

Sclerosing Hemangioma with Lymph Node Metastasis

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Sclerosing hemangioma (SH) of the lung is an uncommon type of tumor, which is composed of polygonal and cuboidal cells. This disease is generally regarded as benign but extremely rare cases with lymph node metastasis have been reported. We report a case of SH with a metastasis to the regional lymph nodes. A 19-year-old girl presented with a 2-year history of coughing. A chest X-ray and a CT scan indicated a large mass in the lower lobe. As a result, a left lower lobectomy with a dissection of the hilar and interlobar lymph nodes was performed. The tumor was a well-defined huge mass with partial adhesion to the mediastinal and parietal pleura. The dissected hilar, interlobar, and intrapulmonary lymph nodes demonstrated metastasis. Histologically, the primary and metastatic tumor consisted of polygonal and cuboidal cells. Both types of tumor cells were uniformly immunoreactive to the epithelial membrane antigen (EMA) and the thyroid transcription factor-1 (TTF-1). However, the cuboidal cells tested positive for pancytokeratin, whereas the polygonal cells tested consistently negative. Postoperatively, the patient received chemotherapy and no recurrence or metastasis 2 years after surgery was noted. Although a pulmonary SH is considered to be benign, this case highlights the need for the evaluation of lymph node metastasis.

Key Words: Sclerosing hemangioma, lung, metastasis

INTRODUCTION

Pulmonary sclerosing hemangioma (SH) was first described by Liebow and Hubell in 1956.¹ A number of SH cases have been reported in a series of case reports.^{2,3} Despite the tumor has been considered to be benign, a few cases with a metas-

tasis have been described.⁴⁻⁷ Devouassoux-Shisheboran et al observed several unusual presentations of SH, which included multifocal lesions, hilar lymph nodes, pleural and mediastinal locations.⁴

The neoplasm shows four histological patterns, papillary, sclerotic, solid, and hemorrhagic. It is composed of two populations of cells, solid-growing round to polygonal cells and cuboidal cells that line the papillary structures. Although its histological appearance is well described, the histogenesis of this tumor is unclear. The polygonal cells have been regarded as the neoplastic component and the cuboidal cells are believed to be entrapped pneumocytes.^{2,8} There have been many suggestions as to the origin of the tumor. These include endothelial,⁹ mesothelial,¹⁰ mesenchymal,¹¹ epithelial,^{3,12} and neuroendocrine origins.^{3,13} Recently, after using the thyroid transcription factor-1 (TTF-1) and the epithelial membrane antigen (EMA), Devouassoux-Shisheboran et al⁴ suggested a primitive respiratory epithelium origin for SH.

Here we present the clinicopathologic findings of a case of SH with a lymph node metastasis. The primary and metastatic deposits contained both polygonal and cuboidal cells that stained positive for EMA and TTF-1. This finding provides strong evidence that pulmonary SH originates from the primitive respiratory epithelium and both the polygonal and cuboidal cells are tumor cells with a different degree of differentiation.⁶

CASE REPORT

A 19-year-old girl presented with a 2-year his-

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tory of coughing. The chest X-ray revealed an abnormal density in the lower lobe of the left lung. Computed tomography of the chest revealed a $12.0 \times 9.7 \times 7.8$ cm sized mass, which was relatively well circumscribed with cystic and hemorrhagic areas with no evidence of calcification (Fig. 1). The patient underwent a left lower lobectomy. In addition, the hilar and interlobar lymph nodes were dissected. Grossly, the specimen consisted of

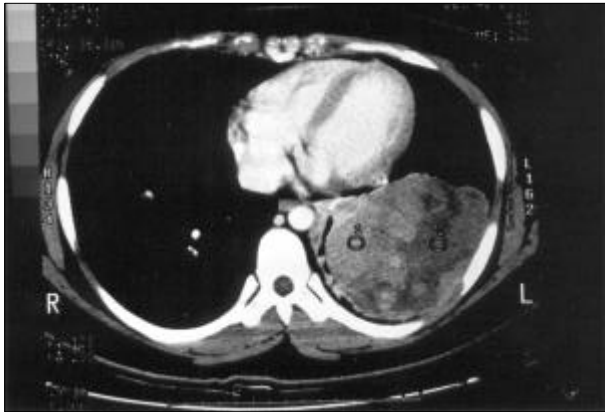


Fig. 1. Chest CT showing an abnormal density in the lower lobe of the left lung.

the left lower lobe of the lung, measuring $20 \times 10 \times 9$ cm and weighing 561 gm. The section revealed a large tumor mass with cystic and hemorrhagic areas, measuring 10 cm in diameter, and two small daughter nodules at the periphery of the main mass. The tumor mass was not encapsulated and was partially adhered to the mediastinal and parietal pleura. A bronchial connection was not found. Enlarged hilar, interlobar, and intrapulmonary lymph nodes were noted, the largest measuring 2.0 cm in diameter. Microscopically, the tumor showed the typical histological features of SH, with variable proportions of papillary (Fig. 2A), sclerotic, solid (Fig. 2B), and hemorrhagic patterns (Fig. 2C). The tumor was composed of solid sheets of round to polygonal cells punctuated by papillae, and the cleft was lined by cuboidal cells. The round to polygonal cells had small, round, centrally located nuclei without discernible nucleoli and slightly eosinophilic but rather clear cytoplasm. The nuclei had a fine dispersed chromatin and few mitoses. The cuboidal cells resembled the bronchiolar epithelium and activated type II pneumocytes, which lined the

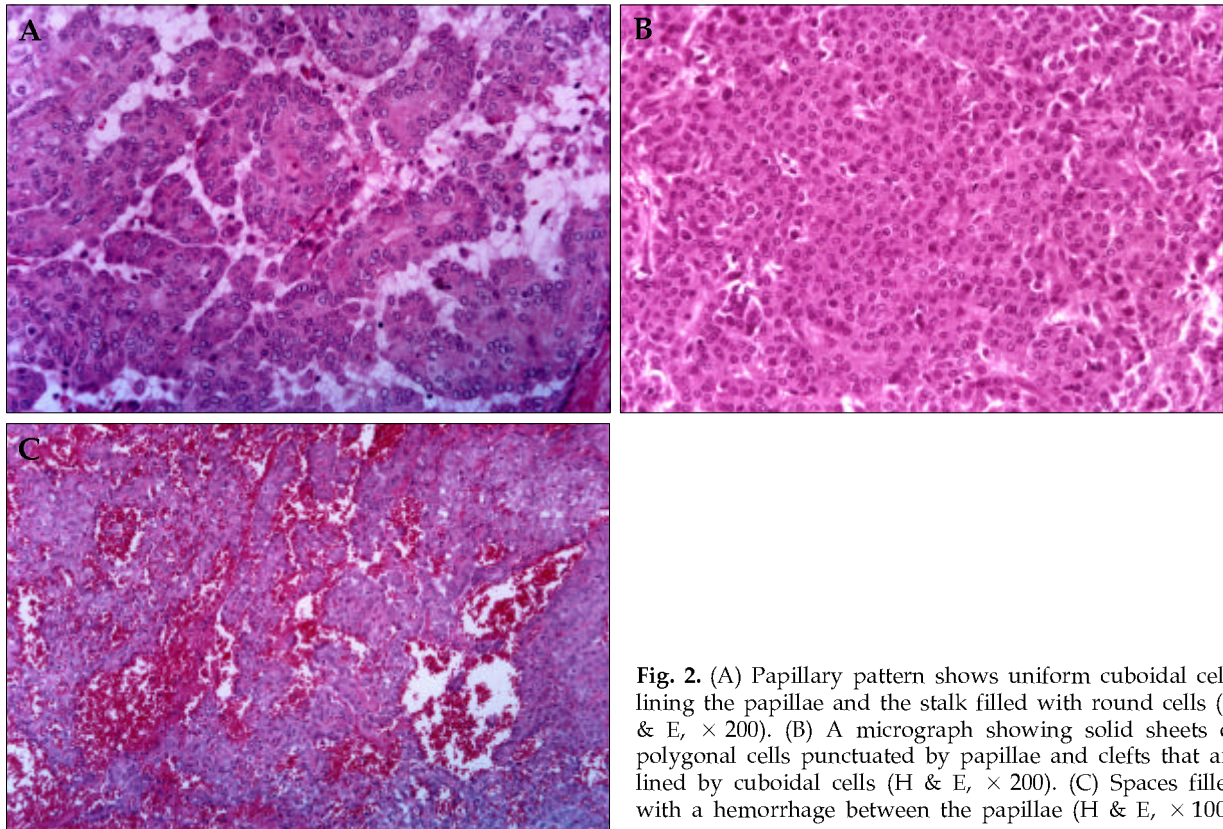


Fig. 2. (A) Papillary pattern shows uniform cuboidal cells lining the papillae and the stalk filled with round cells (H & E, $\times 200$). (B) A micrograph showing solid sheets of polygonal cells punctuated by papillae and clefts that are lined by cuboidal cells (H & E, $\times 200$). (C) Spaces filled with a hemorrhage between the papillae (H & E, $\times 100$).

papillae with a tubular pattern. These lining cells often showed intranuclear inclusions and vacuolated cytoplasm. Necrotic material including macrophages and desquamated type II pneumocytes were often observed in the spaces between the papillae.

There were metastatic foci in five of the dissected hilar, two of the interlobar, and four of the intrapulmonary lymph nodes, which consisted

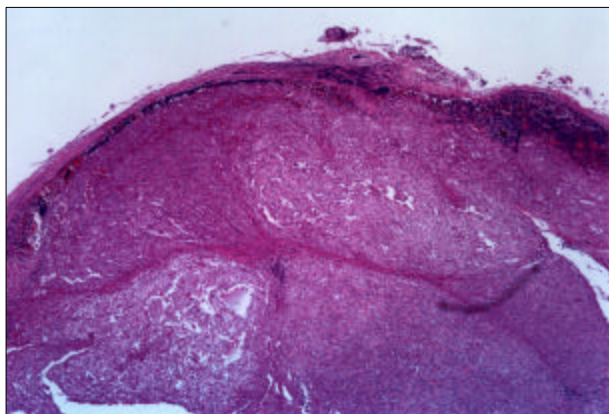


Fig. 3. Metastatic deposits in the lymph node show a mixture of solid and papillary patterns (H & E, $\times 40$).

mainly of round to polygonal cells and partially of cuboidal cells (Fig. 3). The large polygonal cells with a plump and foamy cytoplasm were often found and tested negative for periodic acid-Schiff (PAS) with and without a diastase predigestion and a mucicarmine stain. Immunohistochemically, both the polygonal and cuboidal tumor cells expressed EMA (Fig. 4A) and TTF-1 (Fig. 4B). Pancytokeratin staining was limited to the cuboidal cells that lined the papillae and clefts (Fig. 4C). The polygonal cells tested positive for vimentin. Nuclear staining with progesterone receptor (PR) antibodies was detected in both the polygonal and cuboidal cells. The tumor cells were non-reactive to synaptophysin, chromogranin, S-100, neuron-specific enolase (NSE), desmin, alpha-smooth muscle actin (SMA), the carcinoembryonic antigen (CEA), and the estrogen receptor (ER). Electron microscopy showed that the cuboidal cells contained abundant microvilli at the apical and lateral margins, and were filled with rough endoplasmic reticulum and mitochondria. In addition, numerous osmiophilic lamellar bodies, which are characteristic of type II

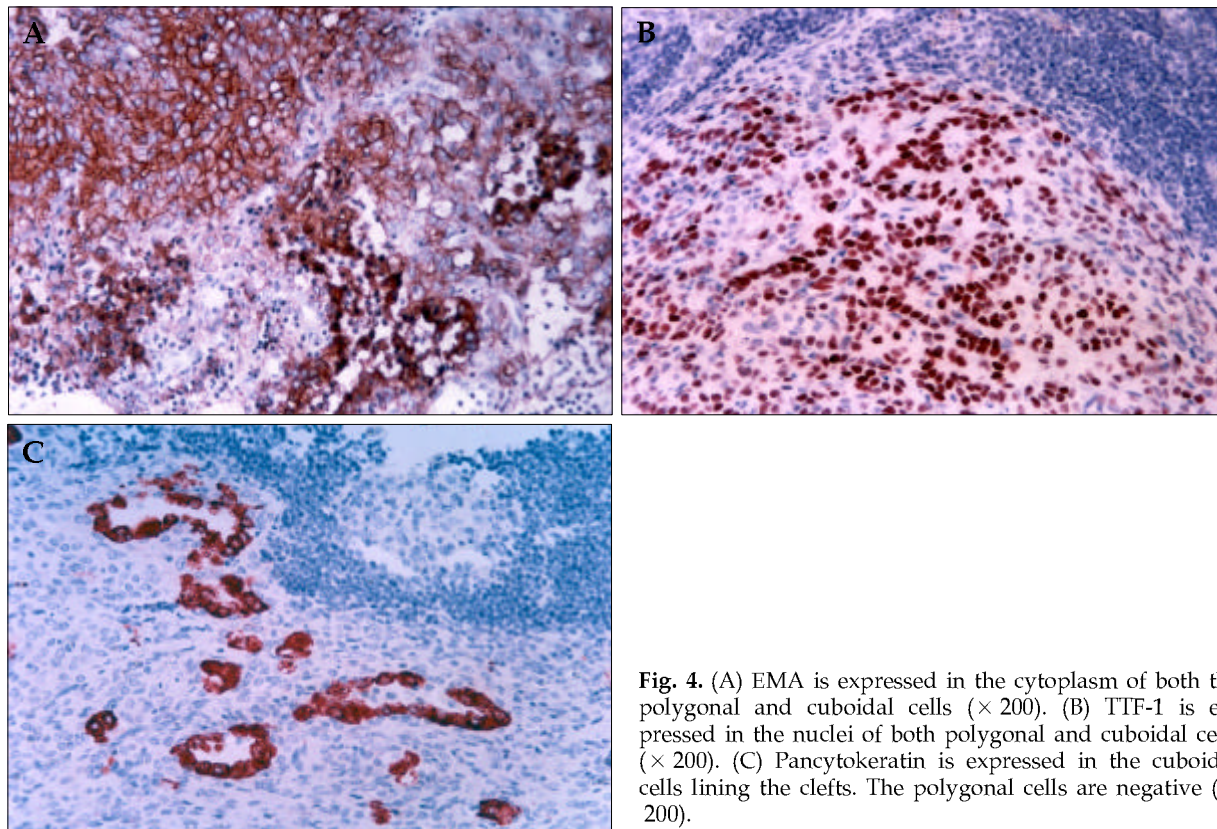


Fig. 4. (A) EMA is expressed in the cytoplasm of both the polygonal and cuboidal cells ($\times 200$). (B) TTF-1 is expressed in the nuclei of both polygonal and cuboidal cells ($\times 200$). (C) Pancytokeratin is expressed in the cuboidal cells lining the clefts. The polygonal cells are negative ($\times 200$).

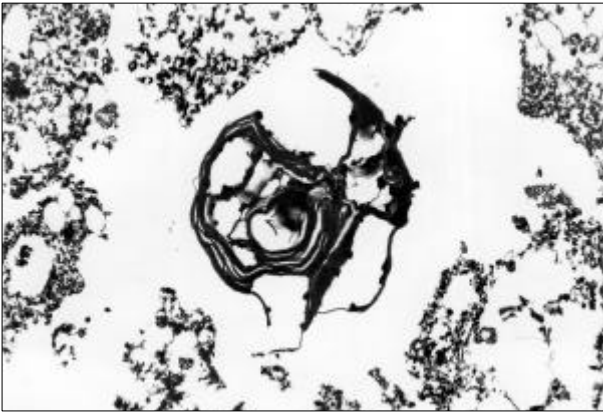


Fig. 5. A higher power view of the osmiophilic lamellar body seen in the cuboidal cell (Electron micrograph, $\times 7000$).

pneumocytes, were noted (Fig. 5). The round cells showed poor cytoplasmic organelle development. Postoperatively, the patient received chemotherapy (Carboplatin and Etoposide), and after two years follow up, no recurrence has been noted.

DISCUSSION

SH of the lung shows varying histological patterns including papillary, sclerotic, solid, and hemorrhagic types. Two populations of cells can be identified. One exhibits a bland cytology with a pale to clear cytoplasm that forms the core of the papillae, lines the angiomatoid spaces, forms the cords of the sclerotic pattern, and makes up the sheets of the solid pattern. These are considered to be the lesional or neoplastic cells. The other is composed of epithelial cells that line the papillae or spaces and are widely considered entrapped pneumocytes. Recently, using microdissection techniques, Niho et al¹⁴ demonstrated that both populations of SH cells were monoclonal in origin and represented a variable differentiation from a common progenitor cell. The presence of papillary projections lined by surface cells in a lymph node metastasis also supports a neoplastic nature of the surface cells.⁵ The architecture of the metastatic lymph node in our case also consisted of both round to polygonal cells and cuboidal cells.

TTF-1 is expressed in the thyroid, lung, and the

diencephalon of the brain.¹⁵ In the lung, it binds to the surfactant A,B,C, and the Clara cell secretory protein genes.¹⁶⁻¹⁹ It is expressed in the columnar non-ciliated cells of the fetal lung as early as 11 weeks of gestation and in the type II pneumocytes and Clara cells of the adult lung.^{15,20} TTF-1 staining was observed in both the polygonal and cuboidal cells. This suggests that both cells are derived from type II pneumocytes and Clara cells. Therefore, the polygonal cells may in fact have originated from the primitive respiratory epithelium or may represent incompletely differentiated pneumocytes or Clara cells, which in some areas can mature into cuboidal cells.⁶ As a result of these findings, the disease was reclassified from the category of tumor-like lesions in the 1981 World Health Organization (WHO) classification of lung tumors²¹ to the category of miscellaneous tumors in the new 1999 WHO/International Association for the Study of Lung Cancer Classification.²²

A SH with multiple lymph node metastasis is extremely rare, and there is little available follow-up data regarding SH with multiple lymph node metastasis. However, although a pulmonary SH is considered to be benign, possible nodal metastases should be considered, particularly when the tumor is huge and the regional lymph nodes are enlarged.

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