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Accurate Diagnosis of Peripheral Small Cell Lung Cancer with Computed Tomography

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Small lesions are frequently detected in the lung with computed tomography (CT) in clinical practice. It is important to know the CT features of small-sized periphearal small cell lung cancer (SCLC) for early-stage diagnosis. We reviewed the CT findings of SCLC that presented as a solitary peripheral nodule without associated lymphadenopathy. This study included 12 patients (11 men and 1 woman; mean age, 68.5 years) with peripheral SCLC of diameters ranging from 9 - 28 mm (mean, 15.4 mm). We evaluated the findings with thin-section CT for each peripheral tumor; emphasis was laid on the predominant internal characteristics (whether the mass is solid), tumor-lung interface characteristics (whether the mass is well-defined with a smooth surface or with lobulation or spiculation), and surrounding structures (the presence or absence of perivascular thickening adjacent to the tumor). In all patients, most portions of the tumor consisted of a non-calcified solid mass. Contrast enhancement in varying degrees was observed in the tumors of all 8 patients, who were evaluated with enhanced CT. The tumor-lung interface characteristics observed on the CT images included a well-defined mass with a smooth surface (n = 5), a well-defined mass with lobulation (n = 3), and a mass with spiculation (n = 4). An irregular perivascular thickening adjacent to the tumor was observed in 4 patients. We conclude that peripheral SCLC without associated lymphadenopathy manifests as a non-calcified solid mass and is occasionally characterized by perivascular thickening. ———— small cell cancer; lung; CT; lung cancer; neuroendocrine tumor.
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Many small lesions of the lung are detected by computed tomography (CT) in clinical practice. It can be difficult to differentiate between malignant and benign nodules, especially when the CT image shows a small non-calcified soft-tissue density mass (Mack et al. 1993; Bernard and the Thorax Group 1996). The detection of small lesions increases the possibility of curing lung cancer, but it may also lead to unnecessary invasive procedures.

Small cell lung cancer (SCLC) accounts for about 20% of bronchogenic carcinomas (Quinn et al. 1996). Most patients with SCLC have extensive disease at the time of diagnosis. SCLCs usually occur centrally, and less than 10% of SCLCs occur peripherally; they present as solitary pulmonary nodules without associated lymphadenopathy on CT images (Gephardt et al. 1988; Quoix et al. 1990). This type of SCLC is potentially curable by surgery (Quoix et al. 1990; Urschel 1994). It is important to know the CT features of solitary SCLCs that are located peripherally and are small in size in order to reduce diagnostic delay and ensure early-stage diagnosis.

To our knowledge, the CT features of SCLC presenting as a small peripheral nodule have not been adequately described (Yabuuchi et al. 1999). The purpose of this study was to evaluate the CT features of small-sized peripheral SCLC (< 30 mm) without associated lymphadenopathy.

Materials and Methods

We reviewed the medical records of patients from 2 institutions who were pathologically diagnosed with SCLC during the period from 1997 through 2007. The institutions provided access to patient records, and patient confidentiality was maintained. On observing CT scans, we found 12 patients with peripheral SCLC without associated lymphadenopathy. The presence of mediastinal or hilar lymph nodes with a short-axis diameter greater than 1 cm was considered as proof of lymphadenopathy. These patients were asymptomatic and comprised11 men and 1 woman (age range, 56 - 79 years; average age, 68.5 years). All the patients had a history of smoking: 8 heavy smokers; ≥ 30 pack-years (cigarette consumption index) and 4 mild smokers; < 30 pack-years. Tumors were detected among these patients during screening of the chest for other diseases (n = 4) and during lung cancer screening (n = 8). A histological diagnosis was obtained by performing surgical resection (n = 10) and CT-guided biopsy (n = 2). The disease stage was classified as T1N0M0 in all the

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patients, on the basis of pathological (n = 10) and clinical (n = 2) findings. The surgical procedure included a lobectomy with lymph node dissection. The pathological materials were examined by 2 pathologists. All the tumors described in the present study could be classified as "classic small cell carcinomas" as per the revised 1999 World Health Organization (WHO) classification system.

CT was performed on the first 2 patients with conventional CT scanners, on 7 patients with single-slice helical CT scanners, and on the last 3 patients with 64-row multi-slice helical CT scanners. In all cases, contiguous 8-mm or 5-mm collimation scans of the entire chest were obtained. Of the 12 CT examinations, 8 tumors were contrast-enhanced and 4 were not enhanced. In all the patients, the lung nodules were characterized by high-resolution CT images (slice thickness, 1 - 3 mm). Two radiologists evaluated thin section CT findings for each peripheral tumor by consensus; emphasis was laid on the predominant internal and tumor-lung interface (marginal) characteristics and surrounding structures. We evaluated the internal characteristics of the tumor, and if it was a solid mass, it was classified as follows: a well-defined mass with a smooth surface, a well-defined mass with lobulation, or a mass with spiculation (marginal characteristics). Further, we examined the surrounding structures for the presence of irregular perivascular thickening adjacent to the tumor. We defined a peripheral tumor as a tumor located within the peripheral two-thirds of the lung without contact with lobar or segmental bronchi, as observed on CT images. A solid mass was defined that mainly consisted of homogeneous soft-tissue density areas on CT images (Sone et al. 1997). Lobulation was defined as an abrupt bulging of the lesion contour. Spiculation was defined as the presence of 2-mm or thicker strands extending from the nodule margin into the lung parenchyma without reaching the pleural surface (Zwirewich et al. 1991).

Results

The mean diameter of the largest tumor observed on the axial images of the 12 patients was 15.4 mm (range, 9 - 28 mm) (Table 1). In all the patients, most portions of the mass were solid (Fig. 1). Contrast enhancement in varying degrees was observed in the tumors of the 8 patients with enhanced CT. Cavity, air space, or calcification was not found in the tumors of any patient.

The marginal characteristics observed on the CT images included a well-defined mass with a smooth surface (n = 5) (Figs. 1 and 2), a well-defined mass with lobulation (n = 3), and a mass with spiculation (n = 4) (Fig. 3). Ground-glass opacity around the mass was not observed on the CT images of any of the patients, except for one whose CT images showed ground-glass opacity around a part of the tumor.

An irregular perivascular thickening adjacent to the tumor was found on CT images in 4 patients (Fig. 1). Of the 4 patients, pleural retraction was found in 2 patients with a mass with spiculation and 1 patient with a well-defined mass with a relatively smooth surface.

Two patients received chemotherapy as the primary treatment (Table 1). Surgery was performed as the primary treatment in 10 patients, one of whom received postoperative chemotherapy. The median survival period from the date of diagnosis was 37 months. Of the 12 patients, 4 are alive and free of the disease, 3 died of recurrent SCLC, 3 died of other diseases, and 2 patients were lost to follow up.

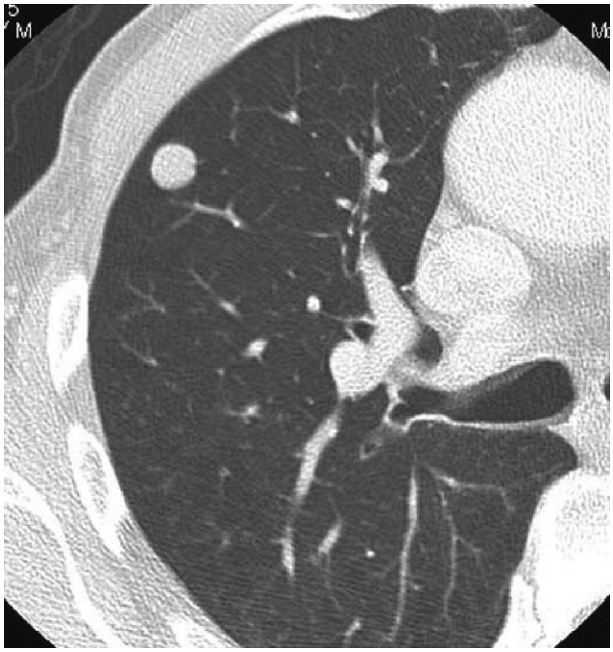
Discussion

Peripheral lung nodules are usually classified as predominantly solid or non-solid (predominantly exhibiting ground-glass opacity) masses. Most of the non-solid masses are considered as well or moderately differentiated adenocarcinomas (Kuriyama et al. 1999; Takashima et al. 2003). In contrast, non-calcified solid masses may be benign or malignant lesions (Munden et al. 1997; Henschke et al. 1999; Bastarrika et al. 2005). Most of the non-calcified solid nodules that were less than 5 mm in diameter were found to be benign in the patients who underwent low-dose CT screening for lung cancer. The frequency of malignancy was found to be high in the cases of larger nodules (Henschke et al. 2004; Bastarrika et al. 2005).

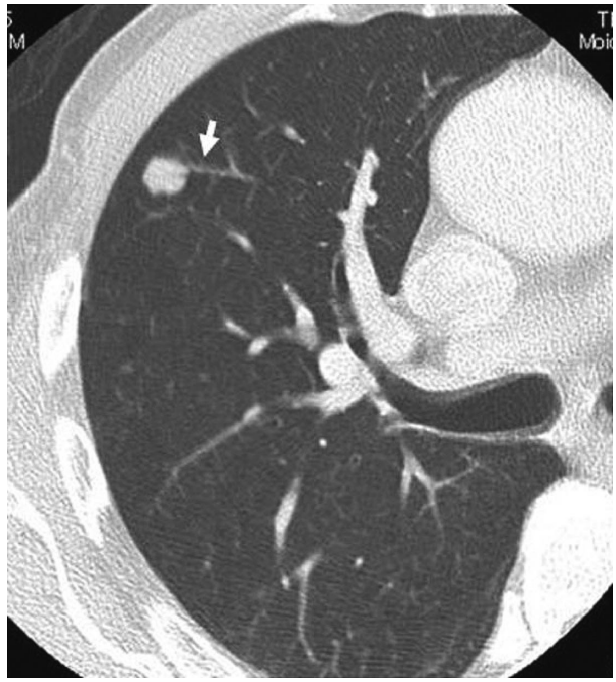
In our study, peripheral SCLC without associated lymphadenopathy appeared as a non-calcified solid mass on CT images. The tumor margins of tumors that were

Table 1. Patient characteristics.

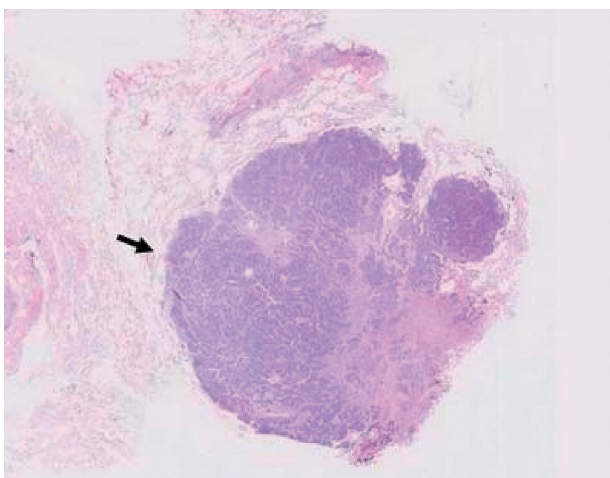
Case	Age(years)/Sex	Diameter(mm)	Solid mass or not	Margin	Vascular wall Thickening	Follow-up
1	56/M	9	Solid	Smooth		Alive, 92 mo
2	70/M	10	Solid	Smooth		Dead, 71 mo
3	78/M	10	Solid	Smooth	+	Alive, 6 mo
4	57/M	11	Solid	Spiculation		Alive, 96 mo
5	77/M	12	Solid	Smooth		Dead, 32 mo
6	72/F	12	Solid	Lobulation	+	Dead, 15 mo
7	64/M	12	Solid	Smooth	+	Alive, 9 mo
8	70/M	14	Solid	Spiculation		Lost, 42 mo
9	68/M	18	Solid	Spiculation		Dead, 13 mo
10	64/M	22	Solid	Lobilation		Lost, 48 mo
11	79/M	27	Solid	Spiculation	+	Dead, 24 mo
12	67/M	28	Solid	Lobulation		Dead, 72 mo



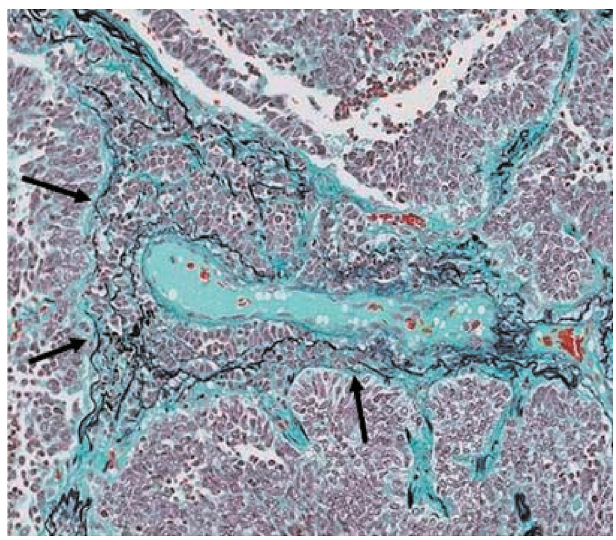
A. Thin-section CT scan obtained with a lung window in the right upper lobe shows a well-defined solid mass with a smooth surface.



B. CT scan obtained 3mm caudal to A. shows an irregular perivascular thickening adjacent to the tumor (arrow).



C. Low-power photomicrograph (hematoxylin-eosin stain) shows a well-defined solid mass with relatively smooth surface (arrow).



D. Medium-power photomicrograph (elastica-mason stain) shows tumor spread of small cell cancer in the perivascular space (arrows).

Fig. 1. Small cell lung cancer in a 78-year-old man.

approximately 10 mm in diameter were found to be relatively smooth, while the margins of those were bigger tended to be irregular. However, these internal and marginal characteristics were not specific to peripheral SCLCs. Poorly differentiated adenocarcinomas and squamous cell carcinomas appear on CT images as a well-defined solid mass showing lobulation or spiculation (Sone et al. 1997; Wang et al. 2000). Large cell neuroendocrine carcinoma appears on CT images as a solid mass with marginal characteristics similar to those observed in SCLCs (Oshiro et al. 2004). It may be difficult to differentiate peripheral SCLCs from carcinoid tumors and benign diseases such as granuloma when peripheral SCLC appears on CT images as a well-defined solid mass with a relatively smooth surface.

The use of dynamic contrast-enhanced CT or positron emission tomography with F-18-fluorodeoxyglucose (FDG-PET) is useful for distinguishing malignant tumors from benign ones. Malignant tumors, including peripheral

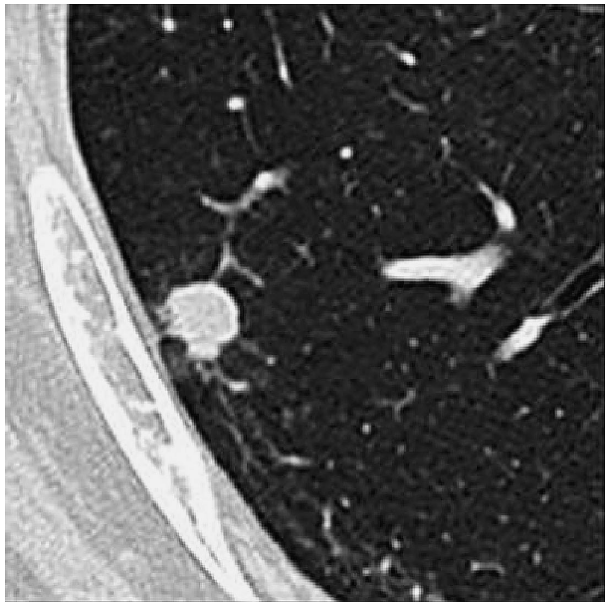


Fig. 2. Thin slice CT scan obtained in a 70-year-old man shows a 10-mm mass with relatively smooth surface in the right lower lobe. Note that pleural retraction is also seen.

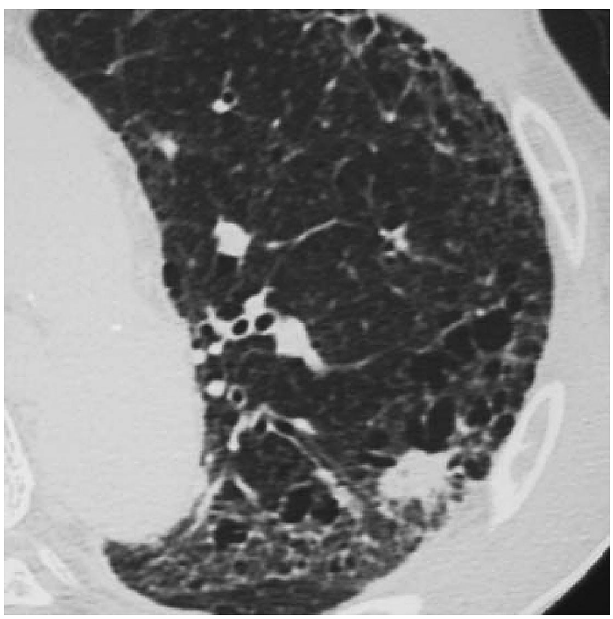


Fig. 3. CT scan obtained in a 57-year-old man reveals an 11-mm mass with spiculation in the left upper lobe. Spiculation might be somewhat enhanced by preexisting emphysema.

SCLCs, tend to exhibit greater enhancement (Zhang and Kono 1997; Swensen et al. 2000; Yi et al. 2004) and increased FDG uptake (Schrevens et al. 2004). The sensitivity of FDG-PET scanning for SCLCs is 100% (Pandit et al. 2003). In our series, we did not evaluate the precise enhancement pattern, since the CT scanners that were used and the injection rate of the contrast medium differed for each patient. We observed various degrees of enhancement for each tumor (n = 8). Typically, a solid mass that is enhanced to a lesser extent is more likely to be of a benign (Zhang and Kono 1997; Swensen et al. 2000; Yi et al. 2004).

In 2 of the 4 patients with perivascular thickening, histological findings revealed spread of the tumor in the perivascular connective tissue. Small cell carcinoma tends to spread in the submucosa and perivascular connective tissue of the lobar or main bronchi (Fraser and Pare 1989). The results of the present study showed that perivascular spread adjacent to the tumor was present in the peripheral SCLC, even though the tumor was in small in size. To our knowledge, this CT finding has not been previously reported and observed in only approximately 33% of the patients in our series; however, perivascular thickening can sometimes occur in the peripheral SCLCs.

There were some limitations to our study. First, we retrospectively evaluated the CT features of peripheral SCLC in a small number of patients. Second, the results of pathological analyses for identifying the cause of perivascular thickening were available for only 2 patients. However, we think that peripheral SCLC should be considered during differential diagnosis in cases when perivascular thickening is present adjacent to the solid mass.

In conclusion, a peripheral SCLC without associated lymphadenopathy appeared on CT images as a non-calcified solid mass with a smooth or lobulated surface or with spiculation on CT scans, this observation was found to be partly dependant on tumor size. In some cases, it was characterized by a perivascular thickening.

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