# A rare aggressive cancer of the urinary bladder – small-cell neuroendocrine tumor

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Small-cell neuroendocrine tumor is an aggressive and extremely rare cancer of the urinary bladder. The authors present a case of a 60-year-old man who was incidentally found to have a urinary bladder tumor on ultrasonography findings. He was then found to have an irregular mass in the right side of the urinary bladder based on cystoscopic and computed tomography examination. On pathological examination following resection of the tumor, the specimen was found to be a neuroendocrine small-cell subtype with muscularis propria invasion. He was then referred to the oncology department for further management.

**Keywords:**
bladder cancer, rare neoplasm, Small cell neuroendocrine carcinoma

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## Introduction

Urinary bladder carcinoma is in the list of top 10 most commonly diagnosed malignancies in males in Malaysia [1]. Neuroendocrine carcinoma, which encompasses carcinoid tumors, large-cell neuroendocrine carcinomas, and small-cell carcinoma, commonly occurs in the respiratory and gastrointestinal systems [2]. Incidence of primary small-cell neuroendocrine carcinoma (SCNEC) of the urinary bladder is extremely rare, with the occurrence is just 0.5–1% of all primary bladder tumors [3]. SCNEC is very aggressive, with poor prognosis when compared with urothelial carcinoma.

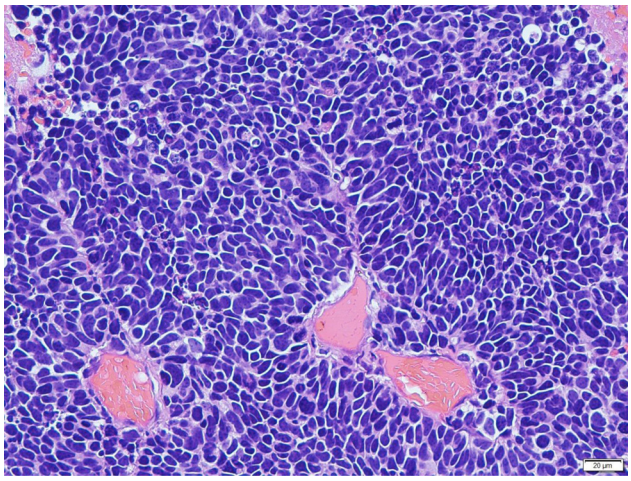
## Case report

A 60-year-old male patient with comorbidities of diabetes mellitus and hypertension presented with bilateral lower limb swelling of 2 months of duration. The patient also had history of smoking 40 pack-years. Ultrasonography of the kidney, ureter, and bladder incidentally revealed a right lateral wall bladder irregular hyperechoic mass measuring 24×26×21 mm. The patient otherwise did not have any genitourinary symptoms. He was then referred to the Urology Hospital Serdang for further treatment. The computed tomography (CT) scans revealed a 61×42×40-mm ill-defined lesion at the right-side dome of the urinary bladder with an exophytic component seen protruding into the perivesical fat. CT also shows scattered tiny lung nodules in the right and left upper lobe, not suggestive of metastasis. There is an enlarged right external iliac lymph node measuring 1.6×2.5 cm with multiple subcentimeter left para-aortic, paracaval, and bilateral inguinal lymph nodes. The patient then underwent transurethral resection of bladder tumor; intraoperatively, large tumor arising from the dome occupying more than half of bladder cavity was extracted. Histopathological examination revealed SCNEC with muscularis propria invasion, T3N1M0, stage 3. On immunohistochemistry, the cells were immunoreactive to CD56, chromogranin, and synaptophysin with Ki-67 80% (Figs 1–4). The patient was then referred to the oncology team for further management.

## Discussion

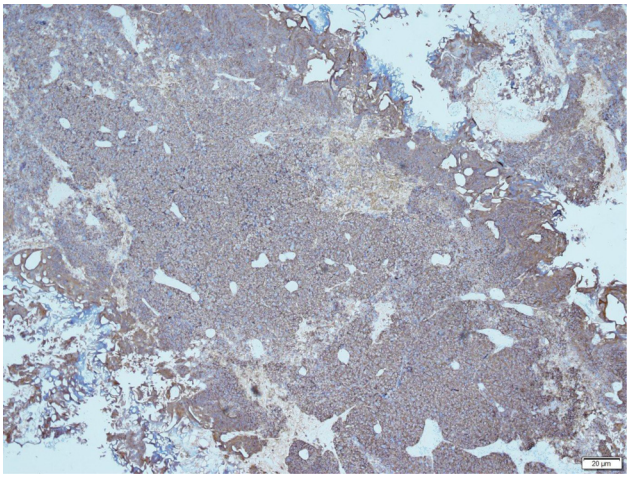
Primary SCNEC is an extremely aggressive and rare neoplasm which accounts for less than 1.0% of all primary bladder carcinomas [3]. The diagnosis of primary SCNEC can only be made by histopathological examination and reactivity for neuroendocrine markers such as synaptophysin, chromogranin A, and neuron-specific enolase [4]. This malignancy is commonly associated with smoking [5], as was the case in our patient and observed in male patients approximately at a mean age of 66 years (range: 36–85 years) [6]. The presentation of primary SCNEC is similar to other

**Figure 1**



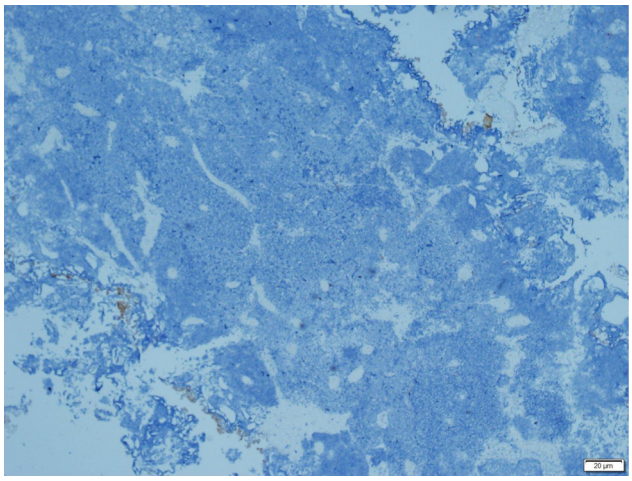
Hematoxylin and eosin-stained section from small cell carcinoma cells showing nuclear molding.

**Figure 2**



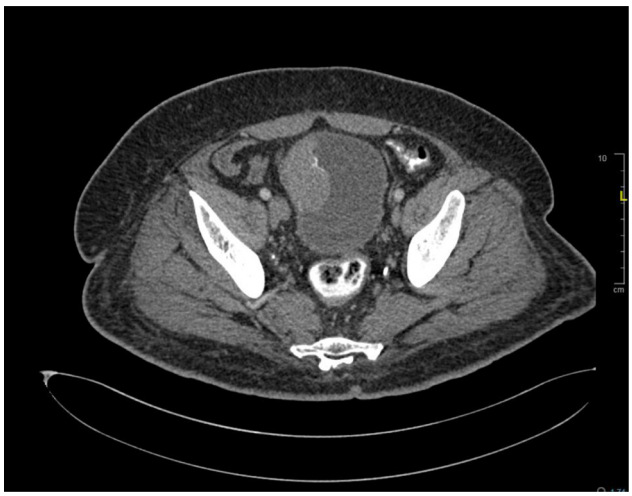
Immunohistochemical staining demonstrates tumor cells with diffuse CD56 expression.

**Figure 3**



Immunohistochemical staining demonstrates chromogranin expressions.

**Figure 4**



Ill-defined lesion over right side of the dome of the bladder with exophytic component protruding out.

types of bladder tumors, which include hematuria, dysuria, urethral obstruction, weight loss, and urinary tract infection.

Diagnosis of primary SCNEC is achieved by cystoscopy examination followed by transurethral biopsy or resection. However, primary SCNEC is indistinguishable from other bladder carcinomas. Precise diagnosis can only be made by histological examination with neuroendocrine markers [7]. Staging of the disease with CT scan of the thorax, abdomen, and pelvis is also warranted before proceeding and deciding for further treatment.

The primary SCNEC has significantly worse prognosis once the tumor has been metastasized. In a study done by Wang and colleagues, the median survival time was only 12 months for patients who did not receive neoadjuvant chemotherapy as compared with 38 months for patients who underwent neoadjuvant chemotherapy before cystectomy. Survival greater than 60 months also has been observed in patients with localized disease and received neoadjuvant chemotherapy [8].

A study conducted by Siefker-Radtke [9] in MD Anderson Cancer Center showed prolonged 5-year survival of 78% for patients receiving neoadjuvant chemotherapy followed by cystectomy as compared with only 36% for patients undergoing cystectomy alone.Another retrospective study of 14 patients by Lohrisch *et al.* [10] reported that the survival rate

was 70% at 2 years and 44% at 5 years when multiagent chemotherapy was combined with local irradiation.

In conclusion, primary SCNEC is a very rare and aggressive tumor, which would require multidisciplinary team approach, with earlier diagnosis being important to improve the survival rates in these cases. Patients would also require long-term follow-up owing to high risk for local recurrence and distant metastasis. Further studies or prospective trials would be required to confirm all the available data right now.

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Nil.

**Conflicts of interest**
There are no conflicts of interest.

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