Demonstration of the skip metastasis pathway for N2 non–small cell lung cancer

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We report the use of an indocyanine green (ICG)–near-infrared fluorescence (NIF) imaging system for the intraoperative detection of lung cancer metastasis directly

to mediastinal lymph nodes without intrapulmonary or hilar lymph node involvement (skip metastasis).

CLINICAL SUMMARY

A 67-year-old woman whose chest computed tomographic scan images showed a 23-mm solid tumor in the right segment 7 without any lobar, hilar, or mediastinal lymphadenopathy was referred to our hospital. Transbronchial endoscopic tumor biopsy revealed the tumor to be an adenocarcinoma. Positron emission tomographic and computed tomographic imaging with fludeoxyglucose F 18 (INN fludeoxyglucose [18F]) showed no marker uptake in any lymph nodes and no distant metastases. Postcontrast magnetic resonance imaging of the brain also indicated no brain metastases.

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FIGURE 1. Intraoperative endoscopic findings. A, A 2-mL dose of indocyanine green was injected into the peritumoral lung parenchyma with a 26-gauge needle. B, White-light mode showing injected indocyanine green. C, Indocyanine green mode showing fluorescence of injection site.

FIGURE 2. Intraoperative endoscopic findings. A, White-light mode showing subcarinal lymph nodes. C, Indocyanine green mode showing 2 subpleural lymphatic vessels and a sentinel node, all of which were illuminated by indocyanine green. C and D, Magnified views of panels A and B, respectively. RLL, Right lower lobe.

The diagnosis of clinical T1b N0 M0, stage IA non–small cell lung cancer (NSCLC) was made, and the patient underwent video-assisted thoracic surgical (VATS) right lower lobectomy with standard mediastinal lymph node dissection.

In our hospital, a clinical study to identify sentinel nodes (SNs) in patients with NSCLC during VATS lobectomy or segmentectomy by means of an indocyanine green fluorescence endoscopy system is ongoing. This patient was enrolled in that study.

After exploration of the thoracic cavity with an endoscope before VATS lobectomy, 2 mL of ICG was injected into the peritumoral lung parenchyma (Figure 1, A–C). After the right lung had been ventilated for 3 minutes to stimulate lymphatic flow, the hilum, intralobar area, and mediastinum were observed with an endoscopic ICG-NIF imaging system (D-LIGHT P; Karl Storz GmbH & Co KG, Tuttlingen, Germany). Two subpleural lymphatic vessels running toward the subcarinal lymph node station were clearly visualized by the ICG mode, and 1 of the vessels reached a lymph node that was also illuminated by ICG (Figure 2, A–D). Other lymphatic vessels or other lymph nodes did not show ICG fluorescence. The illuminated lymph node was sampled as an SN, and other lymph nodes were dissected en bloc. VATS right lower lobectomy with ND2a-2 lymph node dissection was completed uneventfully. Pathologic examination with hematoxylin and eosin staining revealed metastatic adenocarcinoma in the SN. Micrometastases were present in 2 of 6 lymph nodes in station 7 and 2 of 15 lymph nodes in station 4R, although the lobar and hilar lymph nodes

(stations 11, 12, and 13) showed no metastasis. The patient thus was considered to have skip N2 metastasis.

DISCUSSION

Lung cancer often metastasizes directly to mediastinal lymph nodes without intrapulmonary or hilar lymph node involvement. This phenomenon is called *skip metastasis*. Patients with skip metastasis had been reported to be a unique population with a better prognosis than patients with pN2 intrapulmonary or hilar lymph node involvement.¹

The mechanism of skip metastasis has been considered as follows. First, tumors with visceral pleural involvement metastasize to mediastinal lymph nodes through lymphatic vessels of the parietal pleura. Then tumors metastasize to the mediastinal lymph nodes through intrapulmonary lymphatic vessels, bypassing the N1 node. Another possible explanation for skip metastasis may be the failure to note N1 micrometastasis on routine histopathologic examination.

In this case, a subpleural lymphatic vessel running toward one of the subcarinal lymph nodes was clearly visualized with the endoscopic ICG-NIF imaging system. Pathologic examination revealed that the SN was a metastatic lymph node, whereas intrapulmonary and hilar lymph nodes showed no metastasis. In this skip metastasis case, the tumor was considered to have metastasized to the mediastinal lymph nodes through lymphatic vessels of the parietal pleura.

The SN is defined as the first node draining a tumor and should be the first site affected in lymphatic dissemination.

SN navigation surgery has been commonly performed in breast cancer surgery to reduce the extent of lymphadenectomy, leading to a reduction in operative complications. On the other hand, lymphadenectomy has not been found to increase the operative mortality or complications relative to lymph node sampling in NSCLC surgery.²

SN identification has a new significance in recent NSCLC surgery. With the increased incidence of detection of small-sized NSCLC, a phase III randomized trial of lobectomy versus segmentectomy for small-sized peripheral NSCLC is ongoing.³ The eligibility criteria for segmentectomy state that there should be “no lymph node metastasis” and that patients with node-positive cases should undergo lobectomy with standard lymphadenectomy to ensure radical resection. Because the accuracy of clinical nodal staging even with fludeoxyglucose F18 positron emission tomography and computed tomography is still low,⁴ intraoperative sampling and frozen sectioning of lymph nodes are indispensable for segmentectomy. Random sampling of N1 lymph nodes has no meaning, however, because the lymphatic flow of the lung varies. Therefore, SN identification is important for patients with clinical stage I NSCLC who are candidates

for segmentectomy.⁵ Recently, an endoscopic ICG-NIF imaging system became commercially available, and this system can be used during VATS.

In conclusion, this report shows the utility of an endoscopic ICG-NIF imaging system for SN identification during VATS, with especial value in identifying subpleural lymphatic spread.

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Minimally invasive enucleation of a large, extensively calcified esophageal leiomyoma

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Video clip is available online.

A number of gastrointestinal tumors may present with macroscopic calcifications; however, true esophageal

tumors with this characteristic are uncommon. Leiomyomas are the most likely esophageal neoplasms to develop calcifications, and the presence of calcification within an esophageal tumor strongly suggests this diagnosis. We present a case of a rare calcified, distal esophageal leiomyoma that was successfully enucleated through a thoracoscopic approach.

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CLINICAL SUMMARY

A 63-year-old man was referred to our institution with reports of vague left-sided chest pain for the previous 3 months and new-onset atrial fibrillation. A chest radiograph suggested a calcified posterior mediastinal mass (Figure 1, A). Workup continued with a barium esophagogram, which demonstrated a large, smooth-bordered, extraluminal, partially-obstructing distal esophageal mass (Figure 1, B). A subsequent computed tomographic scan of the chest confirmed the intramural, multilobulated, calcified mass measuring 7 cm in maximum diameter