

CASE REPORT  
OLGU SUNUMU

## Pulmonary Sclerosing Hemangioma Exhibiting a High Ki-67 Proliferation Index

## Yüksek Ki-67 Proliferasyon İndeksi Gösteren Pulmoner Sklerozan Hemanjiom

Elif Ülker Akyıldız<sup>1</sup>, Sami Bayram<sup>2</sup>, Akgül Arıcı<sup>1</sup>, Mehtap Kasap<sup>1</sup>ABSTRACT  
ÖZET

Pulmonary sclerosing hemangioma (PSH) is a rare pulmonary neoplasm. This tumour was originally thought to be a variant lesion of hemangioma. Today, however, it has been elucidated to be a tumour of epithelial origin derived from the primitive respiratory epithelium. Previous studies have reported a low Ki-67 proliferation index in cases of pulmonary sclerosing hemangioma (1.4-2.2%). Moreover, the biological nature of this neoplasm, which rarely tends to metastasise to the lymph nodes, has yet to be thoroughly elucidated. A female patient in whom PSH exhibiting a high Ki-67 proliferation index was detected in the lung during follow-up for lymphoma is reported in the present study. While the Ki 67 proliferation index was 3-4% in some areas, it increased up to 15-20% in other areas. No recurrence or metastases were evident at postoperative follow-up.

**Key words:** Lung, hemangioma, sclerosing, immunohistochemistry

Pulmoner sklerozan hemanjiom nadir görülen bir akciğer tümörüdür. Başlangıçta hemanjiomun bir varyantı olduğu düşünülmüştür ancak günümüzde primitif respiratuar epitel hücrelerinden köken aldığı bilinmektedir. Pulmoner sklerozan hemanjiomda Ki-67 proliferasyon indeksinin düşük (%1,4-2,2) olduğu bildirilse de bu tümörün biyolojik davranışı tam olarak bilinmemektedir. Bu yazıda lenfoma tanısı ile takip edilirken akciğerinde yüksek Ki-67 proliferasyon indeksi gösteren pulmoner sklerozan hemanjiom tespit edilen kadın olgu sunulmuştur. Ki-67 proliferasyon indeksi bazı alanlarda %3-4 iken bazı alanlarda %15-20 olarak tespit edilmiştir. Kontrollerinde rekürrens ya da metastaz izlenmemiştir.

**Anahtar kelimeler:** Akciğer, hemanjiom, sklerozan, immünohistokimya

## Introduction

First described by Liebow and Hubbell in 1956, pulmonary sclerosing hemangioma (PSH) is a rare neoplasm (1). This tumour was originally thought to be a variant lesion of hemangioma. Today, however, it has been elucidated to be a tumour of epithelial origin derived from the primitive respiratory epithelium (2). The tumour predominantly affects middle-aged females, and typically presents on chest x-ray as a solitary, well-circumscribed lesion located in the periphery of the lung (3, 4). Previous studies have reported a low Ki-67 proliferation index in PSH cases (3-5). Moreover, the biological nature of this neoplasm, which rarely tends to metastasise to the lymph nodes, has yet to be thoroughly elucidated.

A female patient in whom PSH exhibiting a high Ki-67 proliferation index was detected in the lung during follow-up for lymphoma is reported in the present study.

## Case Report

A 50-year-old female patient was admitted to hospital for the first time with a complaint of severe abdominal pain in 2007. Abdominal computed tomography performed at that time revealed a mass lesion of 5x7x4 cm, located in the head of the pancreas and extending towards the duodenum. In addition, PET (positron emission tomography) also showed a slightly hypermetabolic solitary pulmonary nodule 2 cm in diameter (SUVmax: 2.81). Hilar or mediastinal lymphadenopathy was not evident, and no multilocality and bilaterality were detected. Once the patient was diagnosed with peripheral B-cell lymphoma on the basis of pathological evaluation of the mass located in the pancreatic head, she received eight cycles of chemotherapy. A surgical operation was undertaken for the solitary pulmonary nodule detected in the patient. Furthermore, an intraoperative pathology consultation was requested for the provisional diagnosis of a lymphoma metastasis. The specimen sent for pathological examination was an 8x4x3 cm section of lung tissue with a 2 cm, well-circumscribed, yellowish-brown nodule of subpleural location in the section (Figure 1). Following the evaluation of frozen sections, the tumour was reported as a tumour of vascular origin, not a lymphoma.

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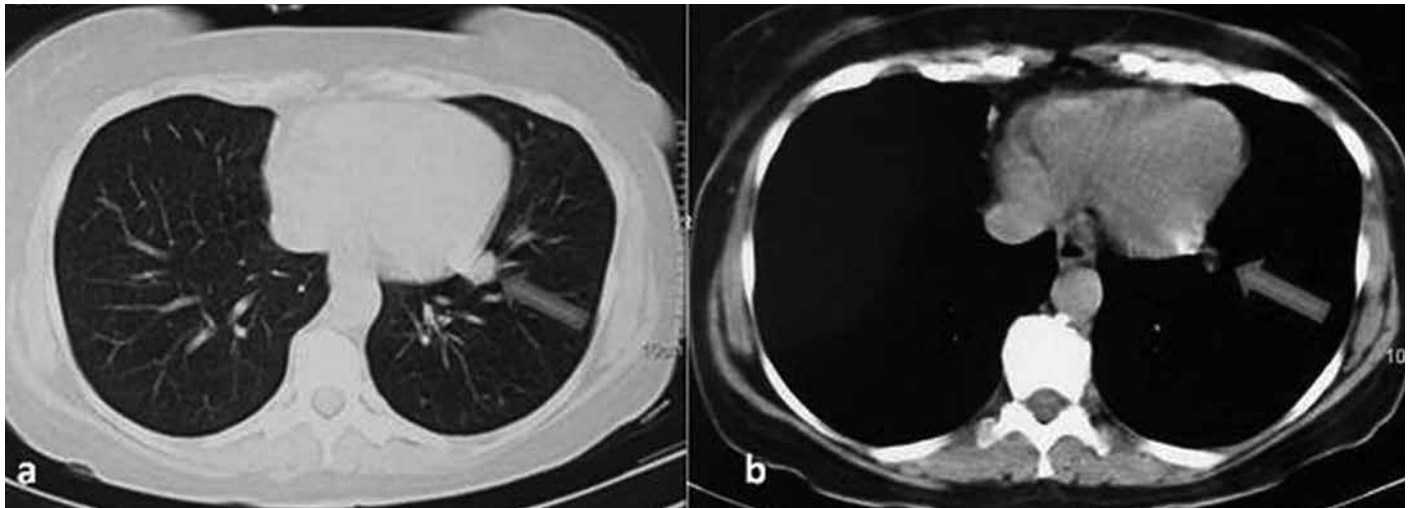
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**Figure 1.** The (a) parenchymal window and (b) mediastinal window images of the pericardial nodule on the thorax CT

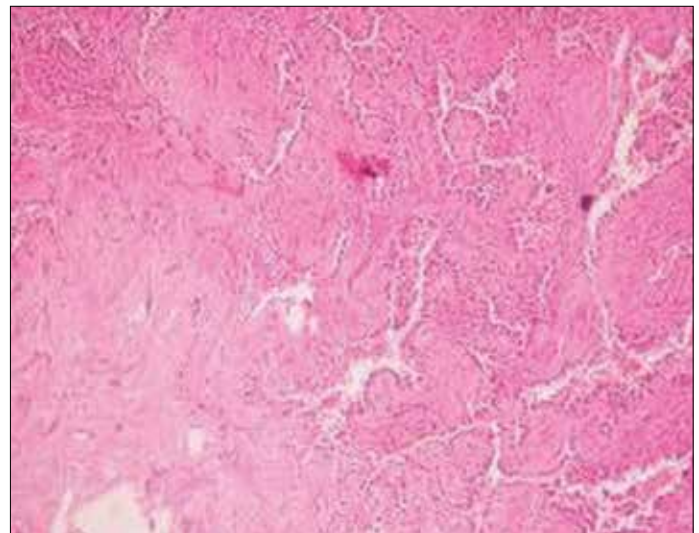
Pathological evaluation after routine tissue processing revealed an unencapsulated, well-defined tumour containing four different histological patterns as solid, papillary, sclerotic and angiomatous. The tumour consisted of two distinctive cell populations: cuboidal cells and stromal cells. The cuboidal cells lined the surface of the papillae and the lacunar spaces, while the polygonal cells were solid, round or oval nucleated cells containing pale or eosinophilic cytoplasm and a small nucleolus located within the solid and papillary areas (Figure 2, Figure 3).

Immunohistochemically, the cuboidal and stromal cells were observed to show strong nuclear positivity for TTF-1 (thyroid transcription factor-1) and diffuse membranous positivity for EMA (epithelial membrane antigen) (Figure 4 and Figure 5, respectively). The cuboidal cells were positive for pancytokeratin and CK7 (Figure 6), whereas no staining was observed for pancytokeratin and CK7 in the stromal cells. 10-20% nuclear positivity was observed for the progesterone receptors in either cell types; no staining was evident for CD34 (not shown). Ki-67 and p53 (not shown) scores were counted on a minimum of 10 randomly selected fields containing representative sections of tumour and calculated as the percentage of positively stained cells to total cells. The Ki-67 proliferation index, albeit variable from one area to another, was found to range from 3-4% to 15-20% (Figure 7). Both cell types exhibited pale nuclear staining for p53 (not shown).

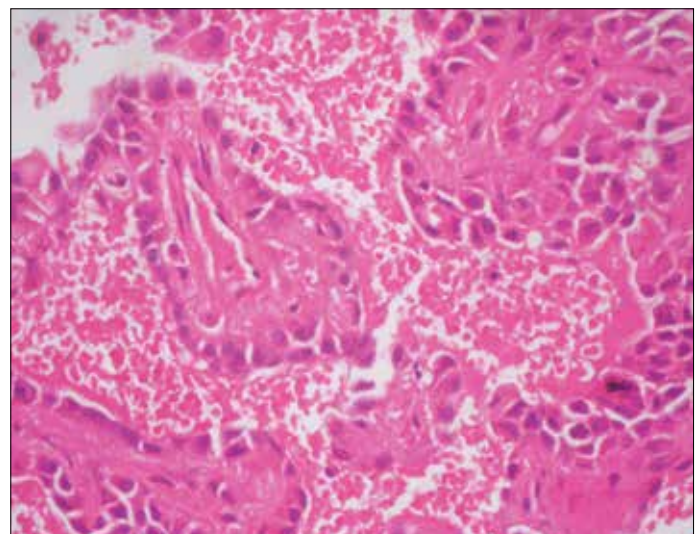
On the basis of the morphological and immunohistochemical findings, the case received a definitive diagnosis of PSH. No recurrence or metastasis was detected in the case during the three-month follow-up period.

## Discussion

Pulmonary sclerosing hemangioma, a rare tumour of the lung, constitutes 1% of all pulmonary neoplasms (6). Affected patients are generally in the fourth and fifth decades of life, with a predilection for women in more than 95% of all cases (3, 7). PSH was originally thought to be derived from vascular structures owing to its rich content of blood vessels, and hence was named incorrectly (1). Today, the tumour is known to be derived from the primitive respiratory epithelium (2). Eighty percent of affected cases are asymptomatic,

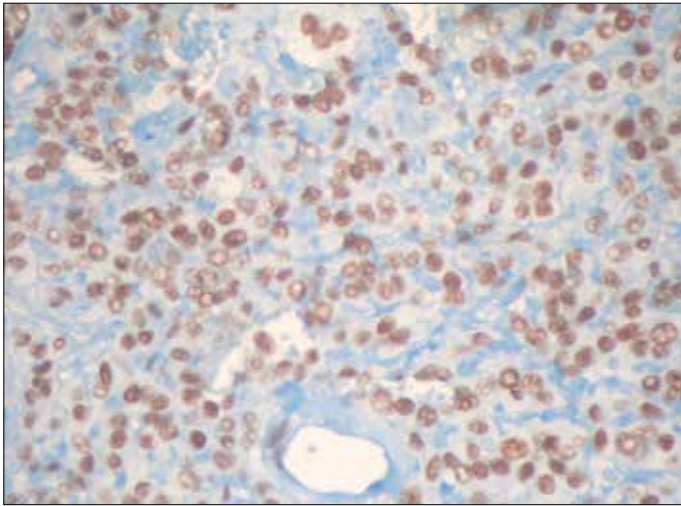


**Figure 2.** Papillary and sclerotic patterns (HE 100x)

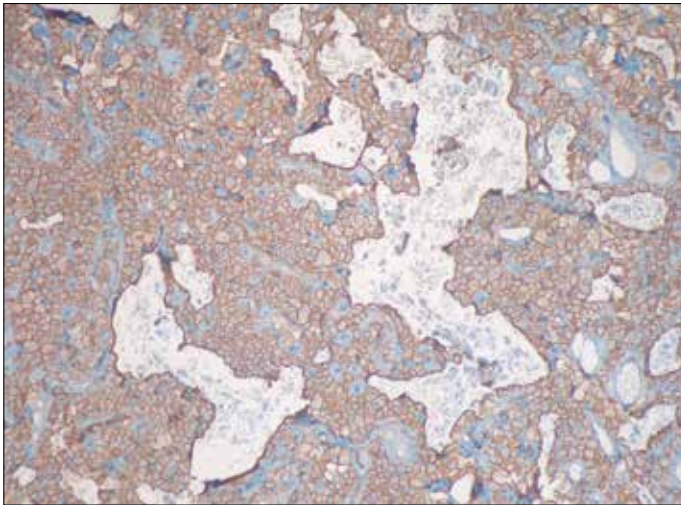


**Figure 3.** Cuboidal lining cells on the surface of the papilla and stromal cells in the interstitial portion (HE 200x)

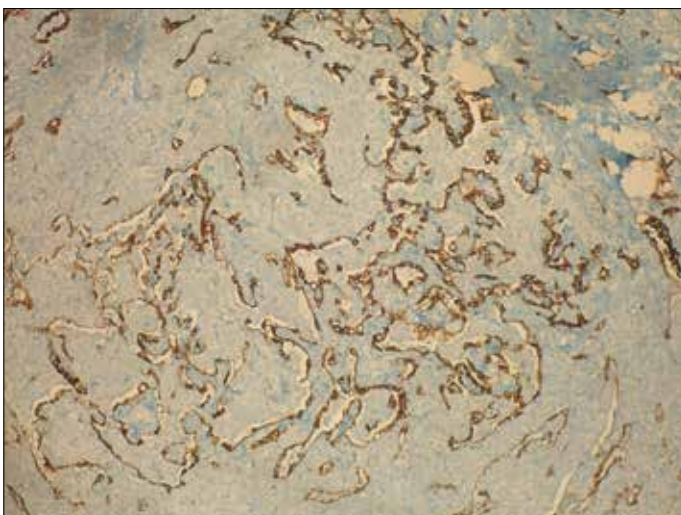




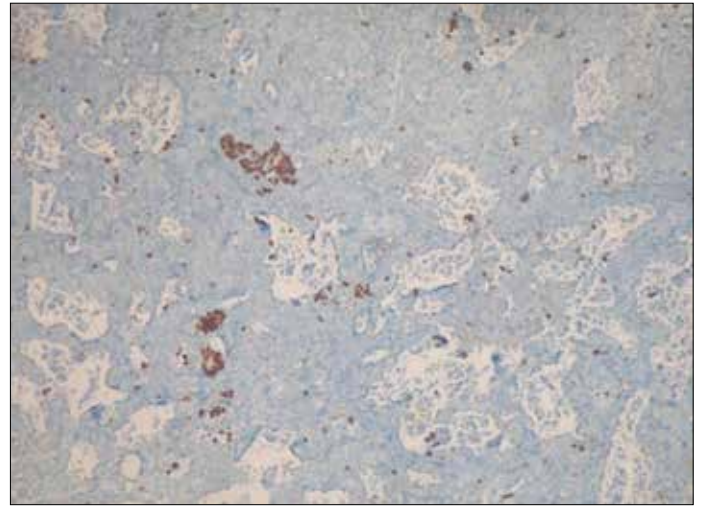
**Figure 4. Strong nuclear TTF-1 positivity in cuboidal cells and stromal cells (200x)**



**Figure 5. Strong membranous EMA positivity in cuboidal cells and stromal cells (100x)**



**Figure 6. Pancytokeratin positivity in cuboidal cells. Stromal cells were negative (100x)**



**Figure 7. Immunoreactivity for Ki-67 in both types of cells (100x)**

thus PSH is mainly detected incidentally. Some patients, however, may present with some complaints such as chest pain, coughing and bloody sputum (3, 4). The symptoms are due to enlargement of the tumour and compression of the surrounding tissue.

A tumour characterised by different histological patterns, PSH is made up of a mixture of papillary, solid, sclerotic and angiomatous patterns. Basically, two types of cell comprise the tumour: cuboidal cells and stromal cells. The cells which line the papillary or tubular structures and contain eosinophilic cytoplasm are termed cuboidal or superficial cells. The other cell type is stromal cells which form layers and contain eosinophilic or clear cytoplasm. These are also called round or pale cells (2).

Both the cuboidal and stromal cells are characterised by positive staining for TTF-1 and EMA, indicating that both cell types are derived from the primitive respiratory epithelium. Moreover, there might be variations in terms of staining for other immunohistochemical markers such as cytokeratin, vimentin, CEA and surfactant protein A between the two cell types. To give an example, while pancytokeratin is positive in the cuboidal cells, it is generally negative in the stromal cells. In our study, TTF-1 and EMA positivity was observed in both cell types, whereas staining for pancytokeratin and CK7 was only positive in the cuboidal cells. Variable results in terms of staining with some immunohistochemical markers have been ascribed to distinct degrees of cellular differentiation in these cell types (2, 5, 8-10).

The predominant occurrence of PSH in women gives an impression that the tumour may be associated with female sex hormones (5). Previous studies have reported positive staining for oestrogen and/or progesterone receptors (5, 11). Detection of positive nuclear staining for progesterone in both the cuboidal and stromal cells in our case supports this idea.

Although accepted as a benign tumour, the exact biological behaviour of PSH is yet to be elucidated. The tumour has been known to be able to metastasise to the hilar or mediastinal lymph nodes, or to recur. Distant metastases, however, have not yet been reported (9, 12-14). Iyoda et al. investigated Ki-67 and p53 expression in an attempt to identify the biological behaviour of the tumour and

compared the results with stage 1 papillary adenocarcinomas of the lung. The Ki-67 proliferation index and p53 expression were documented to be significantly lower in PSH (3). Özlük et al.(5) reported in their study, including five PSH cases, that the Ki-67 proliferation index ranged from 1.4% to 2.2%, along with the absence of p53 expression. Wang et al. (15) detected p53 expression and gene mutation in three out of 19 PSH cases, ascribing this result to a possible potential for malignant biological behaviour of the tumour. Ten percent of both cell types were observed to exhibit p53 protein expression in our case. Moreover, while the Ki-67 proliferation index was 3-4% in some areas and increased up to 15-20% in some other areas. Our case has been under close follow-up for any recurrence or metastasis. No hilar or mediastinal lymphadenopathy was detected prior to surgery; moreover, no recurrence or metastases were evident at postoperative follow-up.

## Conclusion

Pulmonary sclerosing hemangioma possesses a potential for metastasis, although it is accepted as a benign neoplasm. Long-term follow-up of affected cases would therefore be beneficial in understanding the biological behaviour of this tumour.

## Authors' contributions

Conceived and designed the study: EÜA, AA, MK. Examination and follow-up of the patient: EÜA, SB. Analyzed the data: EÜA. Wrote the paper: EÜA, SB. All authors read and approved the final manuscript.

## Conflict of interest

No conflicts of interest were declared by the authors.

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