Case Report

An unexpected SCLC diagnosed by electromagnetic navigation bronchoscopy

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Introduction

Lung cancer remains the leading cause of cancer-related death in China and the United States (1,2). Small cell lung carcinoma (SCLC) constitutes 10–15% of all lung cancer cases (3). Owing to its rapid volume-double time, high growth fraction and greater propensity for early hematogenous spread, it's considered the most aggressive form of lung cancer, its overall 5-year survival rate is around 7%. Traditionally, SCLCs present as a large hilar mass and bulky lymphadenopathy, whereas a peripheral SCLC is rather uncommon. One case with an unexpected peripheral SCLC was reported in our institute. After pathologically diagnosed as SCLC assisted by electromagnetic navigation bronchoscopy-guide trans-bronchial needle aspiration (ENB-TBNA), the patient underwent a standard video-assisted lobectomy and lymphadenectomy and recovered well. The confirmatory procedures as well as imaging demonstrations of peripheral SCLC will be discussed by reporting this case and reviewing related literature.

Case presentation

A 53-year-old female was admitted due to a nodular lesion in the right lower lobe. The patient was free from any respiratory, neurological, or endocrine paraneoplastic symptoms. She had no smoking or radioactive substances exposure history. No history of recurrent pulmonary infections including tuberculosis or family history of cancer was present.

Physical examinations and laboratory tests were unremarkable, particularly the tumor biomarkers including CEA, FRT, NSE, CA125, CYFRA21-1, CA50, SCC were negative.

Computed tomography with contrast of the chest (*Figure 1*) showed a 1.3 cm × 1.4 cm well-defined solitary nodule adjacent to a segmentary artery in the right anterior basal segment. The lesion was homogenous in density; the CT value in the arterial phase was 30 HU and that of the venous phase 48 HU, making the imaging diagnosis a bronchial mucous plug or a pulmonary cyst. Conventional bronchoscopy demonstrated a negative result.

The patient adopted one of the 3 recommendations and underwent an ENB-TBNA (others were 1-month follow-up and an immediate lobectomy). The ENB-TBNA in the case reported was performed by a bronchoscopist in our institute, SuperDimension Bronchus System (SDBS, Herzliya, Israel) was used for navigation, and TBNA was performed using a 22-gauge cytology needle. ENB-TBNA successfully produced a sample (*Figure 2*) and hematoxylin-eosin staining and immunohistochemistry confirmed it to be a SCLC. A subsequent PET/CT scan (*Figure 3*) suggested that it was a limited stage disease without metastatic lymphadenopathy. A multidisciplinary team consultation, consisting of a pulmonologist, a thoracic surgeon, an oncologist and a radiologist was done, which determined the patient was at the cT1N0M0 and stage IA2. EBUS-TBNA was recommended to proceed pathological mediastinal staging according to NCCN guidelines; despite this, the patient refused further invasive diagnostic procedures and demanded surgical treatment. Considering PET/CT suggested no metastatic lymphadenopathy and that even N1 SCLC disease benefit from surgery (4,5), we believed straightforward surgery was reasonable and a video-assisted right lower lobe resection and systematic

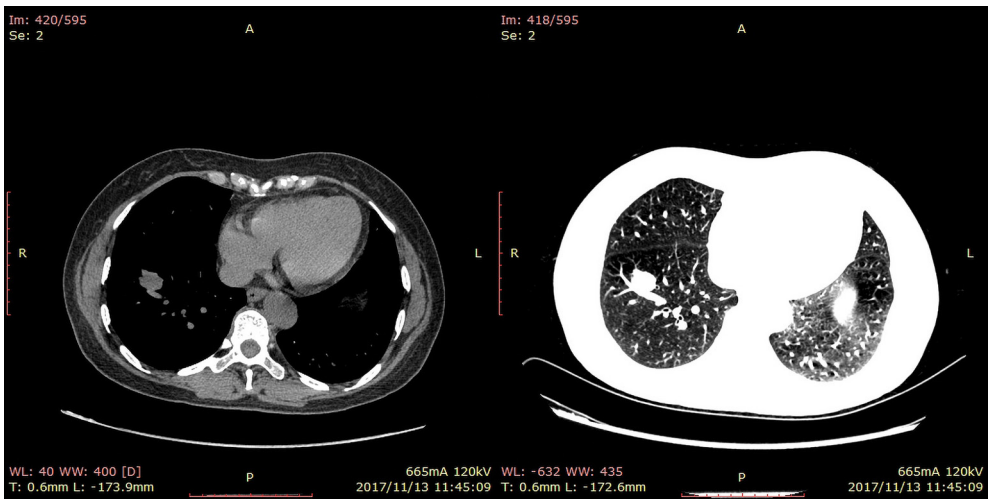

Figure 1 Computed tomography of the chest.

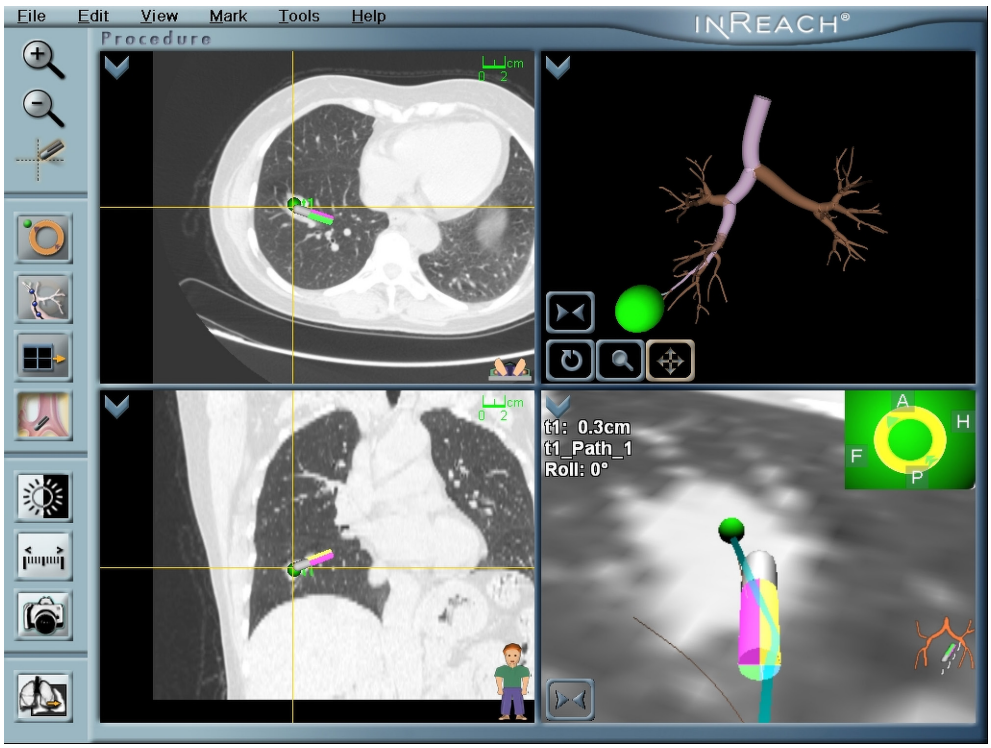

Figure 2 ENB-TBNA procedure. ENB-TBNA, electromagnetic navigation bronchoscopy-guide trans-bronchial needle aspiration.

lymphadenectomy of stations 2R, 3a, 4R, 7, 9R, 10R, 11R and 12R was performed under the patient's consent. The patient recovered well from the surgery with 5-day chest drainage and 7-day hospital stay. Post-operation pathology confirmed it was a right lower lobe SCLC with stations 12R, 11R, 10R metastatic lymphadenopathies. Adjuvant chemotherapy and prophylactic cranial irradiation are to be followed.

Discussion and conclusions

SCLC typically manifests as a hilar mass and bulky

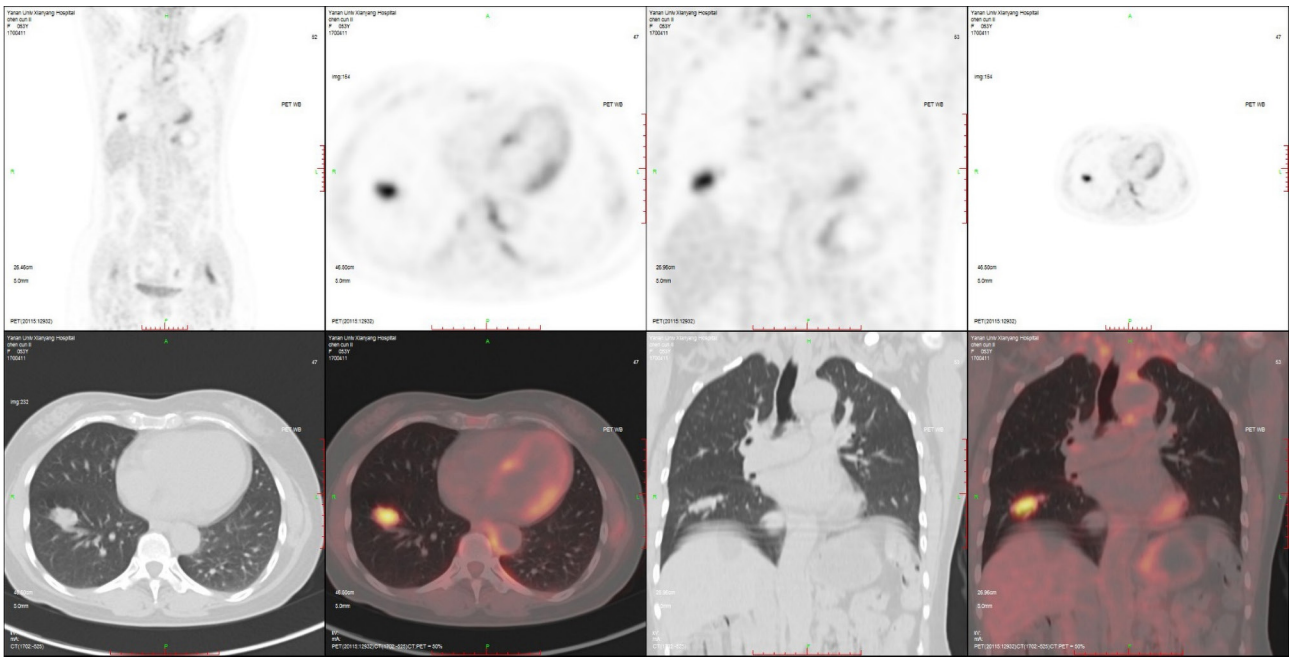

Figure 3 PET/CT scan findings. PET/CT, positron emission tomography/computed tomography.

mediastinal lymphadenopathy and symptoms of widespread metastatic diseases; it's long been believed to be the central-type lung cancer, and the central-located SCLC accounted for about 60% of all the cases (6). Recently, occurrence of peripheral-located SCLC seems to be growing (7-9), which can partly be attributed to the advent of lung cancer screening with low-dose computed tomography (LDCT). Peripheral SCLCs seem to mean less hilar and mediastinum involvement, less extended stage cases, and less distant metastasis. Kanaji *et al.* (9) reported better survival rates in patients with peripheral-type SCLC, and concluded that it resulted from more frequent surgical treatment for peripheral located SCLC, better PS scores, less tumor burden and more limited stage diseased of such cases. Since surgery on high selected cT0-1N0-1 SCLC patients can yield a favorable 5-year survival rates of 40–60% (5,10-13), early detection and surgical intervention in peripheral SCLC cases may be essential to improve the prognosis of the aggressive malignancy.

The treatment modality of peripheral cT0-1N0-1 SCLC is be lobectomy followed by adjuvant chemotherapy and prophylactic cranial irradiation (14); whereas the choice of confirmatory procedure of a peripheral lesion depends on available resources, cost performance, patient preference, practitioner expertise, etc. Currently, the most frequently-used procedures embrace conventional bronchoscopy-guided transthoracic needle aspiration, CT-guided transthoracic needle aspiration, EBUS-guided transthoracic needle aspiration and more aggressive immediate surgery. Apart from the advantages, the drawbacks of the procedures mentioned above should be concerning. First, conventional bronchoscopy has a poor yield between 14% to 62% for small peripheral lesions (15-17). Second, while CT-guided core/fine needle aspiration does have higher sensitivity and precision for peripheral disease, its higher rates of complications such as pneumothorax and bleeding should not be overlooked (18-21). Third, previous studies (22-26) found that the diagnostic sensitivity of EBUS-TBNA ranged from 74.5% to 92% involved with sarcoidosis, lung cancer staging, or undiagnosed mediastinal lymphadenopathy, and the figure was similar with that of ENB-TNBA; whereas the figure dropped when focusing on diagnoses of lung nodules (46% to 88%) (27-32), noticeably in some studies the high upper end resulted from the application of ROSE. This implies that ultrasound guiding techniques may be inferior to ENB on diagnosing lung nodules, especially peripheral lesions. Fourth, surgery is never a good option for the elderly patients or patients with higher Charlson Comorbidity Index, even though it can avoid pitfalls of less invasive procedures for low- to intermediate-risk patients

with suspected cancer; and a lobectomy for small peripheral benign nodules may be much more aggressive.

Electromagnetic Navigation Bronchoscopy can be a good option under the circumstances similar to the case reported. It is recommended for detecting peripheral lesions that are hard to reach with conventional bronchoscopy (33), and its diagnostic yield varies from 60% to 87.5% (34-38), with a pooled sensitivity more than 71% and accuracy more than 73.9% (37,38). Moreover it is safer and the risk of pneumothorax is around 3.1% (37), whereas pneumothorax following transthoracic needle lung biopsy is 15% and hemorrhage 1% (19). Thus, ENB is an effective and safe procedure to investigate peripheral lung lesions; in the cases of peripheral SCLC, it can yield earlier diagnosis, lead to earlier interventions including surgery, and provide the chance for cure.

ENB's higher safety and yield come at a cost. Owing to its low cost-effectiveness ratio, ENB is not as prevalent as bronchoscopy-guided and CT-guided transthoracic needle aspiration. In most cases, computed tomography still plays an important role in the diagnosis of SCLC. Efforts were made to summarize recognizable CT features of SCLC (39-42). It seems that peripheral SCLC is a lobulated (69.6%) or a well-defined (66.1%, 37/56) mass rather than a spiculated mass (17.9%, 10/56). Notably, Yabuuchi *et al.* (39) reported that all the 12 peripheral lesions were homogenous in density. These findings can provide some references for imaging diagnosis, even though they may be nonspecific. On the other hand, as positron emission tomography (PET) with [^{18}F] fluorodeoxy-D-glucose (FDG) emerges as an accurate and superior tool for NSCLC staging, studies aimed at exploring the similar utility of PET in SCLC. A prospective study of 120 consecutive patients with newly detected SCLC concluded that complete agreement between FDG-PET results and other staging procedures were observed in 75 patients (43), but there seemed to be no pathological confirmations. The divergence between PET and pathology does exist, as depicted in the case reported above, metastatic lymphadenopathy in SCLC may not be detected by PET/CT scan. We speculate that the underlying reason is lower tumor burden in metastatic lymph nodes in early stage peripheral SCLC. Thus, the precise workup of peripheral SCLC should be comprehensive, and invasive procedures could be recruited if necessary.

All in all, we conclude that Electromagnetic Navigation Bronchoscopy might be useful for peripheral nodes diagnosis and avoidance of futile surgeries. Particularly in the case reported, Electromagnetic Navigation Bronchoscopy can be beneficial to diagnose peripheral SCLC at the early stage, leading to earlier surgical intervention and providing the chance for cure.

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None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Informed Consent: Written informed consent was obtained from the patient for publication of this manuscript and any accompanying images.

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