Small Cell Carcinoma Presenting with Massive Pleural Spread Mimicking Malignant Pleural Mesothelioma

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Abstract

Small cell carcinoma (SCC) predominantly spreading over the pleura is exceedingly rare and difficult to diagnose without proof of malignant effusion. A 65-year-old man presented with right pleural thickening and effusion and was diagnosed with SCC based on a thorascopic pleural biopsy. He received combined chemotherapy consisting of cisplatin and irinotecan hydrochloride, which resulted in a complete response. Seven months later, local relapse was observed. Thereafter, he received second-, third- and fourth-line chemotherapies and died of tumor progression 21 months after the diagnosis. Considering the possibility of SCC with pleural spread, performing early invasive procedures is important for diagnosing pleural malignancies.

Key words: small cell carcinoma, pleural spread, video-assisted thoracic surgery (VATS), pleural biopsy


Introduction

Small cell carcinoma (SCC) is usually observed as a central type of lung cancer with a highly malignant potential and poor prognosis as a consequence of early metastasis to the mediastinal lymph nodes and distant organs. SCC predominantly spreading over the pleura without any apparent masses in the lung fields or lymph node swelling is exceedingly rare and difficult to diagnose when malignant pleural effusion is not observed. The highly malignant and proliferative potential of SCC requires prompt diagnosis and early treatment in order to obtain a better prognosis.

We herein report the case of a patient who presented with SCC predominantly spreading over the pleura that was diagnosed using video-assisted thoracic surgery (VATS) and subsequently controlled with appropriate chemotherapy.

Case Report

A 65-year-old man with a smoking habit of 80 pack-years presented with right chest pain. Chest X-rays (Fig. 1) and CT scans (Fig. 2) revealed thickening of both parietal and visceral pleurae, nodular masses and pleural effusion in the right thoracic cavity. The concentrations of LDH and total protein in the pleural effusion were 430 IU/L and 3.8 g/dL, respectively, classifying the pleural effusion as exudative according to Light’s criteria. The concentration of hyaluronic acid in the pleural effusion was not significantly increased (21 μg/mL). The cytology of the pleural effusion was negative. The serum levels of progastrin-releasing peptide (ProGRP) and neuron specific enolase (NSE) were 2,578.0 pg/mL (normal range, <46.0 pg/mL) and 39.3 ng/mL (normal range, <16.3 ng/mL), respectively.

Since the possibility of a malignant pleural tumor could not be excluded and the mass could not be identified in the right lung field, VATS was performed to confirm the pathologic diagnosis. VATS revealed pleural thickening with a nodular mass predominantly around the costophrenic angle with some nodules inside of the thoracic cavity, suggesting dissemination. The histology demonstrated small- to intermediate-sized malignant cells with hyperchromatic nuclei, very scant cytoplasm and a partly rosette-like and palisading growth pattern (Fig. 3a, b), confirming the diagnosis of SCC. The origin of the SCC was unclear, even on VATS, which failed to demonstrate a pleural origin. Therefore, considering the rareness of SCC of pleural origin, the very small mass in the peripheral lung field adjacent to the area of pleural thickening was considered to be the origin, indicating invasion to the visceral pleura (stage T2a; the dis-
semilated nodules suggested a stage of M1a). Taken together, the clinical stage was cT2aN0M1a, stage IV. The patient’s chest pain was so severe that oxycodone was prescribed for palliation, and he required frequent visits to our emergency room.

The patient received combined chemotherapy consisting of cisplatin (60 mg/square meter) on day 1 and irinotecan hydrochloride (60 mg/square meter) on days 1, 8 and 15 every 28 days for four cycles, which resulted in a complete response (CR, Fig. 4) accompanied by dramatic relief of the patient’s pain and a reduction in the dose of oxycodone. After seven months of progression-free survival (PFS), local relapse was observed. The same chemotherapy regimen as the second-line treatment was effective and administered for three cycles, resulting in a partial response with four months of PFS. After confirming progressive disease (PD), amrubicin hydrochloride (40 mg/square meter) was administered on days 1, 2 and 3 every 21 days for six cycles, resulting in a partial response with seven months of PFS. As the fourth-line chemotherapy, paclitaxel (200 mg/square meter) was administered on day 1 every 21 days for two cycles, resulting in PD. The patient died of tumor progression 21 months after the diagnosis.

Discussion

SCC usually presents with the central type lung cancer and mediastinal extension (1) with rapid progression and metastasis that requires a prompt diagnosis for early treatment. The frequency of pleural dissemination of SCC is relatively rare (5.9%) (1), while SCC predominantly spreading over the pleura is exceedingly rare, with few case reports. A series of four case reports of SCC simulating pleural mesothelioma was reported in 1995 (2) in which a long history of cigarette smoking was observed in all patients. In addition, one case report of high-grade neuroendocrine carcinoma of the lungs with pleural spread was reported in 2004 (3).

Primary lung cancer mimicking malignant pleural mesothelioma was first reported in 1976 as “pseudomesothelioma...
Pseudomesotheliomatous carcinoma of the lung (4). Pseudomesotheliomatous carcinoma is a rare variant of peripheral adenocarcinoma of the lungs that manifests clinical, radiological and pathological features similar to malignant mesothelioma (5). Following the initial report of adenocarcinoma, the same extension of SCC has been observed (2); however, the occurrence of SCC spreading in this fashion is quite rare and is not well known.

The rareness of SCC predominantly spreading over the pleura sometimes delays the diagnosis too late for treatment, which should be avoided considering the condition’s highly malignant potential and rapid extension.

Making an appropriate diagnosis of pleural malignancies, including malignant pleural mesothelioma (MPM) and carcinomatous pleuritis, is difficult when no malignant cells are observed in the pleural effusion. Thoracoscopy is a safe procedure for observing the thoracic cavity and performing pleural biopsies to make a final histological diagnosis.

The diagnostic rate of detecting pleural tumors has been investigated in patients with MPM. It has been reported that...
the rate of diagnosing MPM is 20.7% on needle biopsies and 26% based on the cytology of the pleural effusion. In contrast, this rate is much higher on VATS at 98% (6).

In the present case, performing early invasive procedures in order to make a diagnosis using VATS was the key to appropriately introducing combined chemotherapy, which obtained the clinical benefits of both subjective pain relief and an objective tumor response accompanied by 21 months of survival after the diagnosis.

We herein described the case of a patient with SCC and massive pleural spread without any masses in the lung fields or lymph node swelling that was diagnosed using a thoracoscopic pleural biopsy. Considering the highly malignant potential and rapid extension of SCC, the early histological evaluation with VATS played an important role in the patient’s survival.

This case suggests the importance of performing early VATS procedures to diagnose pleural tumors in patients without proof of malignant pleural effusion, considering the possibility of SCC predominantly spreading over the pleura.

The authors state that they have no Conflict of Interest (COI).

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**References**