

Pleural Metastasis of Atypical Bronchial Carcinoid

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Pulmonary carcinoids are relatively rare tumors with low metastatic potential. Pleural carcinomatosis of a bronchial carcinoid has only been reported in 4 cases. Due to the rarity of this condition, there are no guidelines for its treatment or management. We report a case of atypical carcinoid with local recurrence and pleural metastases treated by video-assisted thoracoscopic surgery lobectomy and total pleurectomy with photodynamic therapy after non-radical wedge resection.

Keywords: Carcinoid tumor, Neoplasm metastasis, Photochemotherapy, Pleurectomy, Video-assisted thoracoscopic surgery

Case report

A 51-year-old non-smoking woman was admitted to L. G. Sokolov Memorial Hospital 122 due to an area of consolidation in the middle lobe that was found on a chest computed tomography (CT) scan. Two years ago, chest CT was performed due to increasing dyspnea, and revealed a middle lobe neoplasm (Fig. 1). The lesion was solid, centrally located, measuring 16×15 mm, with smooth margins, and caused partial atelectasis of the middle lobe with no enlarged lymph nodes. During video-assisted thoracoscopic surgery (VATS) exploration performed at another institution, the neoplasm in the middle lobe was visualized, as well as multiple small yellowish foci on the parietal pleura, upon which basis pleural dissemination was suspected. Thus, wedge resection of the middle lobe with the entire lesion and biopsy of the parietal pleura were performed. According to the morphologic examination, an atypical carcinoid was verified, the resection margins were clear, and pleural carcinomatosis was confirmed. The patient was treated with octreotide (20 mg once in 28 days) since she had mild symptoms of carcinoid syndrome (the recurrent feeling of blood rushing to the face). Twelve months after surgery, local recurrence was suspected based on follow-up CT (Fig. 2). Significant consolidation was seen in the suture line area, and several small lesions were noted

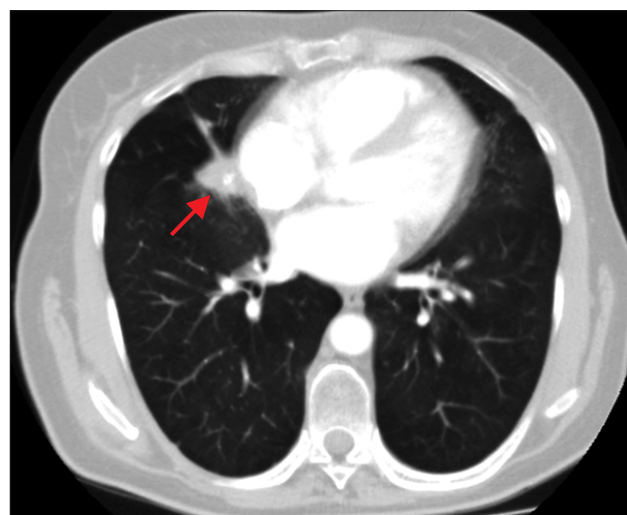


Fig. 1. Computed tomography scan of the chest before the operation, showing a centrally located solid lesion, measuring 16×15 mm, with smooth margins (arrow).

on the parietal pleura. No other signs of distant metastasis or lymph node involvement were found on chest and abdominal CT.

At the time of admission to our hospital, the patient had mild dyspnea. Her Charlson comorbidity index was 3. The level of chromogranin A was elevated. The patient was scheduled for VATS re-exploration of the pleural space to

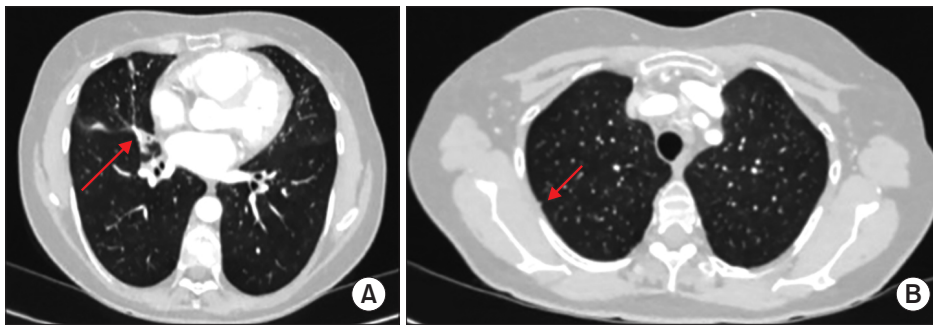


Fig. 2. Computed tomography scan of the chest. (A) Local recurrence in the middle lobe (arrow). (B) Pleural focus (arrow).

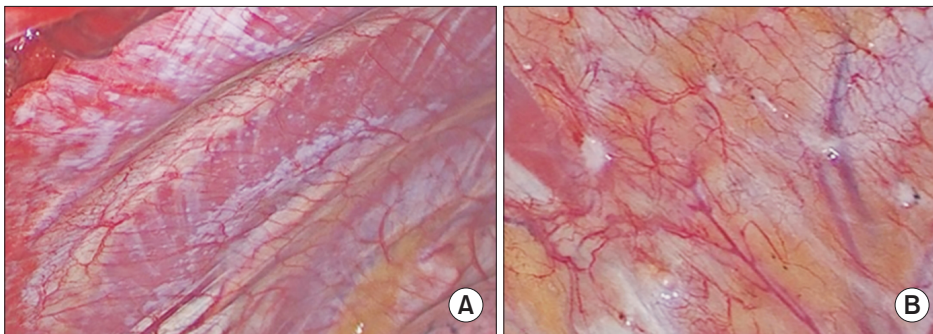


Fig. 3. Intraoperative photos of pleural carcinomatosis. (A) Small lesions on the parietal pleura. (B) Foci in the area of the apex.

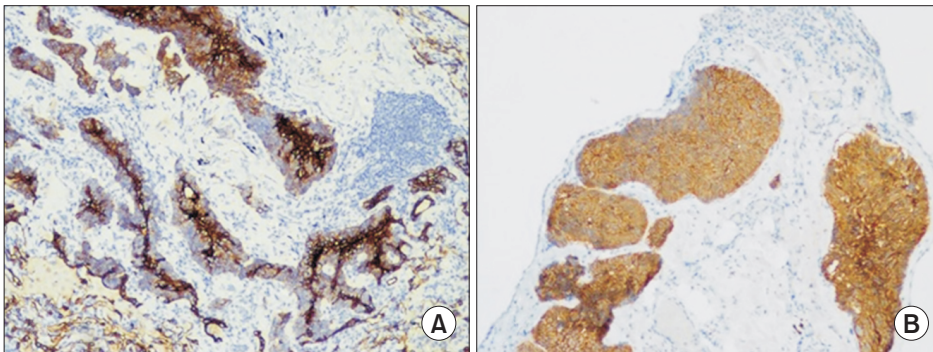


Fig. 4. Immunohistochemical examination. (A) Lung specimen with high expression of cytokeratin 7 (×100, neuroendocrine tumor of the lung). (B) Pleura specimen with high expression of CD56 (×100, pleural metastasis).

prove the presence of recurrence and to evaluate the volume of dissemination and the extent of the previous operation. During surgery, local recurrence in the remaining middle lobe and multiple miliary yellowish foci from 2 to 5 mm in diameter on the parietal pleura were visualized, but the visceral pleura was intact (Fig. 3). Since the consolidation was very close to the hilum, a complete anatomic middle lobectomy with lymphadenectomy was performed. Considering the isolated involvement of parietal pleura, total parietal pleurectomy was also performed, followed by photodynamic therapy (using a neodymium-doped yttrium aluminum garnet laser as the light source, with a 30 mm diffusing fiber with wavelength of 662 nm, light dose of 100 J/cm², and exposure time of 15 minutes). The total

blood loss was 100 mL, and the operative time was 255 minutes. The patient's postoperative course was uneventful and she was discharged on postoperative day 5.

Local recurrence was proven with immunostaining (atypical cells expressing synaptophysin, CD56, thyroid transcription factor 1, cytokeratin 7, and 3%–6% of Ki67) (Fig. 4), with no metastasis in the lymph nodes at stations 12R, 11R, 10R, 7, and 2–4R. The patient took octreotide. Nine months after the operation, no signs of disease progression were found, according to CT scans and low chromogranin A levels. Twelve months after the operation, DOTATATE positron emission tomography/CT was performed, and no metabolic sites were visualized.

The study was approved by the Institutional Review

Board of L. G. Sokolov Memorial Hospital 122 (no. 2, date 17.2.2020). The patient provided written informed consent for the publication of clinical details and images.

Discussion

Pulmonary carcinoids are quite rare tumors of the lung, accounting for approximately 0.2–2 cases per 100,000 population [1]. They constitute only 25% of all carcinoid tumors [2]. During the last 30 years, the incidence of carcinoids has been reported to increase by 6% annually, but this may be explained by the evolution of immunohistochemical techniques, rather than a true growth in the incidence of carcinoids [3]. They represent 1%–2% of all invasive lung neoplasms, with a high predominance of typical forms [1].

Typical carcinoids have an indolent nature, with a median doubling time of approximately 7 years [4]. The average 5- and 10-year overall survival rates have been reported to be 93% and 89%, respectively, and the average disease-free survival rates are 88% and 72% [2]. However, dissemination occurs in 5%–10% of typical carcinoids and in 15%–20% of atypical ones [4]. Among metastatic forms, atypical carcinoid is diagnosed in 69% of cases. Patients with metastatic lung carcinoids are twice as frequently diagnosed with carcinoid syndrome [5].

The most common sites of metastases are the liver, bone, brain, and mediastinal lymph nodes [1]. Extremely rare reported sites include the ovaries, pancreas, subcutaneous tissue, skin, peritoneum, thyroid gland, breast, choroid and ciliary body, spinal cord, and heart [5].

We have found 4 cases of carcinoid pleural dissemination in the literature [6–8]. In all cases, the histologic features of the carcinoids were typical. Three patients were treated with lobectomy and 1 with segmentectomy [6]. All tumors were diagnosed at a non-advanced stage. The time to progression after surgery was 4, 5, 7, and 30 years [6–8]. Only one patient was diagnosed with carcinoid syndrome and was treated with metabolic radiotherapy [6]. Another patient had 2 episodes of local recurrence before dissemination, treated with cryotherapy [6]. Five years later, he was diagnosed with pleural and hepatic metastases and treated with chemotherapy followed by somatostatin analogs. The patient who presented with metastases 30 years after lobectomy underwent surgical cytoreduction through resection of the pleural masses with the sixth and seventh ribs and pericardial resection [8]. Only 2 patients were treated with chemotherapy when pleural dissemination was confirmed [7].

The treatment guidelines for metastatic pulmonary carcinoids are vague [1,5]. Due to their low incidence, no randomized trials have yet been conducted to determine an effective treatment strategy. Cytoreduction surgery is a possible treatment option [9]. Asymptomatic patients may be observed or treated with octreotide. Patients with carcinoid syndrome should be treated with somatostatin analogs. These drugs provide symptom control and have been reported to slow down tumor growth. For patients with progressive metastatic disease, everolimus is a recommended treatment option. Chemotherapy is a possible option, but the tumor response rate is usually low. Treatment with peptide receptor radionuclide therapy may be considered in patients with somatostatin receptor-positive imaging who exhibit disease progression while taking octreotide or lanreotide.

Patients with carcinoid tumors should receive regular follow-up [10]. The observations should be made with chest CT and abdominal CT or magnetic resonance imaging every 3 to 6 months. The biochemical evaluation includes testing chromogranin A levels as a marker of tumor recurrence every 6 months in patients with elevated levels at baseline [9]. The follow-up period should constitute at least 10 years, although according to some studies it may be prolonged for up to 20 years [5].

Photodynamic therapy is an evolving method of treating disseminated tumors that is characterized by few complications. It is widely used for the treatment of pleural dissemination of epithelial tumors. In our center, we usually perform pleurectomy and photodynamic therapy with a chlorine photosensitizer (radachlorin) in cases of pleural carcinomatosis, including thymoma dissemination and mesothelioma. Since pleural dissemination of bronchial carcinoid is an extremely rare condition, there are no previous reports of photodynamic therapy use in such cases. However, several cases of the use of photodynamic therapy to treat choroidal metastasis from pulmonary carcinoids have been reported, with good responses [11]. Considering the absence of other metastatic sites and the indolent behavior of the tumor, we decided to perform pleurectomy and photodynamic therapy to increase the antitumoral effect of the operation.

In our opinion, photodynamic therapy is a viable treatment option for the pleural dissemination of epithelial tumors. Its addition to systemic therapy might prolong the patient's life and relieve the symptoms of tumor progression. If a patient has metastasis limited to the parietal pleura, we propose to perform pleurectomy and photodynamic therapy to affect all sites of neoplasm spread. This proce-

dure does not significantly increase the time or cost of the operation, and extremely rarely causes complications. We hope that the effects of photodynamic therapy on such a slowly growing tumor will prolong the patient's life for decades.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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