Extrapulmonary small cell carcinoma (EPSCC) refers to small cell carcinoma arising outside the lungs. EPSCC is a rare aggressive neoplasm, representing a minority of all small cell carcinomas. Despite its uncommon occurrence, EPSCC has been described in nearly every organ, most commonly in the gastrointestinal and genitourinary systems. As such, it is important for radiologists to be aware of the entity. Although imaging is neither sensitive nor specific for EPSCC, it plays an important role by helping exclude metastases from a primary pulmonary tumor, establish tumor staging, and assess response to therapy. EPSCC is diagnosed by demonstrating pathologic features of small cell carcinoma in an extrapulmonary site. There are two ways to stage EPSCC. One method uses the Veterans Administration Lung Study Group system developed for small cell lung cancer that allocates patients into limited or extensive disease categories. The second approach is the American Joint Committee on Cancer tumor-node-metastasis system applied to other tumor subtypes arising from the same organ. Because of its rare and varied manifestations, the most effective treatment for EPSCC has not been established. Current management recommendations are derived from retrospective studies and single-institution experiences or are extrapolated from small cell lung cancer data. Regardless of therapy, overall survival rates are poor, with 5-year survival rates around 13%. To help radiologists increase their familiarity with EPSCC, this article provides (a) a background for EPSCC based on the literature and (b) a pictorial review of EPSCC in multiple organs, with radiologic-pathologic correlation.

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Introduction
Extrapulmonary small cell carcinoma (EPSCC) refers to small cell carcinoma arising outside the lungs. It occurs most commonly in the gastrointestinal and genitourinary systems but has been described in virtually every organ in the body. EPSCC is a rare neoplasm, constituting only 2.5%–5.0% of all small cell carcinoma cases and 0.1%–0.4% of all cancers (1). EPSCCs often manifest as large aggressive tumors; however, clinical and radiologic manifestations are nonspecific and vary with the organ of origin. Pathologic specimens are used to establish the diagnosis by demonstrating morphologic features of small cell carcinoma, including sheets, ribbons, clusters, or rosettes of small- to medium-sized, round to oval blue cells with scant cytoplasm (2). The role of the radiologist is to exclude metastases from a primary small cell lung cancer (SCLC), characterize tumor staging, and assess response to therapy.
To diagnose EPSCC, two basic criteria must be fulfilled: (a) the tumor demonstrates histologic features of small cell carcinoma and (b) a primary SCLC is excluded.

EPSCC and SCLC are neuroendocrine tumors with shared histologic features.

Immunohistochemistry supplements the morphologic diagnosis; however, EPSCC cannot be diagnosed on the basis of immunoreactivity alone. Neuroendocrine markers are not required to make a diagnosis, but they may be reactive and support morphologic findings of small cell carcinoma.

Imaging and clinical features of EPSCC are nonspecific and vary with the site of origin. Regardless of anatomic site, however, EPSCC is characterized by advanced local disease and early widespread metastases.

Because of its rare and varied manifestations, there is a paucity of data from randomized prospective trials; consequently, there is little consensus on the most effective treatment of EPSCC. Current management recommendations are derived from retrospective studies and small single-institution experiences or are extrapolated from SCLC data.

The purpose of this article is to familiarize radiologists with the clinical, radiologic, and pathologic characteristics of EPSCC through a literature and case-based review. First, the epidemiologic and histopathologic features are discussed. Then, imaging manifestations are described through several examples of EPSCC with radiologic-pathologic correlation. Subsequently, two pertinent staging systems are summarized. Finally, current EPSCC treatment strategies and prognosis are outlined.

Epidemiology

According to the World Health Organization, neuroendocrine tumors are classified into three categories: well-differentiated (true carcinoids), moderately differentiated (atypical carcinoids), and poorly differentiated tumors (small cell carcinomas) (3). SCLC and EPSCC share pathologic features and are both considered poorly differentiated tumors. To diagnose EPSCC, two basic criteria must be fulfilled: (a) the tumor demonstrates histologic features of small cell carcinoma and (b) a primary SCLC is excluded. As such, one important role of the radiologist is to exclude SCLC with chest imaging, preferably computed tomography (CT) with or without fluorine 18 fluorodeoxyglucose (FDG) positron emission tomography (PET).

Duguid and Kennedy (4) described EPSCC in 1930. It is a rare entity with about 1000 new cases diagnosed in the United States each year, representing only 2.5%–5.0% of all small cell carcinoma cases and 0.1%–0.4% of all cancers (1,5,6). The largest series of EPSCC cases demonstrated a median age of 70 years (6). This study also showed a slight female predilection of 1.3:1; however, other studies have reported a higher incidence in men (6,7). Cigarette smoking has been described as a risk factor for genitourinary and head and neck EPSCC (8,9). Other postulated risk factors, including heavy alcohol consumption, have not been verified in the literature. EPSCC most commonly arises in the gastrointestinal and genitourinary systems, including the esophagus, stomach, colon, rectum, anus, gallbladder, cervix, vagina, prostate, and bladder. However, EPSCC has been described in nearly every organ system. In the largest series of which we are aware (1618 EPSCC cases), the esophagus was involved most often (18%), followed by other gastrointestinal sites (15%), the genitourinary system (20%), head and neck (11%), and breast (10%) (6). In another study with 120 cases, the cervix was the most common primary site (20%), followed by the esophagus (17%), bladder (13%), and parotid gland (4%) (10). In 7%–30% of EPSCC patients, a primary site cannot be identified, and the diagnosis is small cell carcinoma of unknown primary origin (5).

Histopathology

Although the pathogenesis is not entirely understood, EPSCC is thought to arise either from a multipotent stem cell that develops neuroendocrine features or as a late-stage phenomenon in the genetic progression of more organ-typical carcinomas (2). Many tumors contain mixed elements with both EPSCC and non–small cell carcinoma cell types; in such cases, the small cell component usually dictates the disease course and management (11).

All small cell carcinomas, regardless of the site of origin, are diagnosed on the basis of their morphology at light microscopy. EPSCC and SCLC are neuroendocrine tumors with shared histologic features (2). Several nuclear qualities are characteristic of small cell carcinomas: salt-and-pepper chromatin without prominent clumps, hyperchromatic and indistinct nucleoli, frequent mitotic figures, and nuclear molding, which describes nuclei conforming to the contour of adjacent cells (Fig 1) (2). Another typical feature is the Azzopardi phenomenon, named after the pathologist John Azzopardi, who first described the feature of basophilic nuclear chromatin diffusing into the walls of blood vessels (12). Finally, the nuclei of small cell carcinomas tend to be delicate and specimens may show smudging, a term for crush artifact that results from cell fragility (2).

Immunohistochemistry supplements the morphologic diagnosis; however, EPSCC cannot be diagnosed on the basis of immunoreactivity alone. Neuroendocrine markers are not required to make a diagnosis, but they may be reactive and...
support morphologic findings of small cell carcinoma. Neural cell adhesion molecule (NCAM or CD56) is the most sensitive neuroendocrine marker (2). Chromogranin A, a protein found in neurosecretory granules, is the most specific marker for neuroendocrine differentiation and yet the least sensitive in EPSCC, with less than 50% reactivity (2). Neuron-specific enolase and synaptophysin are additional neuroendocrine markers with intermediate sensitivity (2). Pan-keratin is positive in all cases. As with SCLC, EPSCC may express thyroid transcription factor–1 (2). As such, thyroid transcription factor–1 positivity does not distinguish SCLC from EPSCC.

**Clinical and Radiologic Manifestations**

Imaging and clinical features of EPSCC are nonspecific and vary with the site of origin. Regardless of anatomic site, however, EPSCC is characterized by advanced local disease and early widespread metastases. Clinically, patients may present with systemic symptoms such as anorexia, weight loss, fatigue, sweating, nausea, and vomiting (5). EPSCCs can secrete hormones and therefore may cause paraneoplastic syndromes such as Cushing syndrome or syndrome of inappropriate antidiuretic hormone secretion (5). Clinical and radiologic findings specific to different organ systems are reviewed.

**Gastrointestinal System**

According to some series, the gastrointestinal tract is the most common site of EPSCC. About 650 cases of gastrointestinal EPSCC have been reported in the literature (13). In a meta-analysis of 544 gastrointestinal EPSCC cases, the esophagus was involved most frequently (53.3%), followed by the colon (13%), stomach (11%), and gallbladder (8.4%) (11). EPSCC represents 0.1%–1.0% of all gastrointestinal malignancies, including 1.0%–2.8% of all esophageal cancers and 0.2% of all colorectal neoplasms (11). The authors of this review found an increased incidence in older males, with a mean age of 64 years (11). Clinically, patients with EPSCC of the gastrointestinal tract may have pain, melena, or bowel obstruction at presentation; symptoms depend on tumor size, extent, and location within the gastrointestinal system (11).

The imaging appearance of gastrointestinal EPSCC is nonspecific. For example, case reports of esophageal EPSCC describe bulky tumors that typically involve the lower two-thirds of the esophagus (14). Gallbladder EPSCC may manifest as nonspecific gallbladder wall thickening that is indistinguishable from adenocarcinoma of the gallbladder or inflammation secondary to cholecystitis (Figs 2, 3). Elsewhere in the gastrointestinal system, EPSCC often mimics tumors that are more common to the site of origin, such as ampullary or pancreatic adenocarcinoma when arising near the second portion of the duodenum (Fig 4).

Gastrointestinal EPSCC is characterized by an aggressive course. The tumor stage is often advanced at diagnosis, with regional lymph node involvement and distant metastases in more than half of cases (11). The most common sites of metastatic involvement include the liver, distant lymph nodes, bones, and bone marrow (11).

**Genitourinary System**

Common EPSCC sites of origin within the genitourinary system include the cervix, bladder, and prostate. Although cervical EPSCC constitutes as much as 20% of EPSCC cases in some studies, it accounts for fewer than 3% of all cervical cancers (1,10). A retrospective review of 188 patients with cervical EPSCC found a median age at diagnosis of 42 years, which is younger than most patients with EPSCC at other sites of origin (15). Tumors in this review were large at presentation, with more than 80% greater than 2 cm.
Figure 2. Small cell carcinoma of the gallbladder in a 69-year-old woman. (a) Coronal T2-weighted magnetic resonance (MR) image shows irregular gallbladder wall soft-tissue thickening (arrows). (b) Coronal contrast material-enhanced MR image shows enhancement of the abnormal soft tissue (arrows), in keeping with suspected malignancy. Multiple liver metastases are also evident (circles). The soft tissue had intense FDG uptake on PET/CT images (not shown). Liver biopsy was performed for tissue diagnosis. (c) Photomicrograph (original magnification, ×4; hematoxylin-eosin stain) of a cell block from liver fine-needle aspiration shows small to intermediate-sized, round to oval blue cells with scant cytoplasm and hyperchromatic nuclei. Nuclear molding and mitotic figures are also seen. The morphologic findings are compatible with small cell carcinoma, in this case metastatic from the gallbladder. (d) Photomicrograph (original magnification, ×4) shows that the tumor cells are strongly positive for synaptophysin. CD56 and neuron-specific enolase were also positive, while chromogranin A and thyroid transcription factor–1 were negative. Immunoreactivity is not required to diagnose small cell carcinoma but does support the light microscopy findings in this case.

Cervical EPSCCs are aggressive neoplasms that commonly have lymph node involvement, vascular invasion, and hematogenous metastases (Figs 5, 6) (16). Cervical EPSCC often responds well to chemotherapy and radiation initially but is more likely than other types of cervical cancer to develop distant metastases (15).

The bladder is also a common site for EPSCC, but accounts for less than 1% of all bladder tumors. Patients most often have macroscopic hematuria at the time of presentation (8). In a series of 20 patients with bladder EPSCC, the tumors arose from the lateral bladder walls most often (54%), followed by the posterior wall (20%), trigone (10%), dome (8%), and anterior wall (8%) (17). This study showed a 3:1 male predominance with a mean age of 68 years (17). Bladder EPSCC cannot be distinguished from more common urothelial neoplasms at imaging or cystoscopy, although bladder EPSCCs tend to manifest as large, broad-based, polypoid masses with extravesical extension (Fig 7) (14,17). As at other sites, bladder EPSCC shows aggressive behavior. Although patients may initially respond well to surgery, chemotherapy, and radiation, they usually relapse. Of the 20 patients in the retrospective series, nine (45%) had extensive disease at the time of diagnosis (17).
Figure 3. Small cell carcinoma of the gallbladder in an 84-year-old woman. (a) Axial contrast-enhanced CT image shows irregular soft tissue along the gallbladder (circle). Gallstones are also noted. (b) Axial contrast-enhanced CT image depicts enlarged necrotic periportal lymph nodes (arrows) compressing the portal vein. The patient underwent cholecystectomy for presumed cholecystitis. (c) Axial unenhanced CT image performed 4 months later shows increased periportal lymphadenopathy (arrows), which resulted in biliary ductal dilatation (circles). New malignant ascites is also evident. The findings reflect progression of metastatic gallbladder carcinoma. (d) Photomicrograph (original magnification, ×10; hematoxylin-eosin stain) shows small to intermediate-sized, round to oval blue cells with scant cytoplasm and hyperchromatic nuclei with nuclear molding and mitotic figures. The morphologic findings are compatible with small cell carcinoma. The immunohistochemical pattern supported the diagnosis, staining positive for CD56 and neuron-specific enolase and negative for synaptophysin, chromogranin A, and cytokeratin 20. Pathologic findings of acute and chronic cholecystitis were additionally noted.

Similar to bladder EPSCC, the prostate is a common site for EPSCC but accounts for fewer than 1% of all prostate tumors (18). In contrast to prostatic adenocarcinoma, serum levels of prostatic-specific antigen (PSA) do not correlate with disease activity or treatment response (18). In fact, PSA levels can be normal. Only a few case reports have described imaging findings of prostatic EPSCC; the appearance is nonspecific and includes prostatomegaly with an enhancing lobulated soft-tissue mass, local invasion, and distant metastases at presentation (19). Additionally, patients tend to present with symptoms of obstructive uropathy from advanced disease (Fig 8) (8). Prostatic EPSCCs are aggressive tumors characterized by a poor response to hormone therapy, early relapse after chemotherapy, and rapid development of visceral and bone metastases (14,18). In one series of 58 patients with bladder, prostatic, and upper urinary tract EPSCC, the patients with prostatic EPSCC had the worst outcomes, with median survival of only 5.1 months (8).

Head and Neck
EPSCC can occur in multiple sites in the head and neck. The larynx is the most frequent site of origin, followed by the salivary glands and sinonasal region (9). Laryngeal EPSCC is three times more common in men, and the majority of patients have a history of tobacco use (9). Among laryngeal sites, the supraglottic region is
Figure 4. Small cell carcinoma in a 48-year-old woman, most likely arising from the pancreatic head. (a) Axial contrast-enhanced CT image of the abdomen demonstrates abnormal soft tissue centered around the pancreatic head and second portion of the duodenum (circle). Subsequent MR imaging examination better delineated the findings. (b) Axial T2-weighted MR image shows the soft-tissue tumor (circle). (c) Coronal T2-weighted MR image depicts an abrupt cutoff of the common bile duct and biliary ductal dilatation from obstruction (arrows). A Whipple procedure was performed. (d) Photomicrograph (original magnification, ×4; hematoxylin-eosin stain) of the duodenal wall shows nests and sheets of tumor cells in the duodenal submucosa. Although neuroendocrine markers were negative, the morphologic features are consistent with small cell carcinoma and are enough to enable the diagnosis. Given its epicenter, the primary tumor most likely arose from the pancreatic head and extended locally into the duodenum.

most common (9). As with other laryngeal cancer subtypes, symptoms may include hoarseness, throat pain, odynophagia, dysphagia, and airway obstruction (9). EPSCC can arise in major and minor salivary glands, most commonly involving the parotid and submandibular glands (9). Salivary gland tumors have demonstrated a slightly better prognosis compared with other head and neck EPSCCs (9).

Head and neck tumors have a tendency for aggressive local infiltration, including early angiolymphatic and perineural invasion (9). Head and neck EPSCCs are also prone to metastasize to regional lymph nodes and distant sites; more than half of patients present with a nodal mass at diagnosis (20). Although imaging findings are nonspecific, EPSCC can be included in the differential diagnosis for head and neck tumors manifesting with extensive cervical lymphadenopathy or distant metastases (14).

Breast
Breast EPSCC is a rare diagnosis that represents fewer than 1% of mammary neoplasms (21). Of note, the first two reported cases occurred in males (21). The average age is 55 years, and about one-half to two-thirds of patients have lymph node involvement at the time of diagnosis (21). The majority of patients present with a palpable breast mass and/or axillary lymphadenopathy (21), although breast EPSCC may even be found incidentally (Fig 9). Core needle biopsy is generally required for diagnosis, as these tumors have nonspecific findings at mammography, US, and MR imaging. There is usually histologic evidence of ductal carcinoma in situ with areas
of ductal, lobular, or papillary differentiation (21). Breast EPSCC inconsistently demonstrates immunoreactivity for neuroendocrine markers as well as reactivity for estrogen or progesterone receptors (21). HER2/neu expression has not been reported (21).

**Differential Diagnosis**

The differential diagnosis for EPSCC usually includes other malignancies. Typically, the main diagnostic dilemma is distinguishing EPSCC from SCLC metastasis, particularly because SCLC is much more common. In every patient with a tissue diagnosis of small cell carcinoma from an extrapulmonary site, SCLC must be excluded by using appropriate chest imaging. Additional workup with sputum cytology, bronchoscopy, or biopsy should be conducted for indeterminate pulmonary findings.

Other entities in the differential diagnosis include carcinoid, lymphoma, melanoma, and Merkel cell carcinoma. In general, carcinoid does not have the same degree of necrosis and mitotic and apoptotic activity as EPSCC (2). Additionally, carcinoid cells are larger with moderate cytoplasm, and the nucleoli are more prominent than in EPSCC (2). Moreover, thyroid transcription factor–1 is usually negative. Immunohistochemistry also helps differentiate the other processes. For example, lymphoma is positive for leukocyte common antigen (CD45) and negative for pan-keratin (2). Melanoma has positive melanoma-specific markers, such as melan-A and HMB-45 (2). Merkel cell carcinoma is thyroid transcription factor1 negative and shows a characteristic punctate perinuclear cytokeratin 20 staining pattern, which is rare in EPSCC (2).
Figure 6. Small cell carcinoma of the cervix in a 74-year-old woman. The patient presented with postmenopausal bleeding. (a, b) Axial (a) and coronal (b) contrast-enhanced CT images of the pelvis reveal a bulky soft-tissue mass centered in the cervix (arrows). Findings are compatible with a primary cervical malignancy without clear evidence of metastatic disease. A cervical biopsy was performed. (c) Axial contrast-enhanced CT image obtained 5 months later shows progression of disease with new liver metastases (circles). New retroperitoneal lymphadenopathy was also present (not shown). (d) Photomicrograph (original magnification, ×10; hematoxylin-eosin stain) reveals small to intermediate-sized, round to oval blue cells with scant cytoplasm and hyperchromatic nuclei with nuclear molding and mitotic figures. Immunohistochemical stains were positive for CD56, neuron-specific enolase, and synaptophysin (not shown), supporting the morphologic diagnosis of small cell carcinoma.

Staging
At present, EPSCC does not have a unique staging scheme; however, two methods are employed most commonly. One method uses the Veterans Administration Lung Study Group staging system developed for SCLC that allocates patients into limited or extensive disease categories. Limited disease refers to a local-regional tumor burden contained within a single radiation therapy field (1). Extensive disease, by definition, extends beyond a single radiation field. The second approach is the American Joint Committee on Cancer TNM staging system applied to other tumor subtypes arising from the same organ. For instance, EPSCC of the gallbladder can be staged in the same manner as adenocarcinoma of the gallbladder. Limited and extensive disease are described more commonly in the literature, although individual cases tend to reflect institution preferences.

Imaging plays an essential role in staging patients with EPSCC. Given the aggressive nature of the disease and its propensity to metastasize, a complete workup should include cross-sectional imaging of the site of origin, as well as of the chest, abdomen, and pelvis. Additionally, our institution usually performs contrast-enhanced brain MR imaging during the staging workup, although routine brain imaging is controversial in the absence of neurologic symptoms (11). EPSCC is FDG avid, and our institution prefers whole-body imaging with FDG PET/CT for both staging and treatment response assessment. One small retrospective study found that FDG PET appropriately influenced patient management in eight of 43 (19%) imaging episodes.
Figure 7. Small cell carcinoma of the bladder in a 70-year-old man. The patient had microscopic hematuria at presentation. (a) Axial contrast-enhanced CT image of the pelvis demonstrates an enhancing soft-tissue mass with coarse calcification arising from the left inferolateral bladder wall (arrow). Biopsy performed at an outside institution confirmed the diagnosis of bladder EPSCC. The tumor was limited to the bladder on the initial study; however, the patient returned with distant metastases. (b) Axial contrast-enhanced abdominal MR image obtained 4 months later shows a new lesion in the right hepatic lobe with peripheral enhancement (circle), reflecting liver metastasis. (c) Axial contrast-enhanced brain MR image obtained 9 months after a shows an enhancing nodule (circle) in the left frontal cortical gray matter, compatible with brain metastasis. (d) Axial unenhanced CT image acquired 11 months after diagnosis shows progression of disease with marked interval growth of the primary bladder mass, which now has a large exophytic component (arrows).

compared with conventional staging; FDG PET/CT depicted additional disease and either changed treatment intent from radical to palliative or altered the radiation therapy field (22). However, the standard use of FDG PET/CT has not been substantiated in the literature.

Treatment and Prognosis
EPSCC has an aggressive natural history characterized by rapid local progression, early widespread metastases, and recurrence following treatment (6). Because of its rare and varied manifestations, there is a paucity of data from randomized prospective trials; consequently, there is little consensus on the most effective treatment for EPSCC. Current management recommendations are derived from retrospective studies and small single-institution experiences or are extrapolated from SCLC data. Surgery, chemotherapy, and radiation therapy have all been used. Regardless of therapy, the prognosis is poor, with median survival ranging from 3 to 27 months and overall 5-year survival rates around 13% (2,7).

By most accounts, tumor stage affects EPSCC treatment strategies more than any other factor. In general, patients with limited disease are treated for potential cure with aggressive combined-modality therapy. Despite aggressive local therapy with surgery and radiation therapy, relapse is common and adjuvant systemic chemotherapy is often implemented. As with SCLC, typical regimens consist of at least four cycles with etoposide and a platinum-based agent such as cisplatin or carboplatin (10). Unfortunately, most patients develop metastases despite adjuvant therapy. Patients with extensive disease, on the other hand, are managed more conservatively, often with palliative measures (11). In extensive disease, chemotherapy is the primary therapeutic option; surgery and radiation are used sparingly to alleviate local symptoms (11).
Figure 8. Small cell carcinoma of the prostate in a 61-year-old man who presented with flank pain. (a) Sagittal unenhanced CT image shows a bulky mass arising from the prostate (arrows), which obstructed the right ureterovesical junction and produced obstructive uropathy. (b) Coronal unenhanced CT image reveals extensive retroperitoneal and pelvic lymphadenopathy (circles). (c) Axial unenhanced CT image shows pulmonary metastases (circle). Liver metastases were also present (not shown). Transurethral resection of the prostate was performed. (d) Photomicrograph (original magnification, ×20; hematoxylin-eosin stain) shows small to intermediate-sized, round to oval blue cells with scant cytoplasm and hyperchromatic nuclei with nuclear molding and mitotic figures. The morphologic findings are consistent with small cell carcinoma. Immunohistochemical stains (not shown) were strongly positive for CD56 and synaptophysin and focally positive for chromogranin A, supporting the diagnosis. Eighty-two of 83 “chips” (microarrays) (>99%) were involved by carcinoma. As commonly reported in the literature, PSA level was normal at 0.035 ng/mL (µg/L).

The role of prophylactic cranial irradiation in EPSCC remains controversial. In SCLC, brain metastases are common, with an incidence ranging from 20% to 30% in limited disease and as much as 40% in extensive disease (23). Stated another way, at least 18% of patients with SCLC have brain metastases at diagnosis, and the incidence approaches 80% at 2 years (23). Prophylactic cranial irradiation is offered routinely to patients with SCLC in complete remission after initial chemotherapy because it has shown a considerable survival benefit (23). Investigators have reported a lower incidence of brain metastases in EPSCC. For instance, in a series of 120 patients with EPSCC, the overall lifetime risk of developing brain metastasis was 13%; the risk was slightly higher in the cohort of patients with extensive disease, but still only 17% (10). In another review of 280 patients with EPSCC, only 18 (6.4%) developed brain metastases (24). At present, the risks of morbidity associated with prophylactic cranial irradiation outweigh data showing its efficacy, and it is not administered routinely in patients with EPSCC (11). The one exception may be head and neck EPSCC, which has higher rates of brain metastases; however, prophylactic cranial irradiation remains controversial even in this setting (5).

In the largest reported series, overall 3-year survival was 28% for limited and 9% for extensive disease (6). This study demonstrated differences in survival rates on the basis of site of origin: Breast EPSCC had the best 3-year survival rate (60%), followed by genitourinary (23%), lymph nodes and unknown primary origin
disease progressed and died of their disease (7). This series also revealed a survival difference between sites of origin: Patients with gynecologic EPSCC had the longest median survival (54.4 months), followed by those with breast EPSCC (40.9 months) (7). EPSCC of unknown primary origin had the worst outcome, with a median survival of only 2.5 months (7).

Although a specific imaging algorithm has not been established for EPSCC treatment response (22%), head and neck (16%), other (11%), and chest (8%), with gastrointestinal having the lowest rate (7%) (6). In another series with 101 patients, the median survival for patients with limited disease was 34 months, and that for patients with extensive disease was 2 months (7). Overall median survival for all patients was 9.83 months from the time of diagnosis (7). In this study, the median progression-free and/or recurrence-free survival in responding patients with limited disease was 20 months, compared with 12 months in patients with extensive disease (7). Seventeen of 38 patients (45%) who achieved complete response eventually developed recurrent disease, and all patients with partial response or stable disease progressed and died of their disease (7).
assessment, our institution prefers FDG PET/CT to characterize local progression and metastases in most cases. Continued investigation is required to determine the most effective clinical and radiologic management of patients with EPSCC to prolong disease-free survival.

**Conclusion**

EPSCC is a rare but aggressive entity that represents up to 5% of all small cell carcinoma cases. Although EPSCC is most commonly described in the gastrointestinal and genitourinary systems, it has been reported in nearly every organ in the body. EPSCC poses diagnostic and therapeutic challenges, as it is characterized by high rates of recurrence and poor survival. It is important for radiologists to gain familiarity with the range of imaging findings to contribute to the multidisciplinary management of patients with EPSCC and improve patient outcomes.

**References**