

SCLEROSING PNEUMOCYTOMA

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Abstract

Sclerosing pneumocytoma is a rare benign tumour of the lung with not fully understood histogenesis. We have studied a case of this unusual neoplasm removed from the lung of a 29-year-old man. Histological, immunohistochemical and ultrastructural findings suggest the origin from type 2 pneumocytes with neuroendocrine differentiation.

Key words

Lung, Sclerosing hemangioma, Pneumocytoma, Neurocrine differentiation

INTRODUCTION

Liebow and Hubbell (6) published a report on sclerosing hemangioma/histiocytoma, xanthoma/ of the lung in 1956. Further studies basing on ultrastructural analysis of neoplastic cells revealed that the tumour histogenesis is by far more complicated.

Hill and Eggleston (3) pointed out the dominant role of the proliferating pneumocytes of type 2. These data were supported by *Palacios et al* (5). The vagueness of the terminology of this tumour is manifested in Czech literature too (1); some synonyms are available with regard to its histogenesis. Nevertheless, recent studies using immunohistochemistry have not succeeded in offering a generally accepted classification of this tumour. *Rodriguez-Soto et al* (10) suggest that the idea of epithelial differentiation of tumour cells is supported by the immunophenotype but the definitive nature of the lesion cells of "sclerosing hemangioma" remains a mystery.

The problem of histogenesis and neuroendocrine activity of the sclerosing pneumocytoma remain an open question and further studies are desirable. That is why we try to contribute to this effort with our observation.

CASE REPORT AND METHODS

CLINICAL DATA

A man of 29 with no significant family history. His complaints were related to chronic rhinitis. The alarming symptoms of his actual disease appeared in August 2001: hemoptysis and physical strain. An x-ray examination revealed a focus situated at the base of the right lung under the hilus. The CT showed a solid well circumscribed lesion of ca. 42x33 mm in diameter /with scattered calcifications/ bordering closely on the right heart atrium. The residual lung parenchyma, mediastinum and regional lymph nodes displayed no alteration. An additional test of respiratory functions and general laboratory screening were normal.

A surgical intervention was indicated. The patient was hospitalized from 5th to 12th November 2001 with the diagnosis: An infiltrative affection of the lower lobe of the right lung 7th segm. A banal posterolateral thoracotomy had been performed and the tumoriform tissue was removed *in toto* from the affected segment. Though inconspicuous, the regional lymph nodes were removed too. The neoplasm displayed a tough but brittle consistency. The result of a preoperative biopsy excluded a malignancy so that no need to perform a lobectomy ensued. The postoperative course was favourable, the wound healed by first intention. The patient was discharged with good respiratory functions and additional rehabilitation was recommended.

MORPHOLOGICAL EXAMINATION

The resected part of the lower lobe of the right lung displayed a well bordered neoplastic node of ca. 3 cm in diameter. The cut surface showed a white-yellowish tissue with patchy consolidation and calcifications.

For histological study, formalin fixed paraffin embedded tissue sections were stained with hematoxylin-eosin, periodic acid-Shiff with and without diastase digestion.

Immunohistochemistry was performed in sections cut from the paraffin blocks.

For the electron-microscopic examination, the paraffin-embedded tissue was processed through a series of xylenes and acetones. This was postfixed in the 2.5% buffered glutaraldehyde and then in 1% osmium tetroxide. Dehydration was accomplished with a series of acetones, and finally the tissue was embedded in Durcupan. The sections were contrasted with lead citrate and uranyl acetate.

HISTOLOGY AND IMMUNOHISTOCHEMISTRY

Both preoperative and postoperative samples /7 pieces/ showed a similar picture varying in the range of the histological entity named "sclerosing pneumocytoma" (*Fig. 1*). The neoplastic cells were arranged in solid, papillary or sclerosing patterns with patchy mineralisation. The tumour cells were relatively uniform with monomorphous nuclei and without mitotic figures. The labelling of Ki67 as a marker of cell proliferation was near zero. The tumour cells expressed cytokeratin markers (7, 8, 18, 20) and granular cytoplasm at places showing positivity for synaptophysin and protein S 100.

The benign course of the neoplasm may be supported by the absence of mitotic figures and relatively monomorphic appearance of the tumour cells (*Fig. 2*). The tumour was well circumscribed at surgical intervention, and no enlarged regional lymph nodes were found. The lymph nodes removed revealed only a reactive hyperplasia of lymphoid tissue and in some sinuses small amounts of siderin-laden macrophages and mild to moderate fibrosis with anthracotic pigment were found. The results of other routine staining /screening/ were irrelevant and the complex histological examination can be summarized in a diagnosis. of "sclerosing pneumocytoma with an epithelial immunophenotype and with patchy neuroendocrine differentiation of some cells".

In the lesion cells we found numerous polymorphic cytoplasmic electron-dense granules which were round, oval, elongated, rod-like or curved in shape. They had a finely striated or granular substructure with an indistinct peripheral limiting membrane (*Fig. 3*). This alteration may be due to the double processing of the samples described in the paragraph "Morphological examination", and will be discussed later.

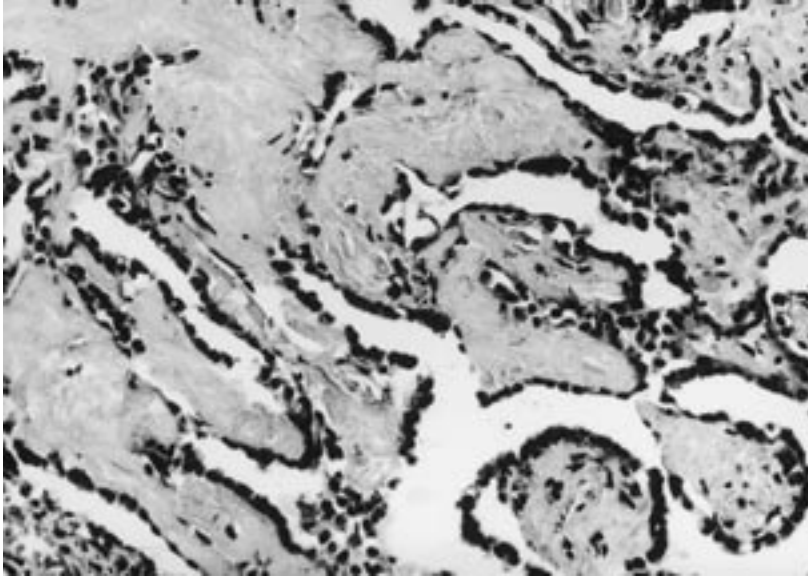


Fig. 1

Papillary and sclerosing growth pattern of the sclerosing pneumocytoma, hematoxylin - eosin, original magnification x200.

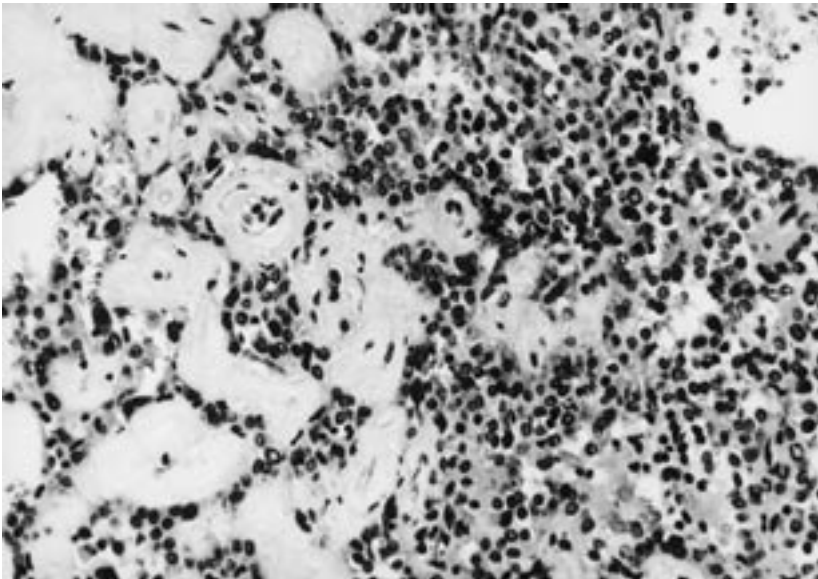


Fig. 2

Solid and papillary arrangement of neoplastic cells lacking atypia and mitotic activity, hematoxylin - eosin, original magnification x200.

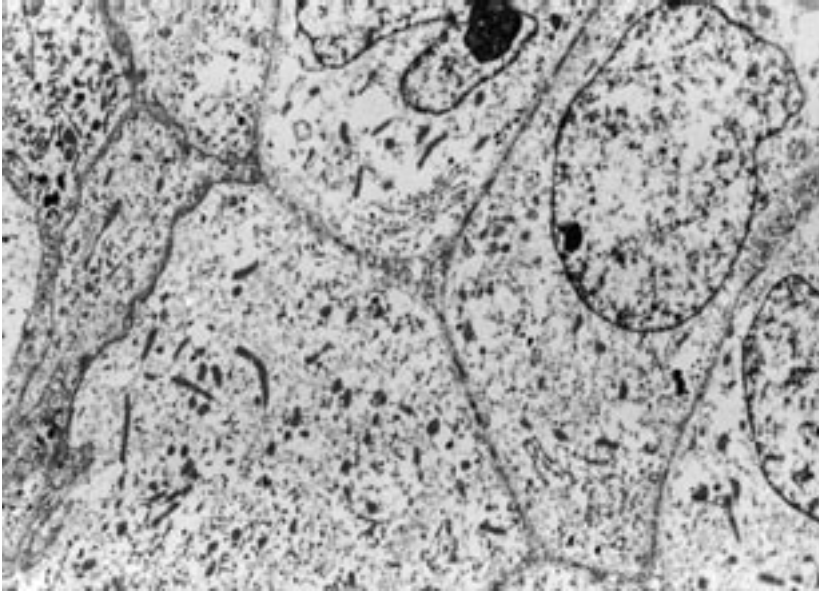


Fig. 3

Electron microscopic view of neoplastic cells with regular rounded nuclei. The cytoplasmic electron-dense granules showed pleomorphism and variability in shape (x6000).

DISCUSSION

Sclerosing pneumocytoma is a rare pulmonary neoplasm which was identified by *Liebow and Hubbell (6)* in 1956 and termed sclerosing hemangioma of the lung owing to prominent sclerotization and vascularization of the tissue. The neoplasm occurs in young as well as in old persons, the peak age incidence being in the 5th decade. Women are affected by this tumour more frequently. The symptomatology is poor, cough is not constant. The tumour is well circumscribed but lacking a definite capsule. It grows expansively, compressing the neighbouring parenchyma. The histological picture is characterized by alternating areas of papillary, solid and angiomatoid structures with papillary predominance. The papillary surface cells are uniform with mild eosinophilia of the cytoplasm and with oval nuclei which show tiny nucleoli at places. Mitotic figures are rarely observed. The tumour tissue displays secondary regressive changes with sclerotization and patchy lipophage accumulation. The angiomatous components reveal continuous, irregular channels filled with blood.

As regards the histogenesis and classification of this tumour, there exists no general agreement. In 1956, *Liebow and Hubbell (6)* identified this tumour and found it analogous to the sclerosing hemangioma of the skin. This evaluation proved false

by the studies of *Hill et al.* (3). They proved that the proliferating elements in this neoplasm took their origin from the respiratory epithelia. The ultrastructure of these cells was similar to that of type 2 pneumocytes. This was supported also by *Palacios et al* (5). *Nagata et al* (7) published a report representing a larger series of patients and confirmed the epithelial origin of the so-called "sclerosing hemangioma". They pointed out the heterogeneity of epithelial cells by an immunohistochemical assay. *Xu et al* (4) confirmed the results of Nagata et al and demonstrated neuroendocrine differentiation of the proliferating cells. Nevertheless, neurocrine activity was not positive in the group studied by *Rodriguez-Soto* (10).

The WHO classification (8) includes this tumour in a marginal category and sets apart four subgroups: solid, papillary, hemorrhagic, and sclerotic. *Corrin* (9) terms this tumour "sclerosing pneumocytoma" pointing out that the proliferating element is the type 2 pneumocyte, which may show a neuroendocrine differentiation. The vascular and fibrous components are of secondary significance. The key arrangement of the proliferating cells is papillary.

As regards the neuroendocrine activity of the neoplastic cells, some additional remarks must be added. Normal histology demonstrates granular neuroendocrine cells among respiratory epithelia. These neuroendocrine cells release catecholamines or polypeptides and are in contact with nerve terminals (2). Now the question may arise about the origin of the neuroendocrine cells present in the sclerosing pneumocytoma. Are these cells mutants of the proliferating pneumocytes of type 2 or do they represent co-proliferating or only hyperplastic normal neuroendocrine pulmonary cells?

Hill et al (3) disclosed cytoplasmic granules with one or two membranes by electron-microscopic analysis, but they do not clearly attribute an incretory nature to them. *Palacios et al* (5) show dense membrane inclusions bound in the apical cytoplasm of some of the cells and believe that these cells are similar to those of Clara. A neurocrine activity comprising the identification of some hormones was presented by *Xu and al* (4). These authors do not discuss the putative origin of the tumour endocrine cells. Our own ultrastructural results are only marginal and not relevant owing to the material used, which was fixed in formalin and embedded in paraffin. Nevertheless, we cannot exclude that the dense granules found in the cytoplasm of some neoplastic cells (*Fig 3*) might be the substrate of endocrine activity regardless of the fact that they are devoid of the membranes. The absence of the membranes may be elucidated by the influence of the fixative and paraffin used. As regards the neuroendocrine activity, we can rely to a certain degree on the positivity of synaptophysin and protein S 100.

DIFFERENTIAL DIAGNOSIS

Xu et al (4) differentiate between the so-called sclerosing hemangioma and papillary adenoma or between carcinoid tumour and others. *Corrin* (9) points out the

differential diagnosis against xanthoma and histiocytoma and epithelioid hemangioendothelioma, etc. We believe that a large series of histo- and immunohistochemical methods prevent confusion with the majority of the above-mentioned tumours.

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SKLEROZUJÍCÍ PNEUMOCYTOM

S o u h r n

Sklerozující pneumocytom je vzácný benigní nádor plic, jehož histogeneza není zcela jasná. Zjistili jsme tento tumor u 29-letého muže na základě histologického, imunohistochemického a elektronmikroskopického nálezu a přikládáme se k názoru, že jde o derivát pneumocytů 2. typu, jež se diferencují neuroendokrinně.

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