

# Large cell lung carcinoma with rhabdoid phenotype: case report

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## SUMMARY

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**Large cell carcinoma of the lung with a rhabdoid phenotype is very rare. We report a 62-year-old male patient admitted to our hospital due to chest pains and hemoptysis. The computed tomography scan of the lungs revealed a massive consolidation of the parenchyma in the upper right lobe. The right upper lobectomy and mediastinal lymph node sampling were carried out. The microscopic appearance suggested a large cell carcinoma with a rhabdoid phenotype, with no foci of any other carcinomatous components. The tumor cells had eosinophilic cytoplasmic globules and eccentric nuclei. Immunohistochemically, vimentin was diffusely positive. The epithelial membrane antigen and neuron-specific enolase were focally positive. We expect a good outcome for this patient because the diagnostic procedure and successful operation were performed in the early stage (IA-T1aN0) of the disease.**

**Key words:** Lung Neoplasms; Carcinoma, Large Cell; Neoplasms, Glandular and Epithelial; Rhabdoid Tumor

## INTRODUCTION

Large cell lung carcinomas (LCLC) make about 10% of all lung cancers (1-3). It is estimated that approximately 1% of these eventually develop the rhabdoid phenotype during tumor evolution (3). It appears that the large cell lung carcinoma with a rhabdoid phenotype (LCLC-RP) comprises between 0.1% and 1% of all lung malignancies (4). A tumor can be diagnosed as LCLC-RP only when an undifferentiated large cell carcinoma contains a rhabdoid cell component that makes at least 10% of the tumor mass (5). A rhabdoid cell is characterized by large intracytoplasmic eosinophilic paranuclear inclusions consisting of intermediate filaments, which may be positive for vimentin and cytokeratin. Malignant cells with a rhabdoid phenotype have been described in several renal and extrarenal tumors, and are known to occur in many different histological variants of lung cancers (adenocarcinoma, sarcomatoid carcinoma, squamous cell carcinoma, combined large cell neuroendocrine carcinoma, combined small cell lung carcinoma (6-9). Tumors containing rhabdoid cells are important to be recognized because of their aggressive biologic behavior and bad prognosis. In this report, we described the clinicopathologic characteristics of a tumor diagnosed in the lung.

## CASE REPORT

A 62-year-old male was admitted to hospital, complaining of chest pain and occasional hemoptysis lasting for 10 days. He reported smoking about 40 cigarettes per day and he had been treated for hypertension. In October 2009, he had a spontaneous pneumothorax due to bullous emphysema of the right superior lobe of the lung, and then had an emergency operation. During the hospitalization in July 2010, the physical examination of the patient resulted in the detection of respiratory abnormalities, hyperresonance, and decreased respiratory auscultation noise in the right hemithorax. No pathogenic bacteria were registered in his sputum culture. Other systems' physical findings were completely normal. The hemoglobin level was 149 g/l, red blood cell count was  $4.76 \times 10^{12}$  and white blood cell count was  $6.6 \times 10^9$ . Blood gas analyses, blood electrolytes, blood glucose level, bilirubin, urea, creatinine and uric acid blood levels were normal. The chest X-ray showed consolidation of the

lateral aspect of the right upper lung lobe and signs of pneumothorax. The computed tomography scan of the thorax revealed a partial pneumothorax of the right hemithorax and inhomogeneous consolidation of the parenchyma subapically and posterolaterally in the right upper lobe. Pleural thickening of the adjacent pleura was also noted (Figure 1). In July, the patient was operated, performing right upper lobectomy and mediastinal lymph node sampling. The patient recovered well and his control chest X-ray was satisfactory.

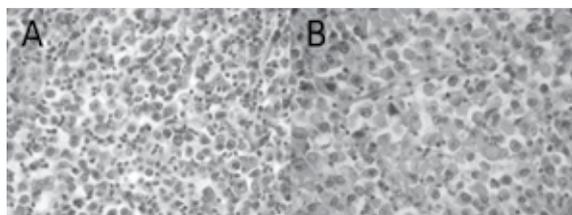


**Figure 1.** Thorax computed tomographic axial scan showing inhomogeneous consolidation of lung parenchyma subapically and posterolaterally in right upper lobe, local pleural thickening and small amount of air in right pleural cavity.

The macroscopic examination of the lobectomy-obtained material showed the right upper lobe of the lung with preserved lumens of the segmental bronchi of medium width with grayish and smooth mucosa. The pleura was thin and grayish. The old surgical scar on the pleura, equipped with a metal clip, was present. The alveolar tissue was partly solid, gray-pink in color and partly pale with increased aeration. Subpleurally, there were numerous extended bullae. Inside the upper lobe, there was a partly gray-white and partly yellow cavitated node (1.5x1x0.5cm). The surrounding alveolar tissue was less aerated, darker and firmer.

The fresh surgery-obtained tissue was fixed in formalin, paraffin-embedded, and sectioned for hematoxylin and eosin (HE) staining. The antibodies applied for immunohistochemical staining included: cytokeratin 7 (CK7) (Dako), thyroid transcription factor-1 (TTF-1) (Dako; 1:50), vimentin (Dako), desmin (Dako), neuron-specific enolase (NSE) (Dako), epithelial membrane antigen (EMA) (Dako), leukocyte common antigen (LCA) (Dako), high-molecular-weight cytokeratin (HWCK) (Dako), Epstein Barr virus (EBV) (Dako), chromogranin (Dako), and synaptophysin (Dako).

On light microscopy, the examined tissue showed large areas of bulbous emphysema and large areas of interstitial fibrosis with chronic inflammation signs (plasma cells and lymphocytic interstitial infiltrate). The examined portion of the lung tissue had the so-called honeycomb appearance. Focal areas of atypical alveolar hyperplasia were also seen. The microscopic examination of the node showed areas of polygonal and oval tumor cells with vesicular, eccentric localized nuclei and prominent nucleoli. The cytoplasm of these cells contained large globular eosinophilic inclusions (Figure 2). There were no foci of any other carcinomatous components. The tumor cells showed intraalveolar dissemination, spreading through the alveolar septa. These cells were surrounded by lymphocytes. Bronchial invasion and lymph node metastases were not detected.



**Figure 2.** (A) Microscopic appearance of the polygonal-shaped tumor cells (HE, x20). (B) Cytoplasm of rhabdoid phenotype tumor cells contains large eosinophilic inclusions and round vesicular nuclei (HE, x40).

Immunohistochemically, the tumor cells were vimentin diffusely positive while EMA and NSE were focally positive. The performed assays confirmed the diagnosis of the large cell lung carcinoma with a rhabdoid phenotype (LCLC-RP).

The patient was discharged from hospital after 13 days and scheduled for oncological consultation.

## DISCUSSION

Malignant rhabdoid tumors were first reported in the kidney (10) and the tumor cells morphologically resembled rhabdomyosarcoma cells, but further immunohistochemical investigation did not reveal rhabdomyoblastic differentiation (11). Extrarenal tumors located in the brain, skin, liver and mediastinum have also been reported (12). The series of 5 and 26 cases of malignant soft tissue tumors with a rhabdoid phenotype were also reported (13, 14). The lung localization of LCLC-RP is extremely rare. Most of the cases reported were adenocarcinomas, squamous and neuroendocrine lung cancers with a rhabdoid phenotype (15). This phenotype usually occurs in a poorly differentiated component of LCLC. In one large series of 902 surgically resected lung cancers, only 3 cases (3%) were diagnosed as LCLC-RP, in another highly selected series of

large cell carcinoma cases, 4 of 45 tumors (9%) were diagnosed as rhabdoid phenotypes (4). Our case was the large cell lung carcinoma with a pure rhabdoid phenotype.

Histopathology results showed that the tumor cells had abundant eosinophilic cytoplasm and intracytoplasmic inclusions. Ultrastructurally, in some reports, the inclusions were described to be composed of elongated accumulation of intermediate filaments that were immunohistochemically positive with vimentin (4, 13, 14). We could not perform the electron microscope analysis, but our case was vimentin-positive. Some of the rhabdoid-phenotype tumors showed neuroendocrine differentiation and some cases were positive with EMA and cytokeratins (4, 5, 13). Our case showed the focal positivity with EMA antibody, but cytokeratin 7 was negative. Among neuroendocrine markers, the NSE was focally positive but chromogranin and synaptophysin were negative. For rhabdomyoblastic differentiation, we applied desmin, but the result was negative. All cases reported in the literature had a poor prognosis due to the aggressive behavior of these tumors. Some studies suggest that, as the proportion of rhabdoid cells in the tumor increases, the prognosis tends to worsen (4). Interestingly, there are case reports of rhabdoid carcinomas recurring after unusually long periods. One report described a very early stage patient whose tumor recurred 6 years after the initial treatment (16). We reported a patient who was successfully operated in the early stage (IA-T1aNO) of the disease.

In conclusion, we have evaluated our case as immunohistochemically vimentin-positive, focally EMA and NSE positive, CK7, desmin, TTF1, chromogranin and synaptophysin negative, large cell carcinoma of the lung with a rhabdoid phenotype. The pathological stage of the disease was IA (T1aNO).

## Conflict of interest

We declare no conflicts of interest.

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