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Case Report

Sclerosing Angioma of the Lung

Case Report and Electron Microscope Investigation

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Summary. Electron microscopy of a sclerosing angioma of the lung, a coincidental finding in the upper lobe of a 32-year-old woman. The rare, benign tumor, whose vascular proliferation by light microscopy is reminiscent of an angioma, exhibits a clear epithelial structure by electron microscopy. The tumor may develop out of immature pneumocytes. The paper discusses histogenesis and problems of differential diagnosis (potential confusion with carcinomas).

Key words: Angioma – Lung – Carcinoma – Pneumocytes – Ultrastructure.

Zusammenfassung. Elektronenmikroskopische Untersuchung eines sog. sklerosierenden Hämangioms der Lunge, das im Oberlappen einer 32jährigen Frau zufällig entdeckt wurde. Der seltene gutartige Tumor, der lichtmikroskopisch wegen seines Gefäßreichtums an ein Hämangiom erinnert, zeigt elektronenmikroskopisch eine eindeutige epitheliale Struktur. Die Geschwulst entwickelt sich möglicherweise aus unreifen Pneumocyten. Histogenese sowie differential-diagnostische Probleme (Verwechslungsmöglichkeit mit Carcinom) werden diskutiert.

The sclerosing angioma of the lung is a relatively rare, benign tumor predominantly found in young and middle-aged females (Spencer, 1977; Thurlbeck, 1978). Sometimes the tumor causes mild haemoptyses, but frequently it is a coincidental finding in the course of routine chest radiology, appearing as a round, sharply delineated shadow. It occurs most commonly in the lower lobes, although it may be found in other lobes of the lung. In the first decriptions, by Scott et al. (1948) and Ford et al. (1950), the tumor was considered to be a xanthoma. "Sclerosing angioma" was the term employed by Liebow and

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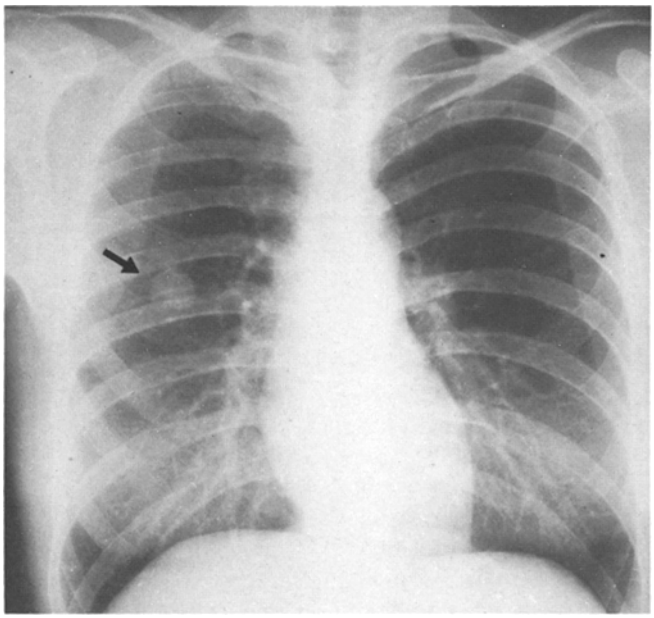

Fig. 1. Radiographic appearance of a sclerosing angioma (arrow) of the lung

Hubbel (1956), who interpreted the tumor, by analogy to the sclerosing angioma of the skin, as a primary vascular proliferation accompanied by proliferation of the connective tissue.

In the present case, the aim was to gain information on the origin of the tumor cells by means of light and electron microscopy.

Clinical History

In November 1977, a routine X-ray for a duodenal ulcer in a 32-year-old female revealed a circular focus (2 cm in diameter) in the right upper lobe of the lung (Fig. 1). The patient was not conscious of any respiratory symptoms. In view of the unknown nature of the circular focus, a thoracotomy was done although it had not grown and the round tumor was removed. Intraoperative frozen section examination was consistent with a scar carcinoma, and it was decided to resect the upper lobe as a radical treatment. The correct diagnosis was made after a histological study of paraffin wax embedded material had been made. There were no postoperative complications, and checks at six and twelve months post-operatively showed the patient to be completely free of symptoms, and radiological abnormalities in the chest.

Material and Methods

The operation specimen sent for frozen section examination comprised a portion of the right upper lobe of the lung with a round, sharply delineated, whitish tumor, about 2 cm across. For

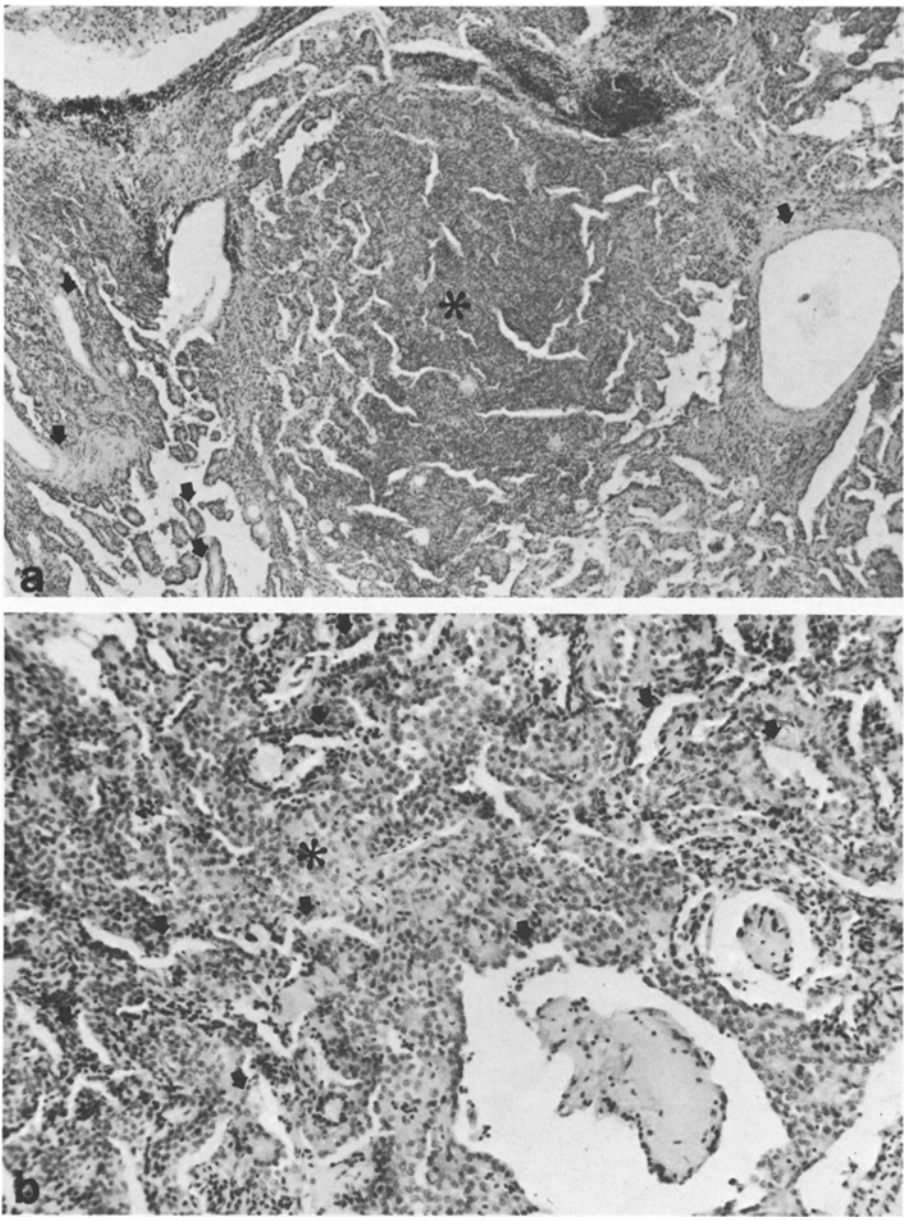

Fig. 2. **a** View of a sclerosing angioma with a central cellular area (*) and vessels at the edge of the tumor (arrows). HE, ×25. **b** Cellular area (*) with vessel-like (arrows) clefts lined with cuboidal epithelia. HE, ×40

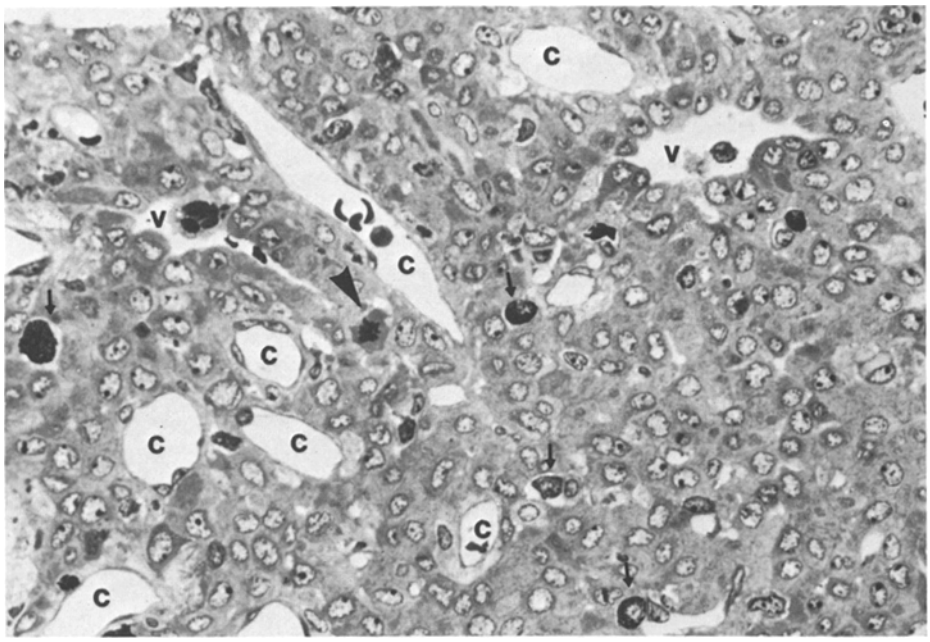

Fig. 3. So called (Spencer, 1977) "alveolar epithelial hyperplasia" with vessel-like clefts (*v*) and true capillaries (*c*). Arrows indicate mast cells and the arrow-head a tumor cell mitosis. Semithin, Methylene-blue, ×250

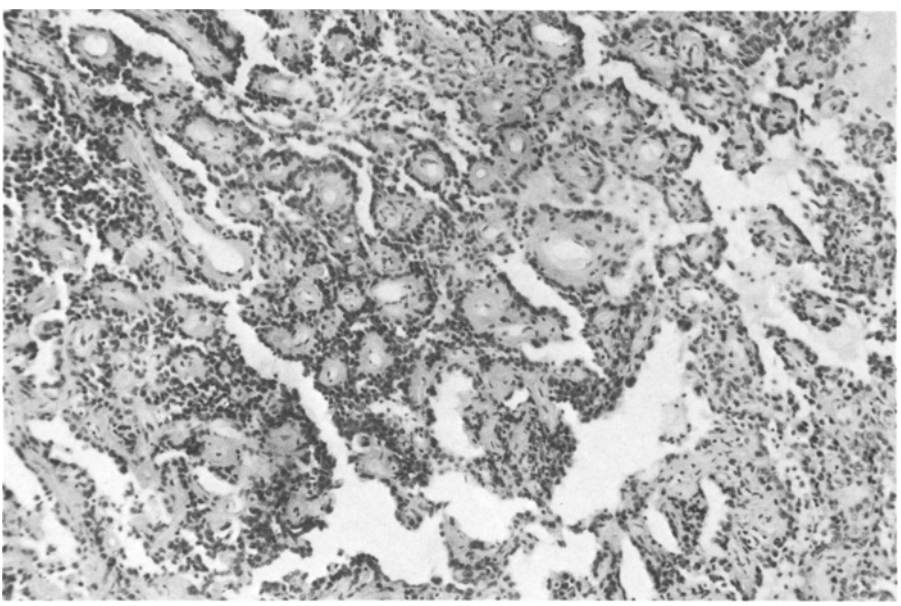

Fig. 4. Characteristic branching buds covered with cuboidal epithelium. At the centre of the buds capillaries are surrounded by a fibrous hyaline tissue ring. HE, ×100

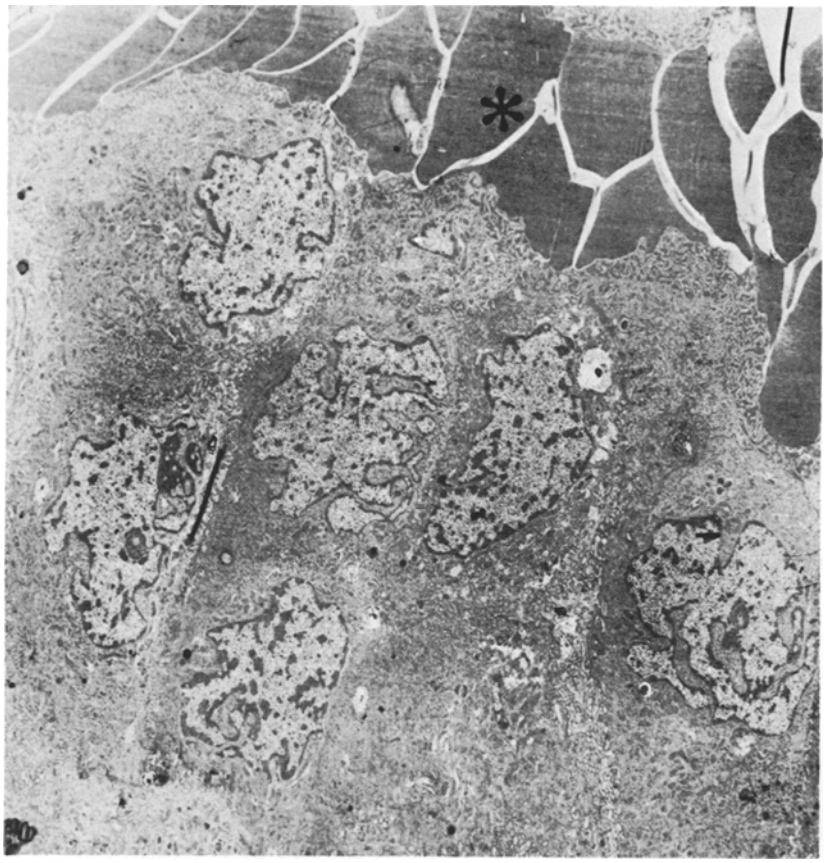

Fig. 5. Electron-microscopic appearance of the sclerosing angioma of the lung. Tumor cells are lining a blood filled space (*) imitating blood vessel in light microscopy. × 1,900

light microscopy, the tumor was fixed in 4% formaldehyde embedded in paraffin and stained with hematoxylin, eosin, PAS, van Gieson and Gomori stains. For electron microscopy, formaldehyde-fixed specimens were postfixed with phosphate buffered (0.15 M, pH 7). 6.5% glutaraldehyde, followed by postfixation with Dalton's chrome-osmium tetroxide. The specimens were dehydrated with acetone, embedded in Durcopan, and sectioned on a Reichert "Ultracut". Semi-thin sections were stained with methylene-blue and thin sections with uranyl acetate, lead citrate, and examined with a Zeiss electron-microscope EM 9 S.

Results

Light Microscopy

The tumor, which had suggested a scar carcinoma in frozen section, was formed of cells arranged partly in solid and partly in papillary complexes (Fig. 2a), of which two types could be differentiated by light microscopy. The predominant cells had lightly stained, round or oval nuclei, a delicate chromatin structure

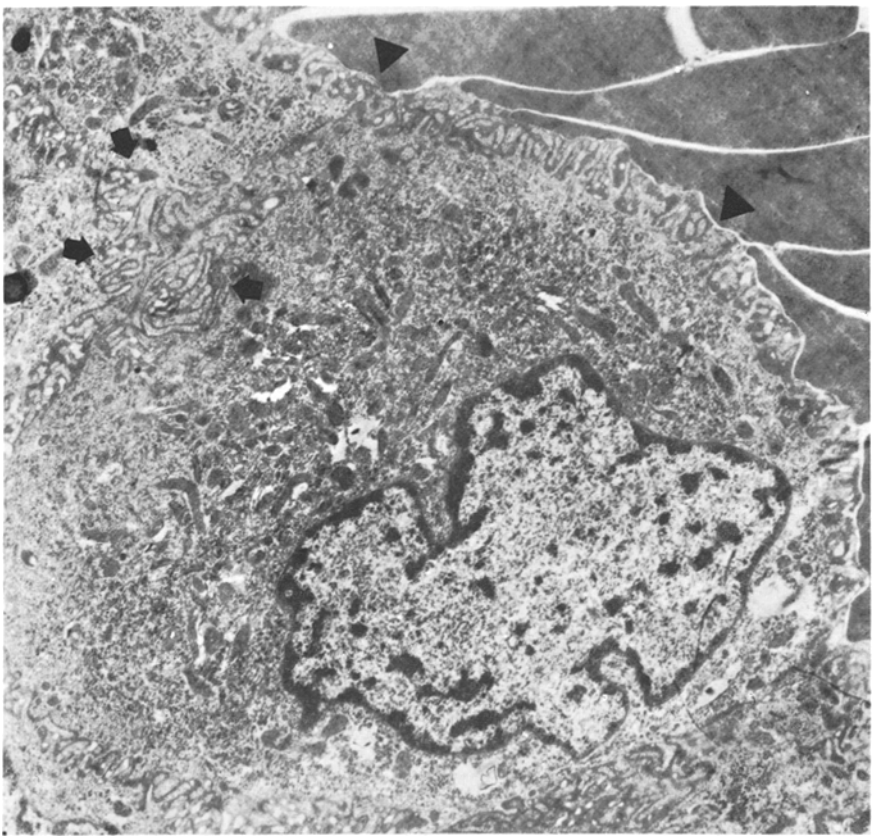

Fig. 6. Tumor cells with microvilli (arrow-heads) on the free surface and interdigitating folds between adjacent cells (arrows). ×4,500

(Figs. 2b and 3), and light and frequently foamy cytoplasm. The other cells were cuboidal with small, mostly round nuclei, a coarser chromatin structure and dark eosinophilic cytoplasm.

Numerous reticular, interconnected cavities were found, corresponding most likely to the terminal bronchioles of the normal lung tissue (Fig. 2). They were mostly lined with the cylindrical eosinophil cells or, less frequently, the lighter type of cell. These cavities were surrounded by solid tumor masses of densely arranged, light cells (Fig. 3). On the fringe of the tumor a marked proliferation of capillaries and arterioles was found, the latter often having become hyalinised (Fig. 4). Extensive haemorrhage in the cavities was found in the vicinity of the proliferating capillaries.

Between the tumor cells, isolated mast cells, plasma cells and lymphocytes were found (Fig. 3).

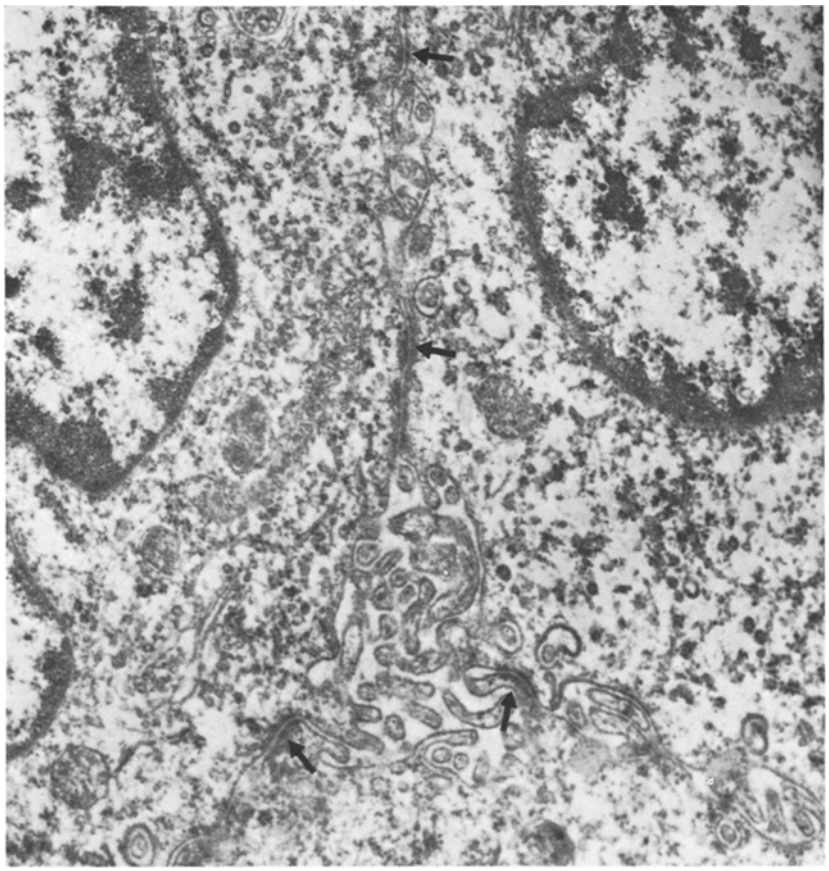

Fig. 7. Desmosome-like junctions between closely apposed tumor cells (arrows). × 12,000

Electron Microscopy

With electron microscopy the two types of cells distinguished by light microscopy show little differentiation (Fig. 5). Both had large, strongly lobed nuclei. The cytoplasm contained an abundance of mitochondria, a granular, endoplasmic reticulum and a rudimentary golgi apparatus. The cytoplasm of the light cells contained less mitochondria and a few glycogen particles. Both cell types had many-layered lamellar inclusions, as found in type 2 pneumocytes. Both had clear epithelial differentiation with a long, microvillus-like folding of the cell membrane (Fig. 6) and clearly identifiable attachment devices, usually desmosomes (Fig. 7). Electron microscopy showed numerous mast cells between the tumor cells. The sinusoidal cavities seen by light microscopy and which contained erythrocytes in their lumina, were clearly lined with tumor cells and not with endothelial cells (Fig. 5). In some places lamellar formations were found in the interstitial tissue and were possibly layers of mucus or the products of

cell death. Between the tumor cells independent capillary development (tumor stroma) was seen.

Discussion

The morphological complexity of the tumor has led to some confusion in the terminology. According to which component was dominant in light microscopy, the tumor has been designated sclerosing angioma, xanthoma, pulmonal histiocytoma, xanthofibroma, fibroxanthomatous pseudotumor etc.

Liebow and Hubbel (1956) believed the tumor to be an angioma with haemorrhage and histiocytic reaction. Mori (1968) and Haas et al. (1972) also considered it an angioma, interpreting the sclerosis and hyalinisation as the result of an ageing processes.

On the basis of their examinations with tissue cultures Sherwin et al. (1965) came to the conclusion that the tumor was a mast cell granuloma, while Wentworth et al. (1968), having conducted quantitative evaluation of the lipid inclusions, proposed a xanthomatous pseudotumor. In our case, however, inflammatory cells were insignificant, and the tumor cells whose foamy cytoplasm suggested a certain similarity with histiocytes, were identified by electron microscopy as cells of epithelial origin with lipid inclusions. Electron microscopy in our case revealed clear epithelial differentiation in the form of desmosomes, microvilli, interlocking of the cells, and lamellar inclusions in the cytoplasm. The equivalents of the tumor cells in normal lung tissue were probably the membranous granular pneumocytes, while the cavities corresponded to the terminal branches of the bronchi and bronchioles. The blood-filled cavities were lined not with endothelial cells but with cells of epithelial origin. Thus the vascular proliferation and haemorrhage, which were located predominantly on the fringes of the tumor were a secondary reaction.

Spencer (1977) suggested that the tumor was formed through the proliferation of indifferent alveolar epithelial cells. On the basis of electron microscopy Hill and Egglestone (1972) and Heilman and Feiner (1978) came to the same conclusion. According to Hill and Egglestone since pneumocytes (types I and II) originate from the cylindrical epithelial cells lining the primitive fetal bronchioles, the cells of the clerosing angioma derive from such primitive, incompletely differentiated epithelial cells. The various morphological forms of the tumor cells merely correspond to the various degrees of differentiation. The histological differential diagnosis from carcinoma of the lung is of great practical importance. In view of the abundance of collagenous tissue and the morphology of the tumor cells in the sclerosing angioma, there is the danger, especially with intraoperative frozen section examination, of confusion with a scar carcinoma or alveolar carcinoma (Thurlbeck, 1978) as occurred in the present case. The danger is all the greater as the possibility of sclerosing angioma is less likely to be considered because of the rarity of the tumor. The macroscopic findings (yellowish, clearly defined circular focus) and clinical findings (no symptoms, young females) are highly significant aids in the differential diagnosis. As a sclerosing angioma of the lung is a benign, isolated lesion (Thurlbeck, 1978), no further treatment of the patient is required.

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