

## SIGNIFICANCE OF ELECTRON MICROSCOPIC EXAMINATION IN THE DIAGNOSIS OF PULMONARY NEOPLASMS

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**The significance of electronic microscope examination (EM) in the diagnosis of pulmonary neoplasms was evaluated in 40 cases of patients with different kinds of pulmonary neoplasms. In 27 of the 40 cases, final diagnoses were made by light microscope (LM) examination, while in the remaining 13 cases, LM failed to reach definite diagnoses which were established with the help of EM. By analyzing our data, we conclude that in the following situations, EM helps most in the diagnosis of pulmonary neoplasm: 1. diagnosis of neuroendocrinal carcinomas of the lung; 2. diagnosis of some rare pulmonary neoplasm; 3. documentation of the histologic origins of the metastatic pulmonary neoplasms and 4. differentiation of malignant mesothelioma with pleural metastasis of pulmonary adenocarcinoma.**

**Key words: Electronic microscope, Neoplasm, Lung.**

The diagnosis the selection of management and the prognosis prediction of pulmonary neoplasms depend largely upon the accurate histological classification of the tumors, which in some circumstances cannot be achieved by light microscope examination (LM) alone. And observation of the ultrastructure of tumor

tissues or tumor cells by electronic microscope (EM) is often indicated to give a final diagnosis. The present work is aimed to make a preliminary attempt to evaluate the clinical significance of EM examination in the diagnosis of pulmonary neoplasms.

### MATERIALS AND METHODS

For LM and EM examinations, specimens were obtained from unselected 40 cases with pulmonary neoplasms in our hospital since 1988, among which 34 cases were male and 6 were female. Average age was 54.15 years old. Chest X-ray films revealed solitary mass in 28 cases, multiple nodules in 2 cases and pleural effusion in 10 cases respectively. Clinical manifestations included cough (n=22), bloody sputum (n=13) and chest pain (n=10). Some patients presented fever, hoarseness, fatigue or symptoms of metastatic diseases. Of particular, ectopic ACTH syndrome was noted in one case with carcinoid.

Specimens were obtained from fiberoptic bronchoscope (FB) biopsy (n=22), pleural effusion (n=9), surgical resection (n=7), and other sources (n=2). FB biopsy and surgical resection specimens were all

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obtained from the same sites. Specimens were fixed with 10% formalin for LM examination and with 2.5% glutaraldehyde for EM examination. Pleural effusion fluids for LM examination underwent no any pretreatment, while those for EM examination were anticoagulated with heparin. After centrifugation, the cellular precipitates were collected and fixed with 2.5% glutaraldehyde.

## RESULTS

Diagnoses were established by LM examination in 27 cases, including squamous cell cancers (n=9), adenocarcinoma (n=7), lymphomas (n=2), tracheal liposarcoma (n=1), bronchial squamous epithelioma (n=1), small cell cancer (n=5), thymoma (n=1) and metastatic renal cancer (n=1).

In the remaining 13 cases, LM failed to give definite diagnoses, which were made with the help of EM examination (Table 1).

## DISCUSSION

By analyzing our data, we believe that in the following situations, EM examination are most indicated for diagnosing pulmonary carcinomas.

### Diagnosis of Neuroendocrinal Carcinomas of the Lung

Diagnosing neuroendocrinal carcinoma is chiefly through identifying cytoplasmic NE granules. In 4 of our patients (Case 1 through 4 in Table 1), LM examination of FB biopsy specimens revealed poorly differentiated lung cancers, which was insufficient for us to make decisions for treatment. EM examination documented few small NE granules and other features of small cell lung cancer (SCLC). Because there exist great differences between SCLC and NON-SCLC in terms of management and prognosis, early diagnosis is no doubt very important.

Table 1. 13 cases of pulmonary neoplasms diagnosed by EM examination

Case number	The sources of specimens	Diagnosis by EM	Differential diagnosis
1-4	FB biopsy	SCLC	
5	FB biopsy	Bronchial carcinoid	SCLC
6	Surgical resection	Atypical carcinoid	SCLC
7	Surgical resection	Primary pulmonary MFH	Spindle cell tumor
8	Surgical resection	Primary pulmonary Schwannoma	
9	Surgical resection	Primary pulmonary hemangiopericytoma	Hemangiopericytoma
10	Pleural effusion	Pleural metastasis of hepatic cellular carcinoma	
11	Biopsy of the mass in left thigh	Pulmonary metastasis of ASPS	Chemodectoma and rhabdomyosarcoma
12	Pleural effusion	Pleural mesothelioma	Pleural metastasis of pulmonary adenocarcinoma
13	Pleural biopsy	Pleural metastasis of pulmonary adenocarcinoma	Pleural mesothelioma

Abbreviations: SCLC: small cell lung cancer; MFH: malignant fibrous histiocytoma; ASPS: alveolar soft part sarcoma.

We also diagnosed one case of carcinoid (Figure 1) and one case of atypical carcinoid (case 5 and 6 in Table 1). The clinical picture, chest X-ray findings and FB manifestations of pulmonary carcinoid resembles those of lung cancer very much.<sup>1</sup> Under LM pulmonary carcinoid is frequently confused with SCLC. However, the treatment is quite different: surgical resection remains the main choice of treatment for carcinoid, whereas SCLC requires combined therapy of chemotherapy, surgical resection and radiotherapy. Prognosis of carcinoid is much better than that of SCLC. Therefore, if doubts exist in the distinction between carcinoid and SCLC, it is justified to examine the specimen under EM for correct diagnosis.

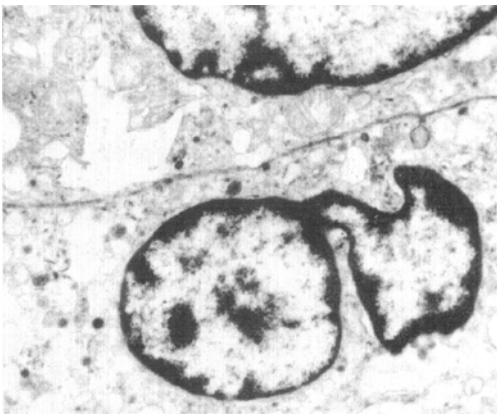


Fig. 1. Bronchial carcinoid. (EM;  $\times 16000$ )

### Diagnosis of Some Rare Pulmonary Neoplasms

Some rare pulmonary neoplasms are often without characteristic presentations clinically and roentgenographically. And differentiation with other tumors are frequently difficult by LM observations. EM examination may play an important role in this respect.<sup>2-4</sup>

In this series, case 7, 8 and 9 suffered from primary pulmonary malignant fibrous histiocytoma (MFH), primary pulmonary schwannoma (Figure 2) and primary pulmonary hemangiopericytoma respectively. In case 7, LM examination only suggested malignant tumor, and in case 8, diagnosis made by LM examination was poorly-differentiated lung cancer. EM

consultations established final diagnoses in these two cases. In case 9, although LM observation suggested vascular tumor, it was unable to judge whether it was hemangiopericytoma or hemangi endothelioma. The definite diagnosis was made with the aid of EM examination (Figure 3).

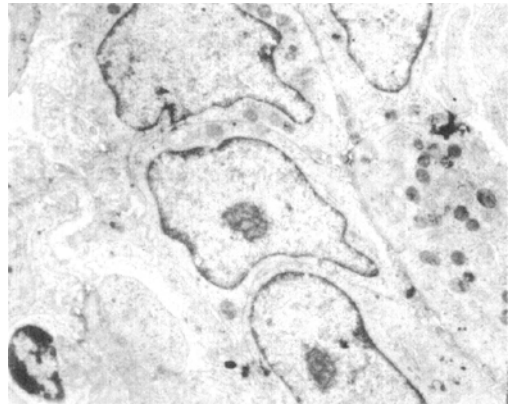


Fig. 2. Pulmonary schwannoma. (EM;  $\times 8000$ )

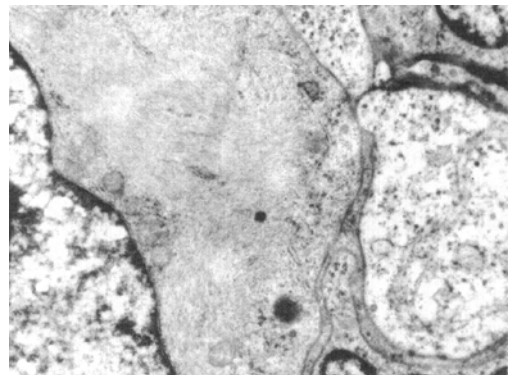


Fig. 3. Pulmonary hemangiopericytoma. (EM;  $\times 16000$ )

### Documentation of the Origins of the Metastatic Pulmonary Neoplasms

Case 10 was a middle-aged male patient presenting with right-side pleural effusion of unknown origin. EM examination of the pleural fluid documented the formation of bile canaliculus within the mass of the tumor cells and other features consistent with hepato-

cellular carcinoma, thus making it clear that the pleural effusion in this case was the result of pleural metastasis of hepatocellular carcinoma.

Alveolar soft part sarcoma is rare and apt to metastasize to remote sites, and in most cases, to lungs.<sup>5</sup> Under LM, alveolar soft part sarcoma is frequently confused with chemodectoma and alveolar rhabdomyosarcoma. A young male patient (case 11) entered our hospital because of hemoptysis and slight dyspnea. A chest X-ray film taken outside revealed multiple nodules in both lung fields. On physical examination, an oval mass of about 2cm×3cm×3cm was palpated in his left thigh, from which a biopsy specimen was taken. And a transthoracic needle aspiration of the pulmonary mass was done. Pathological observation with the help of EM established a diagnosis of alveolar soft part sarcoma of the left thigh with metastasis to both lungs in this case (Figure 4).

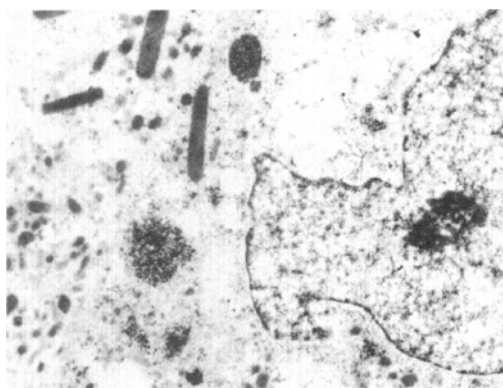


Fig. 4. Pulmonary metastasis of ASPS (EM; ×12000)

### **Differentiation of Malignant Mesothelioma with Pleura Metastasis of Pulmonary Adenocarcinoma**

Distinction between pleural mesothelioma and adenocarcinoma of the lung with pleural metastasis often presents diagnostic challenge clinically, or even pathologically. The regimens of treatment are quite different between these two diseases, therefore the correct diagnosis is of great importance to patients.

Case 13 suffered from right-side pleural effusion without other pulmonary lesions on his chest CT films. LM failed to yield a definite distinction between mesothelioma and pleural metastasis of pulmonary adenocarcinoma. EM examination of the biopsied pleural specimens found acinas and secretory granules which was consistent with adenocarcinoma.

Obviously, most of the pulmonary neoplasms can be diagnosed by LM examination. In this series, 27 of the total 40 cases were diagnosed by LM examination (67.5%). EM examination is relatively expensive. For the sake of saving expense for the patients, it is necessary for clinicians to be familiar with the indications of EM examination.

From the clinical point of view, the goal of laboratory examinations is to assist in diagnosis and selection of managements. In the above-mentioned situations, EM examination can meet these clinical needs. On the other hand, the value of accurate classification in the management of neoplasms has not been fully appreciated because of the limited choices of treatments. Taking the chemotherapy of pulmonary carcinomas as an example, clinicians choose regimens primarily according to the rough classification of SCLC and NON-SCLC. Li Weihua pointed out in his work that LM observation alone was insufficient for accurate classification of lung cancers.<sup>6</sup> Pulmonary neoplasms with different histogenesis exert different biological behaviors and may show different response to treatment. Therefore, re-classification of pulmonary neoplasms according to their histogenesis with the aid of EM observation may have important therapeutic implications.

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