

## Oncology

# Primary small cell carcinoma of the adrenal gland: Case presentation of a rare extrapulmonary small cell carcinoma

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## ABSTRACT

Small cell carcinoma (SCC) is an aggressive histologic subtype of neuroendocrine tumor and is most commonly of bronchogenic origin. However, it can present in an extrapulmonary fashion. Primary extrapulmonary small cell carcinoma (EPSCC) is a rare disease entity, especially within the genitourinary system and furthermore of the adrenal gland. There are scarce case reports that describe management of primary adrenal SCC. We present a case of localized primary adrenal SCC diagnosed on adrenal mass biopsy and successfully treated via neoadjuvant chemotherapy and extirpative surgery.

## Introduction

Small cell carcinoma (SCC) is a poorly differentiated neuroendocrine tumor typically of bronchogenic origin. Small cell lung cancer (SCLC) is characterized by early metastasis commonly to liver, bone, and brain.<sup>1</sup> In addition to SCLC, there are rare instances of primary extrapulmonary small cell carcinoma (EPSCC).

EPSCC represents less than 5% of SCCs or approximately 1000 annual cases in the United States.<sup>1,2</sup> Common extrapulmonary sites include gastrointestinal (20%), genitourinary (GU) (18%), and gynecologic organs (11%), with prostate and bladder comprising the most commonly involved GU organs.<sup>2</sup> Sparse literature exists for primary EPSCC of GU origin, and thus there are few standard treatment guidelines.

We present a case of localized primary adrenal non-metastatic SCC treated with neoadjuvant chemotherapy and surgery.

## Case presentation

A 61-year-old female with past medical history of spontaneous pneumothorax and chronic hepatitis C, who is a current smoker with a 68-pack year history, was referred for an adrenal mass found on workup for flank pain. Index CT revealed a right adrenal soft tissue mass measuring 11.4 × 6.5cm, abutting the right hepatic lobe (Fig. 1). MRI

confirmed the mass was abutting the diaphragm, liver, inferior vena cava (IVC), and right renal hilum.

A chest CT for staging was negative for intrathoracic malignancy. FDG PET/CT showed increased activity in the right adrenal mass with central necrosis. There were no other concerning regions of increased uptake to suggest an extra-adrenal primary tumor or distant metastasis (Fig. 2). Endocrine workup suggested a metabolically inactive process, with index labs revealing normal AFP, normal cortisol, and mildly elevated normetanephrine (less than 3x normal).

Due to concern for local invasion, systemic therapy was proposed as an alternative to up front surgical resection. CT-guided biopsy was used to aid in diagnosis, which revealed SCC via positive staining for keratin AE1/AE3, synaptophysin, thyroid transcription factor-1 (TTF-1), and a high Ki-67 index. Medical oncology recommended four cycles of cisplatin and etoposide, of which the patient completed three due to excessive fatigue and diarrhea.

Subsequent imaging revealed a significant treatment response with the right adrenal mass now measuring 5.0 × 4.9cm (Fig. 3). The patient underwent an uncomplicated open right adrenalectomy and liver wedge resection. There was no invasion into the vena cava. The subsequent hospital course was uneventful, and the patient was discharged on postoperative day 5. Surgical pathology revealed negative surgical margins and a completely resected SCC. The portion of liver resected was negative for carcinoma.

**Abbreviations:** small cell lung cancer, SCLC; extrapulmonary small cell carcinoma, EPSCC; small cell carcinoma, SCC; genitourinary, GU; inferior vena cava, IVC; thyroid transcription factor-1, TTF-1; adrenocortical carcinoma, ACC.

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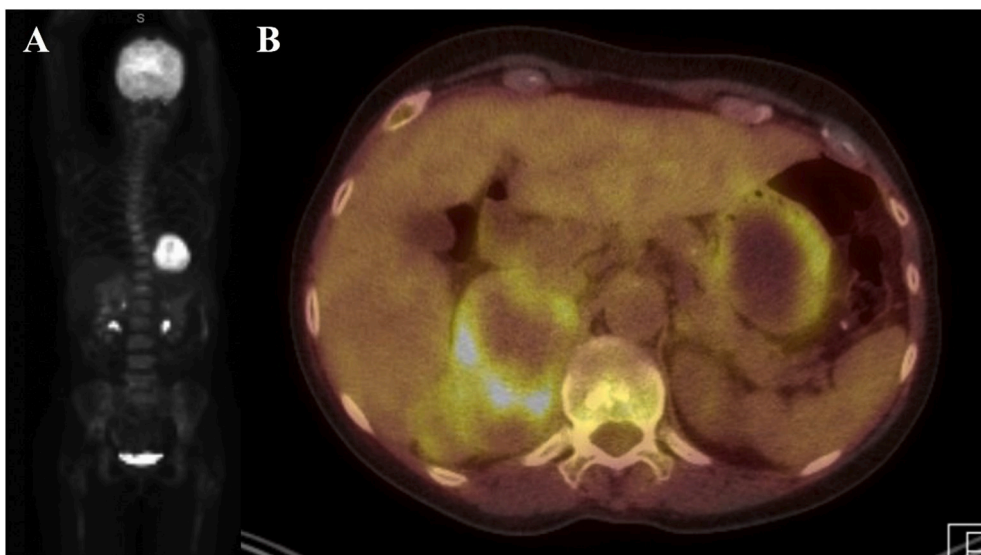
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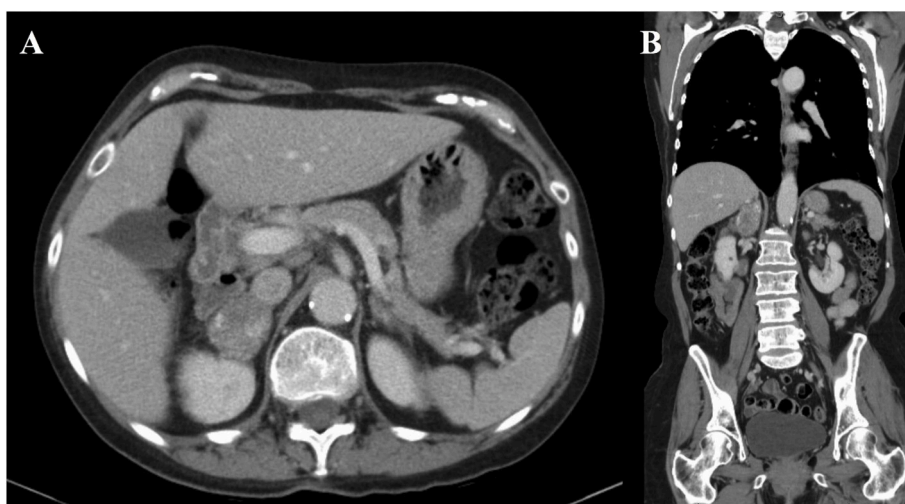
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**Fig. 1.** Initial CTAP revealed a right adrenal soft tissue mass measuring 11.4 × 6.5cm, abutting the right hepatic lobe and inferior vena cava in axial (A) and coronal (B) representation.



**Fig. 2.** FDG PET/CT was completed to work up the adrenal mass as a presumed metastatic site. PET/CT revealed increased activity in the right adrenal mass with central necrosis and no additional site of uptake [coronal (A) and axial (B) representation in color]. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)



**Fig. 3.** After 3 courses of etoposide and cisplatin, subsequent imaging revealed a significant treatment response with the right adrenal mass measuring 5.0 × 4.9cm in axial (A) and coronal (B) representation.

## Discussion

This case highlights complexities in the work-up and management of adrenal masses, contributes to discussion on adrenal mass biopsy, and provides insight to management of a primary adrenal SCC.

When evaluating an adrenal mass, a tumor measuring greater than 6cm has high sensitivity and specificity (91% and 80%, respectively) for a histologic diagnosis of adrenocortical carcinoma (ACC).<sup>3</sup> Generally, adrenal mass biopsy is not recommended due to the potential morbidity of biopsy complications outweighing a minimal benefit, as adrenal mass biopsy does not often change subsequent management.<sup>4</sup> However, when an adrenal mass is deemed surgically inoperable, a confirmatory biopsy can be used prior to initiation of systemic therapy.<sup>4</sup> In this case, biopsy of the adrenal mass was paramount in the accurate diagnosis of SCC and the selection of systemic therapy.

When the diagnosis of EPSCC is suspected, it is important to thoroughly rule out an extra-adrenal primary tumor, as SCC metastases to the adrenal gland are more common than primary adrenal SCC. There are very few treatment guidelines for EPSCC of genitourinary origin. Median overall survival of EPSCC in the GU tract has been described at approximately 10.6 months, including patients who received only chemotherapy or multimodal therapy.<sup>2</sup> In SCLC, cisplatin has been the chemotherapeutic agent of choice, displaying median survival improvement for patients with thorax-confined disease from 14 to 20 months. Additionally, EPSCC demonstrates favorable treatment responses to cisplatin.<sup>1</sup>

However, it is important to note that primary adrenal SCC cases are underrepresented in various EPSCC studies due to disease rarity. To our knowledge, only three case reports exist describing primary adrenal SCC, and this case report joins Ogawa et al. as the only descriptive report of adrenal confined disease.<sup>5</sup> Various management strategies have been employed for primary adrenal EPSCC. A patient with metastatic disease was managed with chemotherapy (etoposide and cisplatin) with 3-month survival. Two patients were treated surgically, with SCC being diagnosed at the time of extirpative surgery. One of the two patients underwent adrenalectomy for organ confined disease, but developed metastatic disease at 3-months postoperatively, followed by mortality at 11 months. The second patient was found to have a renal vein thrombus and was treated by adrenalectomy and nephrectomy.<sup>5</sup> Our case complements these reports, as it is the first case report to describe a biopsy proven primary adrenal SCC that was treated with neoadjuvant cisplatin and etoposide followed by extirpative surgery.

## Conclusion

This case report highlights several takeaways:

- 1) EPSCC is a rare, aggressive disease entity, and due to limited experience, there is no consensus in management. Although rare, EPSCC must be considered in the differential diagnosis of an adrenal mass.
- 2) SCC of the adrenal gland is likely a metastasis, and if diagnosed, a primary site should be meticulously searched for.
- 3) Biopsy of an adrenal mass should be considered on a case-by-case basis and implored if a mass is deemed surgically inoperable before proceeding with systemic therapy
- 4) Surgical management continues to be a hallmark in management of localized adrenal masses and should be considered on a case-by-case basis for metastatic lesions. Surgery should be performed at high-volume, multidisciplinary centers due to the complexities in extirpative surgery.

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## Declaration of competing interest

None.

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