatients department with a three-month history of painless intermittent visible haematuria and irritative lower urinary tract symptoms. He previously smoked and had a 10-year pack history. He was HIV-positive with a suppressed viral load on first-line antiretrovirals since 2019.

He was in a good state of health with an unremarkable general examination. His abdomen was soft and no masses were palpable. A digital rectal exam was done and an enlarged, smooth prostate was noted. His urogenital examination had no abnormal findings.

The side room urine analysis found 3 + blood, 1 + protein. A bedside abdominal ultrasound was performed which showed a large irregular mass on the left lateral wall of the bladder with no hydroureteronephrosis. The urine cytology was negative for high-grade urothelial carcinoma. Blood parameters were within normal limits.

He subsequently underwent a white light cystoscopy. At the cystoscopy a large bladder mass was identified on the left lateral wall of the bladder and a complete resection was performed. Histology showed a high-grade carcinoma containing a neuroendocrine differentiation of the bladder with a sarcomatoid component. There was no deep muscle represented in the specimen.

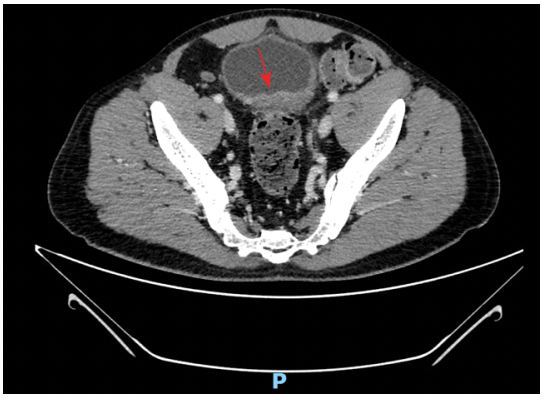

Figure 1: Initial CT demonstrating bladder mass as indicated by the arrow, prior to chemotherapy

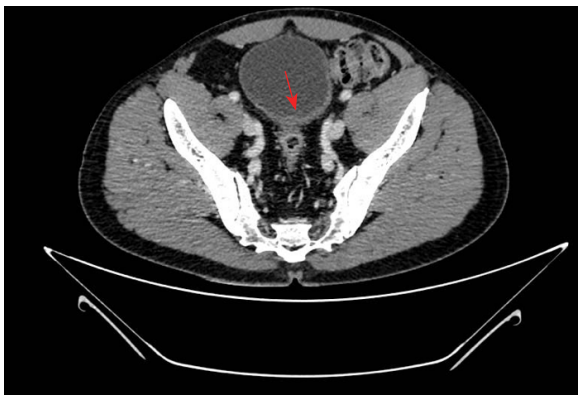

Figure 2: Coronal view of bladder post neo-adjuvant chemotherapy showing residual bladder wall thickening

The staging computed tomography (CT) scan showed posterolateral bladder wall thickening, with no signs of distant metastasis. A repeat cystoscopy was performed after six weeks which found residual bladder tumour and a resection was performed. The repeat histology reported an invasive neuroendocrine carcinoma with small cell morphology and no deep muscle involvement. The tumour stained positive for CK7, chromogranin, TTF1 and negative for CK20, which is in keeping with a small cell neuroendocrine carcinoma.

The patient was referred to the oncology department with the intention to initiate neoadjuvant chemotherapy, prior to definitive radical cysto-prostatectomy. He received four cycles of carboplatin with etoposide which was well tolerated. A CT scan was done after completion of neoadjuvant chemotherapy. He had a good response, with reduced tumour bulk and no extravesical spread.

The patient unfortunately did not return for the radical surgery and was lost to follow-up.

He re-presented to the oncology outpatient's department, two months post-chemotherapy, complaining of headaches and non-specific abdominal pain. He was admitted and an abdominal ultrasound showed a new liver lesion. A biopsy of the liver lesion was performed, however, the histology was not representative of the lesion.

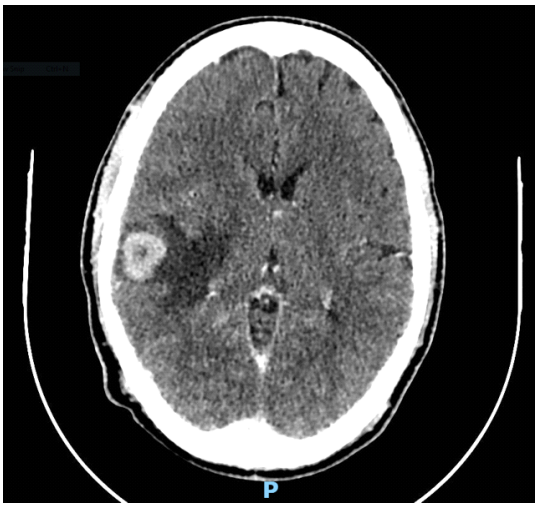

Figure 3: Suspected brain metastasis

During this hospital admission the patient developed new-onset seizures and a dense left-sided hemiplegia.

The subsequent CT brain showed two large brain lesions, thought to be metastasis.

The patient was restaged as a metastatic bladder cancer with poor prognosis. In consultation with the family, the decision was taken to continue with palliative therapy. The patient was discharged for home-based care.

Discussion

Primary neuroendocrine tumours of the bladder are rare tumours with an incidence reported as less than 1% of all newly diagnosed bladder tumors.[1] The index case of a primary bladder neuroendocrine tumour was first reported in 1981 by Abenoza et al.[2]

In 2016, the World Health Organization (WHO) classified neuroendocrine tumours of the bladder into small cell neuroendocrine carcinoma, large cell neuroendocrine carcinoma, well differentiated neuroendocrine tumours and paraganglioma. Neuroendocrine tumours of the bladder are regarded as high grade, biologically aggressive tumours with patients generally exhibiting a poor prognosis.[3]

Small cell carcinomas are the most common type of neuroendocrine tumours of the bladder. It favours a male predominance and typically affects patients over the age of 60. At diagnosis, approximately 60% of patients have metastasis, speaking to the aggressive nature of the tumour.[3]

Risk factors include tobacco smoking, chronic cystitis and bladder calculi. Patient presentation typically consists of haematuria and irritative lower urinary symptoms.[4]

The aetiology of neuroendocrine tumours of the bladder is not known. The prevailing theory is that the cell of origin is a multipotential undifferentiated cell or stem cell.[3] Other theories propose that it arises from the enterochromaffin cells (kulchitsky cells) or from cells which are not usually present in urinary bladder mucosa.[3]

The microscopic appearance of small cell neuroendocrine carcinomas consists of sheets or nests of small or intermediate cells with moulding, scant cytoplasm, inconspicuous nucleoli and evenly dispersed salt and pepper chromatin. Immunohistochemical stains typically show high positivity for chromogranin A, synaptophysin and CD 56 which collectively have a specificity of 96% and a sensitivity of 100% in distinguishing neuroendocrine tumours from urothelial carcinomas.[3]

Chromogranin A has a reduced sensitivity for large cell neuroendocrine tumours vs small cell neuroendocrine tumours. Other stains supporting the diagnosis of small cell neuroendocrine tumours include CD 7, TTF-1, neuron specific enalase, CAM 52, Keratin 7 and epithelial membrane Antigen (EMA). CK 20 is generally negative in small cell neuroendocrine bladder tumours, but positive in 40–70% of urothelial carcinomas.[3]

Due to the low incidence of small cell neuroendocrine carcinoma (SCC), it is difficult to identify a standard treatment guideline. From our literature search, patients are categorised into localised and metastatic disease.[4]

For patients with localised disease, our literature review recommends systemic chemotherapy followed by either a radical cystectomy or radiation therapy.[4] This was first proven beneficial by Anderson et al. who reported that patients receiving preoperative chemotherapy had an improved cancer-specific survival as opposed to those who underwent an initial cystectomy (78% vs 36%).[5] Due to the lack of guidelines for SCC, most chemotherapy regimens are extrapolated from small cell lung cancer protocols. A platinum-based chemotherapy agent is usually combined with etoposide. Cisplatin is recommended, however carboplatin is an alternate if cisplatin is contraindicated or unavailable.[4]

Sroussi et al. performed a retrospective cohort study, looking at all neuroendocrine carcinomas of the bladder in 18 French institutes between 1997–2017. They found that the use of carboplatin-based chemotherapy showed an inferior outcome when compared with cisplatin-based chemotherapy. They also discovered that during early-stage disease, there was no significant difference in disease-free survival between radical cystectomy vs radiotherapy treatment.[6]

Deuker et al. retrospectively reviewed the SEER database base from 2004 till 2016, looking at patients with variant histology bladder cancer (VHBC) limited to T1N0M0 lesions. The endpoint of interest was cancer-specific survival (CSS) and the effect of radical cystectomy for stage T1 VHBC vs other modalities. They reported a superior five-year CSS in T1 SCC patients who had a radical cystectomy (100%) compared to those who did not (66.8%).[7]

For patients with metastatic disease, the median survival was approximately seven to 13 months. Systemic chemotherapy is the treatment of choice. The agents commonly used are cisplatin, etoposide and carboplatin.[4] Sroussi et al. found no difference in median overall survival in patients with metastasis, receiving cisplatin or carboplatin chemotherapy.[6]

SCC of the lung has a proclivity to metastasising to the brain; for this reason, prophylactic cranial irradiation is routinely done. SCC

of extrapulmonary origin does not share this metastatic preference and routine prophylactic cranial irradiations have no benefit in these patients.[4]

The role of checkpoint inhibitor immunotherapy for treatment of small cell carcinoma is currently being investigated.[4]

In summation, small cell carcinomas of the bladder pose a challenge to clinicians due to the lack of treatment consensus. Where possible, an aggressive approach should be taken in patients with localised disease due to the high risk of metastasis. This case report serves to highlight this risk. More studies are required to further understand SCC and to improve treatment protocols.

Conflict of interest

The authors declare no conflict of interest.

Funding source

No funding was required.

Ethical approval

Written informed consent was obtained from the patient for anonymised use of information and images to be published in this case report.

ORCID

S Chetty https://orcid.org/0000-0002-7407-1704
K Makamba https://orcid.org/0000-0003-4301-1079
L Scheepers https://orcid.org/0000-0001-5788-4546

References

1. Hata S, Tasaki Y. A case of the large cell neuroendocrine carcinoma of the urinary bladder. Case Rep Med. 2013;2013. https://doi.org/10.1155/2013/804136.
2. Coelho HMP, Pereira BAGJ, Caetano PAST. Large cell neuroendocrine carcinoma of the urinary bladder: case report and review. Curr Urol. 2013;7(3):155-9. https://doi.org/10.1159/000356270.
3. Kouba E, Cheng L. Neuroendocrine tumors of the urinary bladder according to the 2016 World Health Organization classification: molecular and clinical characteristics. Endocr Pathol. 2016;27(3):188-99. https://doi.org/10.1007/s12022-016-9444-5.
4. Siefker-Radtke AO, Pinney CP, Abrahams NA, et al. Evidence supporting preoperative chemotherapy for small cell carcinoma of the bladder: a retrospective review of the MD Anderson cancer experience. J Urol. 2004;172(2):481-4. https://doi.org/10.1097/01.ju.0000132413.85866.fc.
5. Quek ML, Nichols PW, Yamzon J, et al. Radical cystectomy for primary neuroendocrine tumors of the bladder: the University of Southern California experience. J Urol. 2005;174(1):93-96. https://doi.org/10.1097/01.ju.0000162085.20043.1f.
6. Sroussi M, Elaidi R, Fléchon A, et al. Neuroendocrine carcinoma of the urinary bladder: a large, retrospective study from the French genito-urinary tumor group. Clin Genitourin Cancer. 2020;18(4):295-303.e3. https://doi.org/10.1016/j.clgc.2019.11.014.
7. Deuker M, Stolzenbach LF, Rosiello G, et al. Radical cystectomy improves survival in patients with stage T1 squamous cell carcinoma and neuroendocrine carcinoma of the urinary bladder. Eur J Surg Oncol. 2021;47(2):463-9. https://doi.org/10.1016/j.ejso.2020.05.006.