Histol Histopath (1992) 7: 209-212

Histology and Histopathology

Sclerosing haemangioma of the lung.

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Summary. The present paper describes a case of sclerosing haemangioma of the lung. Immunohistochemical analysis further supports its origin from respiratory epithelium, and confirms its minimal proliferative activity.

Key words: Lung neoplasm, Benign, Immunohistochemistry, Sclerosing haemangioma

Introduction

Sclerosing haemangioma of the lung is a rare pulmonary neoplasm, first described by Liebow and Hubbell (1956).

Its histogenesis has long been controversial: the proliferating cells had been considered to be either endothelial (Liebow and Hubbell, 1956; Carstens and Schrodt, 1974), mesothelial (Katzenstein, 1983), epithelial (Spencer and Nambu, 1986; Satoh et al., 1989) or mesenchymal (Huszar et al., 1986).

The present paper report a case of sclerosing haemangioma of the lung along with immunohistochemical findings supporting its origin from respiratory epithelium.

Materials and methods

A 38-year-old woman suffering from cough and chest pain underwent chest x-ray and was found to have a rounded parahilar nodule in the left lung. The nodule was surgically resected and submitted for histology.

Two years after operation the patient is alive and well.

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Macroscopically the tumour was rounded, 1 cm in diameter, not encapsulated, but well demarcated. The cut surface was fleshly, spongy and deep red in colour, with some white-grey areas.

For light microscopy, sections of the formalin-fixed, paraffin-embedded samples were stained with H-E, P.A.S., Masson thrichrome and silver impregnation for reticulin. Sections were also immunostained with the avidin-biotin complex (ABC) technique. Antisera and antibodies are listed in Table 1. Negative controls were obtained by substituting primary antiserum/antibody with corresponding non-immune antiserum/antibody.

Results

Histologically, the tumour disclosed a predominantly solid architectural pattern, composed of monomorphous polygonal or rounded cells (S cells). Cytoplasm was clear or slightly eosinophilic. Nuclei were vesicular, with a loose chromatin pattern. Stromal tissue was generally scarce, except for a few areas showing hyalinization. Slit-like spaces lined by cuboidal epithelial-like cells were clearly seen among the solid cell nests, especially at the periphery of the neoplasm (Fig. 1). The cells lining most of the spaces showed bronchiolar features, sometimes with clearly-defined cilia. In some areas the spaces were wider and the lining epithelial cells were larger and had foamy cytoplasm (Fig. 2). Areas of hemorrhage, hemosiderin deposition and blood vessel hyalinization were also present.

Immunohistochemistry (Table 2) revealed positivity of the neoplasm for EMA, Clara cell antigen and surfactant apoprotein (Fig. 3). The polygonal cells generally stained weaker than the cells lining the slit-like spaces. The cells with bronchiolar epithelial features lining these spaces were strongly positive for cytokeratin and EMA, and a few were positive for chromogranin A (CGA) and Leu-7 antigen (Fig. 4)

Table 1. Antisera and antibodies used in the present study.

Reagent	Source	Clonality
Anti-epithelial membrane-antigen	Dako	M
Anti-surfactant apoprotein	G. Singh, M.D. Pittsburgh, PA	R
Anti-Clara-cell antigen	G. Singh, M.D. Pittsburgh, PA	R
Anti-cytokeratins (AE1/3)	Lipshaw	M
Anti-chromogranin A (PHE5)	A.M. Gown, M.D.	M
Anti-Factor VIII	Dako	R
Anti- S-100 protein	Dako	R
Anti-Leu-7	Beckton & Dickinson	M
Anti-PCNA (19A2)	American Biotech	M

M: mouse monoclonal
r: rabbit polyclonal

bulk of the available data favours the epithelial hypothesis (Aiba et al., 1988; Yousem et al., 1988; Satoh et al., 1989). Other hypotheses suggested a histogenesis related to endothelial (Carstens and Schrodt, 1974), mesothelial (Katzenstein, 1983) and mesenchymal cells (Huszar et al., 1986). The results of the most recent immunohistochemical studies performed on SHL are summarized in Table 2, along with the results of our own study.

As shown in Table 2, the immunophenotypic properties of SHL support its epithelial nature. There are, however, some immunohistochemical differences between the cells forming the bulk of the neoplasm (S cells) and the cells lining the spaces found within the tumour. Aiba et al. (1988) demonstrated that these spaces were of two types, lined by two different cell types. One called L1, is lined by cells with histochemical similiarities to the polygonal cells of the neoplasia, and the other, called L2, is lined by cells with immunohistochemical

Table 2. Literature review of the most comprehensive immunohistochemical studies performed on SHL along with the results of our own case.

References	1	2	3	4		5		6	7	
				S	L1 L2	P	L		S	CC
CK	+	nd	+	–	+	±	+	–	–	+
EMA	+	nd	nd	+	+	±	+	+	+	+
CEA	+	nd	nd	–	–	nd	nd	nd	nd	nd
VIM	+	nd	+	+	–	±	+	–	nd	nd
SAP	+	+	nd	–	+	±	+	nd	+	–
CCA	+*	nd	nd	nd	nd	nd	nd	nd	+	+*
S100	–	nd	nd	nd	nd	nd	nd	nd	–	–
Leu-M1	–	nd	nd		nd	nd	nd	nd	nd	nd
MUR	nd	–	nd	nd	nd	nd	nd	nd	nd	nd
FVIII	–	–	nd	nd	nd	–	–	nd	–	–
Leu-7	nd	nd	nd	nd	nd	nd	nd	nd	–	+**
CGA	nd	nd	nd	nd	nd	nd	nd	nd	–	+**

Legends:
CK: cytokeratins; EMA: epithelial membrane antigen; CEA: caecinoembrionic antigen; VIM: vimentin; SAP: surfactant apoprotein; CCA: Clara cell antigen; S100: S-100 protein; MUR: muramidase; FVIII: factor VIII-related antigen; CGA: chromogranin A.
*: focally positive
**: positivity restricted to scattered cells among those lining the spaces.
References: 1) Yousem et al., 1988; 2) Nagata et al., 1985; 3)Huszar et al., 1986; 4) Aiba et al., 1988 (S: solid growing cells; L1: cuboidal cells lining the spaces; L2: Large, foamy cells lining the spaces); 5) Satoh et al., 1989 (P: pale cells of the tumour; L: cells lining the spaces); 6) Haimoto et al., 1985; 7) Present case (S: solid growing cells; CC: polygonal cells lining the spaces).

PCNA immunostaining showed very few positive cells (less than 2%).

Discussion

Sclerosing haemangioma of the lung (SHL) is a rare lesion, formerly classified as a hamartoma, which is now generally placed in the category of true neoplasms with low metastatic potential (Shimosato and Kodama, 1987). Its histogenesis is still not definitively confirmed, but the properties of type II pneumocytes.

We too observed two different kinds of space, one lined by foamy cells, not reacting to CK, and the other lined by cuboidal cells, reactive to CK, with intercalated CGA and Leu-7-positive neuroendocrine cells and with clearly evident cilia. This latter kind of space seems to be more frequently distributed at the periphery of the lesion and, in our opinion, may represent bronchiolar epithelial structures entrapped in the neoplasm. On the other hand, the foamy cells may represent a kind of differentiation of the

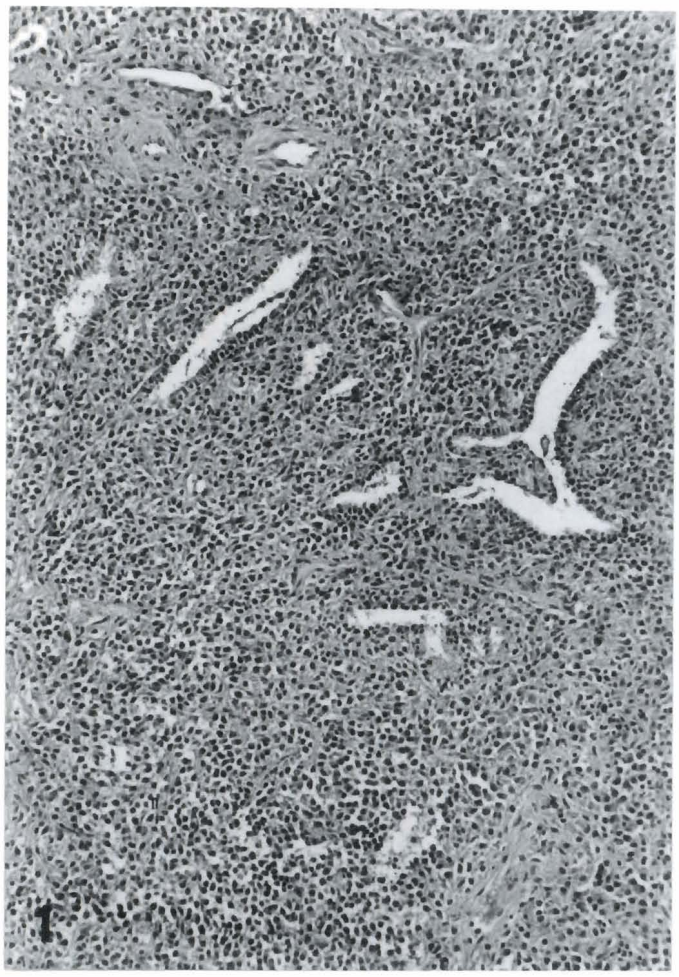

Fig. 1. Sclerosing haemangioma: predominantly solid growth pattern with interspersed slit-like spaces lined by cuboidal epithelial cells. H-E. × 100

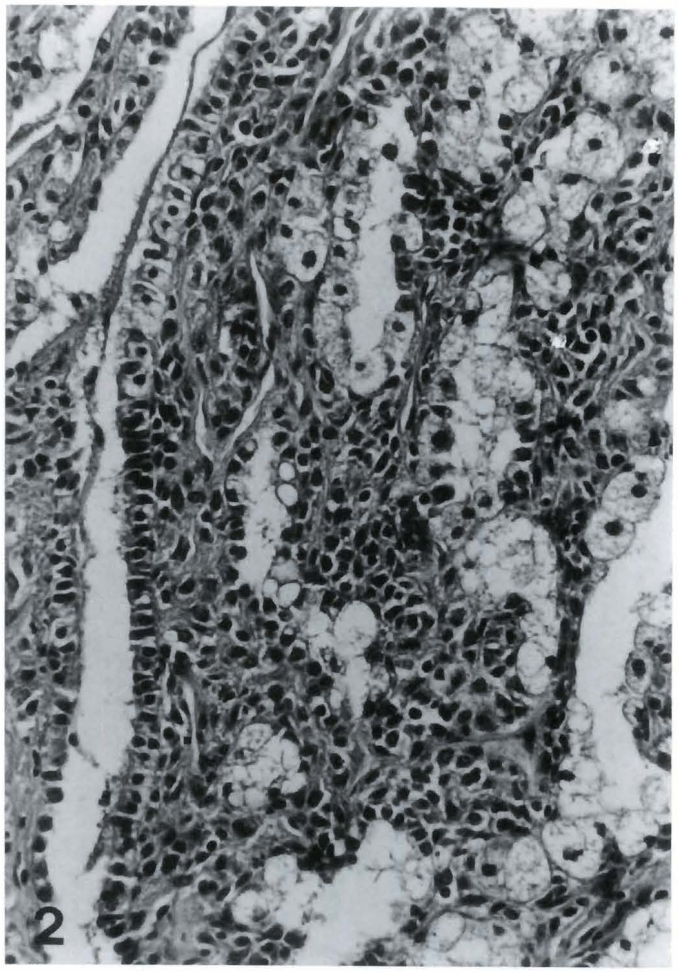

Fig. 2. Two types of slit-like spaces are clearly evident: left is a space lined by cells with bronchiolar features, with cilia; right are multiple spaces lined by foamy cells. H-E. × 250

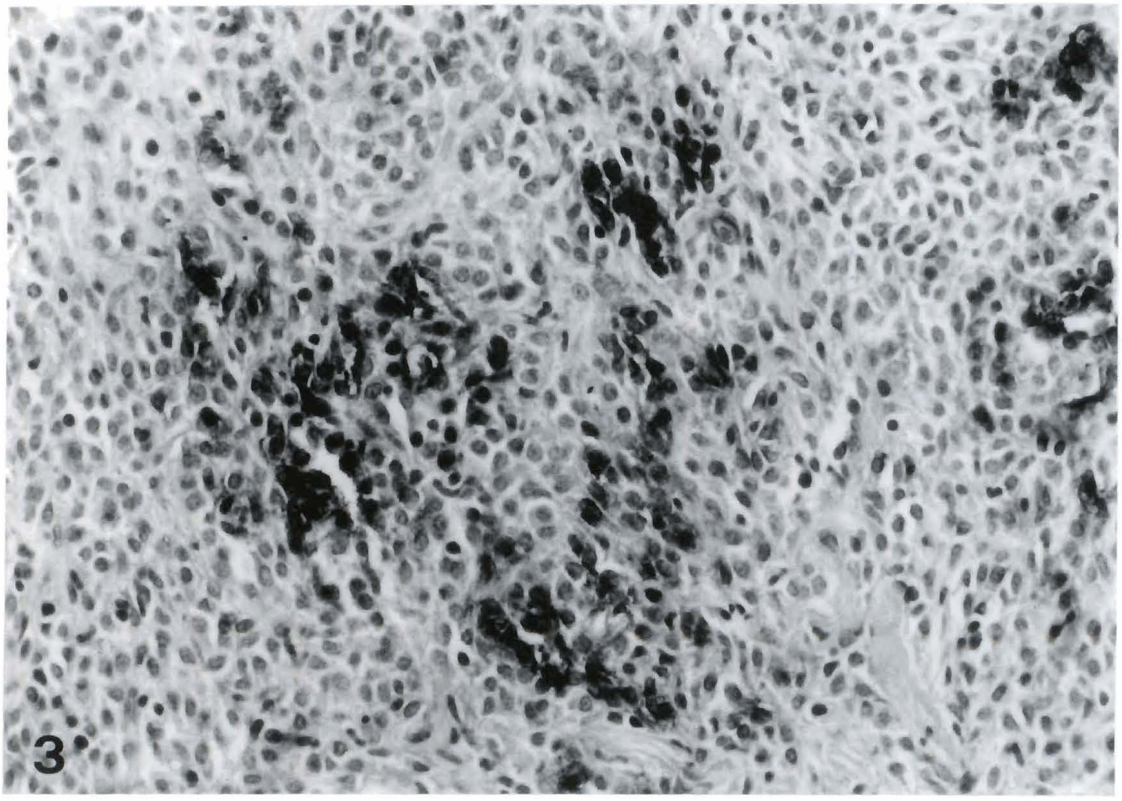

Fig. 3. EMA-positive cells are either singly scattered among the other non-reactive cells, or are grouped in small aggregates. ABC, nuclear counterstain. × 250

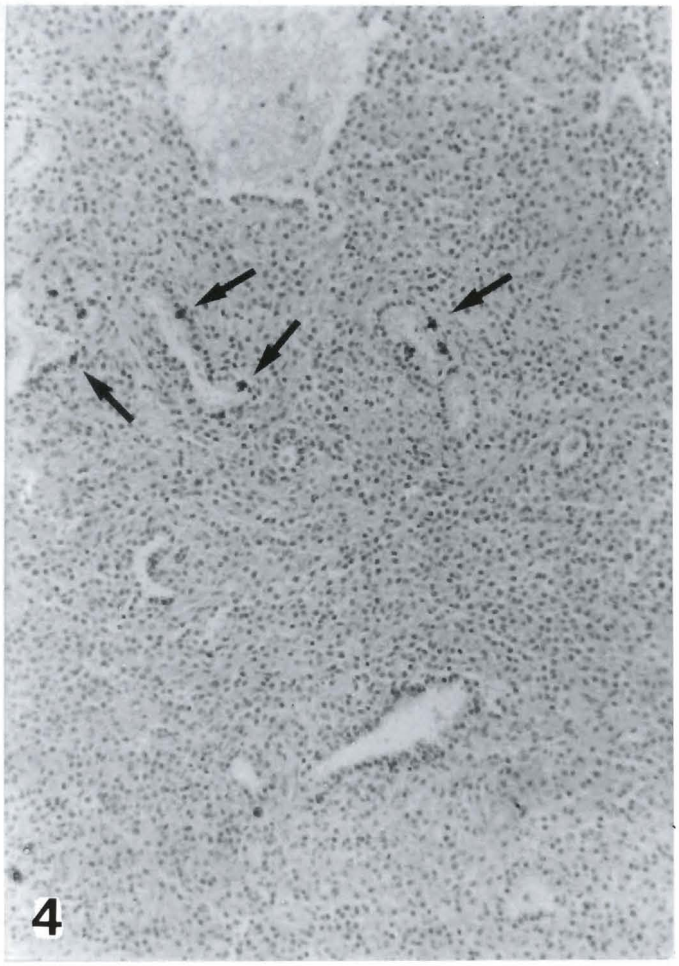

Fig. 4. Bronchiolar type of slit-like spaces with intercalated positive neuroendocrine cells (arrows). ABC, with nuclear counterstain. × 100

neoplasm into a more defined epithelial structure.

The results of immunostaining with PCNA, a newly developed marker of cell proliferation (Dawson et al., 1990), are in keeping with the concept that SHL is a very low-grade neoplasm with minimal proliferative activity.

In conclusion, data from literature, along with ours, show that SHL is a very low-grade neoplasm which may display various differentiative features i.e.: may show features of type two pneumocytes, of Clara cells and of bronchiolar cells.

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Accepted October 15, 1991