Imaging features of extra-pulmonary small cell carcinoma

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Learning objectives

To highlight the imaging features of extra-pulmonary small cell carcinoma in different organs with various imaging modalities.

To emphasize the radiological patterns of metastasis of these uncommon tumours.
Background

Small cell carcinoma is a poorly differentiated neuroendocrine tumour that principally arises in the lung and commonly displays aggressive features with widespread metastasis at presentation. Extra-pulmonary small cell carcinoma (EPSCC) accounts for 2-9% of all small cell carcinomas.\textsuperscript{1-3} The most common site of origin of EPSCC is the gastrointestinal tract, particularly the oesophagus, followed by the gynaecological and genitourinary systems.\textsuperscript{2}

No guidelines currently exist on the optimal management of EPSCC and most clinicians have adopted similar treatment principles to small cell lung carcinoma due to its pathological similarities.\textsuperscript{4} The tumours often respond well to initial local therapy, however EPSCC are usually fatal due to distant metastasis.\textsuperscript{5}

Study Methods:

We conducted a search of our institution’s prospectively maintained histopathology database for cases of small cell carcinoma diagnosed between July 2006 and June 2012. Ethics approval was granted by our institution’s IRB committee for this retrospective study and consent was not required. All cases of small cell carcinoma were reviewed manually to identify those with an extra-pulmonary origin. We defined extra-pulmonary small cell carcinoma as a histopathological diagnosis of small cell carcinoma in the absence of any radiological evidence of a pulmonary origin. Patients diagnosed with merkel cell carcinoma and patients with a history of small cell carcinoma of the lung were excluded from our study. A retrospective analysis was then performed of the imaging features of EPSCC in the remaining cohort of patients.

Based on the radiological appearances, patients were divided into limited or extensive stage disease. Limited stage disease was defined as disease confined to the organ of origin with or without regional lymph node involvement or alternatively disease which could be safely encompassed within a tolerable radiation field. Extensive stage disease was defined as disease beyond locoregional boundaries.
During the six year time period, 357 small cell cancers were diagnosed. 28 (7.8%) of these originated from extra-pulmonary sites. 12/28 (42.9%) patients with EPSCC had extensive disease on initial presentation. Table 1 on page 11 shows the distribution of the primary disease sites of patients with EPSCC as well as the disease stage at presentation.

<table>
<thead>
<tr>
<th>Disease Site</th>
<th>Number of patients</th>
<th>LD;ED</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oesophagus</td>
<td>11(39.3%)</td>
<td>6;5</td>
</tr>
<tr>
<td>Stomach</td>
<td>1(3.6%)</td>
<td>0;1</td>
</tr>
<tr>
<td>Anus</td>
<td>1(3.6%)</td>
<td>1;0</td>
</tr>
<tr>
<td>Gynaecological:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cervix</td>
<td>4(14.3%)</td>
<td>2;2</td>
</tr>
<tr>
<td>Genitourinary:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bladder</td>
<td>3(10.7%)</td>
<td>3;0</td>
</tr>
<tr>
<td>Prostate</td>
<td>1(3.6%)</td>
<td>0;1</td>
</tr>
<tr>
<td>Head and neck:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Parotid</td>
<td>2(7.1%)</td>
<td>2;0</td>
</tr>
<tr>
<td>Thyroid</td>
<td>1(3.6%)</td>
<td>0;1</td>
</tr>
<tr>
<td>Breast</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2(7.1%)</td>
<td>2;0</td>
</tr>
<tr>
<td>Unknown</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2(7.1%)</td>
<td>0;2</td>
</tr>
</tbody>
</table>

Table 1: Primary disease sites of patients with EPSCC and disease stage at presentation. (LD: Limited disease, ED: Extensive disease)

References: Radiology, St. James's Hospital - Dublin/IE

Gastrointestinal EPSCC

The most common extra-pulmonary site for small cell carcinoma was the gastrointestinal (GI) tract. 13 (46.4%) EPSCC were GI in origin. Oesophageal small cell carcinoma
accounted for the majority of these with 11 cases identified (39.3% of all cases). Other GI sources included 1 gastric and 1 anal small cell carcinoma.

Small cell carcinomas arising from the GI tract share a similar pattern of spread, with the liver the most common site of metastasis, followed by distant lymph nodes and then bone. This is consistent with our study findings, with one GI EPSCC patient presenting with liver metastasis only, five patients presenting with both liver and distant nodal metastases and one patient presenting with liver, distant nodal and osseous metastases (Fig. 1 on page 11).

Fig. 1: A 55 year old female with small cell carcinoma of the oesophagus. A: Fused PET/CT image demonstrating the 18F-FDG avid primary tumour (arrow, SUV max 8.0) and adjacent nodal disease (arrowhead). B: PET scan MIP image showing widespread metastatic disease to the liver, lymph nodes and bones despite small primary tumour (arrow) (arrowhead depicts adjacent nodal disease). C: Fused PET/CT image showing an 18F-FDG avid metastatic deposit in the body of T10.

References: Radiology, St. James's Hospital - Dublin/IE

In our series, all 11 oesophageal small cell tumours had concentric wall thickening visible on axial CT imaging. The mean +/- SD of the greatest axial tumour diameters was 4.2 cm +/- 1.7cm (range 2 cm - 7.4cm). This measurement was <2.5cm in 3 patients, 2.5cm- 5cm in 4 patients and >5cm in 4 patients. 10 of the 11 oesophageal tumours occurred in the lower third of the oesophagus (from the inferior pulmonary vein to the gastro-oesophageal junction). 9 of the 11 oesophageal tumours had regional lymph node involvement at presentation and in 6 cases these nodes were bulky with a diameter of #3cm. 5 of the 11 patients with oesophageal small cell carcinoma had extensive disease at presentation including one patient with an axial tumour diameter of 2.3cm (Fig. 2 on page 12). Thus, features of an oesophageal tumour in this series which raises the possibility of a small cell carcinoma are concentric wall thickening, a locally advanced primary tumour,
bulky regional lymph node involvement in association with a small tumour and distant metastasis.

![Image of CT scans](image-url)

**Fig. 2:** A 60 year old female with small cell carcinoma of the oesophagus. A: Axial CT demonstrating the primary tumour as an area of circumferential wall thickening in the distal oesophagus (arrow). B: Axial CT demonstrating multiple low attenuation liver metastases in association with upper abdominal lymphadenopathy (arrowheads).

**References:** Radiology, St. James’s Hospital - Dublin/IE

In the patient with gastric small cell carcinoma, coronal CT images revealed a poorly enhancing, exophytic mass arising from the lesser curve of the stomach, measuring 8.5cm in maximal diameter. This patient had extensive disease with multiple bilobar liver metastases at presentation and responded poorly to chemotherapy (Fig. 3 on page 12).
Fig. 3: A 68 year old male with small cell cancer of the stomach. A: Fused PET/CT image showing intense 18F-FDG uptake in the primary tumour (arrow, SUV max 14.4) and liver metastasis. B: Coronal CT image post iv contrast after 4 cycles of carboplatin and etoposide demonstrating interval disease progression with an increase in the size and number of the liver metastases (arrowheads). Note the poorly enhancing exophytic primary tumour (arrow).

References: Radiology, St. James's Hospital - Dublin/IE

In our study, 7 patients with oesophageal small cell carcinoma and the single patient with gastric small cell carcinoma underwent PET/CT for initial staging. In this cohort of patients, all identifiable disease was 18F-FDG avid (mean SUV max of primary tumour =11.2). PET is of proven value in patients with EPSCC for staging and response assessment and has been shown to influence patient management.7

Gynaecological EPSCC

The uterine cervix was the second most frequent site of EPSCC origin in our study. 4(14.3%) patients with EPSCC had a cervical origin.

The greatest axial diameters of the cervical tumours in our series were 1.5cm, 4cm, 6cm and 6.5cm. Two (axial diameters of 6cm, 6.5cm) of the four tumours were noted to have radiological evidence of parametrial invasion (Fig. 4 on page 13). No tumour invaded adjacent organs. Two of the four patients had regional lymphadenopathy on initial staging and both of these patients had extensive disease. The extra-cervical sites of spread for extensive stage disease were inguinal and intra-abdominal lymph nodes in one patient.
with a primary tumour of 1cm in axial diameter and the liver in a patient with a cervical tumour of 6.5cm in axial diameter.

Fig. 4: A 22 year old female with small cell carcinoma of the cervix. A: Coronal oblique T2 MR image demonstrating left parametrial invasion of the primary tumour (arrow) beyond the vaginal fornix (arrowhead). B: Sagittal T2 weighted MR image demonstrating the primary tumour as a soft tissue mass extending into the posterior vaginal fornix (arrow). C: Sagittal T2 weighted MR image post completion of chemoradiation therapy demonstrating an interval significant reduction in tumour size and return of normal signal to the cervix (arrow).

References: Radiology, St. James's Hospital - Dublin/IE

Two patients with cervical EPSCC underwent a PET scan as part of their initial staging. All gross disease demonstrated $^{18}$F-FDG avidity.

Genitourinary EPSCC

There were 4(14.3%) EPSCC of genitourinary origin in our cohort of patients. 3 of these cases originated from the bladder and a single case originated from the prostate gland.

In our study, CT imaging identified 2 of the 3 bladder small cell carcinomas as an irregular mucosal thickening occurring on the lateral and postero-lateral bladder walls. Both tumours invaded the peri-vesical fat but not adjacent organs. One tumour was associated with regional lymph node involvement. The final tumour had the appearance of a broad based polyloid mass arising from the posterior bladder wall on CT imaging. It invaded the prostate gland but did not involve regional lymph nodes. All 3 bladder tumours enhanced post contrast administration. No patient with bladder EPSCC in our series had distant metastasis on presentation.
The single patient with prostate cancer presented with a soft tissue mass 5.3cm in axial diameter which was intimately related to the rectum and invaded the bladder base and seminal vesicles. This mass displayed heterogeneous attenuation suggestive of areas of necrosis (Fig. 5 on page 14). This patient also had extensive local and distant lymph node involvement as well as mixed sclerotic and lytic osseous metastasis.

**Fig. 5:** An 82 year old male with small cell carcinoma of the prostate. Sagittal T2 weighted MR image demonstrating the primary tumour as an ill-defined soft tissue mass abutting and possibly invading the anterior rectum (arrow). A metastatic deposit is visible within the bladder (arrowhead).

*References:* Radiology, St. James's Hospital - Dublin/IE
No patient with GU EPSCC in our series underwent a PET scan. Although FDG PET is not a helpful imaging modality for evaluating prostatic adenocarcinoma, numerous case reports have reported $^{18}$F-FDG avidity in prostate small cell carcinoma.$^{8-10}$
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Conclusion

Although a rare diagnosis, EPSCC is an important radiological consideration due to its aggressive nature. In our study, the oesophagus, uterine cervix and bladder were the most common sites of origin of EPSCC. Advanced locoregional disease, the presence of lymphadenopathy even with small tumours and distant metastasis were all common radiological findings with these uncommon tumours. All patients who underwent PET/CT demonstrated $^{18}$F-FDG uptake of the primary tumour and gross metastases highlighting its role in the staging of these tumours.
References

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