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Alveolar adenoma of the lung: further characterization of this uncommon tumour

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Abstract Alveolar adenoma of the lung is a poorly characterized, uncommon pulmonary lesion with proliferation of alveolar epithelium and septal mesenchyme. We describe the electron microscopy, immunohistochemistry and DNA flow cytometry in a case of alveolar adenoma in a 55-year-old woman. Alveolar adenoma appears to be a distinct benign neoplasm of the alveolar structures. Our findings further suggest that it is not a precursor of bronchioloalveolar carcinoma or other type II pneumocyte lesions of presumed malignant potential.

Key words Alveolar adenoma · Lung neoplasms · Flow cytometry · Electron microscopy · Proliferating cell nuclear antigen

Introduction

In 1986, Yousem and Hochholzer [28], reported six cases of a pulmonary neoplasm resembling the alveolar structure of the lung histologically, that they designated as alveolar adenoma. Since then only three other cases have been published in the literature [2, 22, 23]. The rarity of this tumour has not allowed a definitive characterization, especially in terms of its histogenesis, although immunohistochemical and ultrastructural findings [22, 23, 28] support the hypothesis that this lesion is a "true" adenoma with proliferation of both epithelial and mesenchymal alveolar components.

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We report a case of alveolar adenoma in a 55-year-old woman, with emphasis on electron microscopic findings, immunocytochemistry and DNA ploidy. We believe these studies support the histogenetic hypothesis proposed by Yousem and Hochholzer. In addition, we also discuss the relationship of alveolar adenoma with other lung lesions exhibiting type II pneumocyte differentiation.

Case history

A 55-year-old white woman was seen at the Instituto Português de Oncologia de Francisco Gentil in February 1993 for evaluation of a right lung mass, discovered during the work-up for an insidious chronic non-productive cough. Chest X-rays and CT scan showed a well circumscribed 4 cm mass in the right lower lobe of the lung. No other abnormalities were detected.

Fibreoptic bronchoscopy showed total occlusion of the basal medial bronchus by a bulging mass that was covered by normal appearing mucosa. Biopsy showed normal lung tissue. A fine-needle aspiration biopsy of the mass done under ultrasound guidance was considered non-diagnostic. The patient underwent an exploratory thoracotomy with a lung segmentectomy performed after frozen-section diagnosis of a benign lesion consistent with lymphangioma. She is currently well and asymptomatic 32 months after surgery.

Materials and methods

Tissue was fixed in 10% buffered formalin, and paraffin-embedded sections were stained with haematoxylin and eosin. Selected sections were stained with alcian blue-periodic acid Schiff (PAS).

Immunohistochemical studies using the enzyme labelled avidin-biotin method [8] were performed on formalin-fixed, paraffin-embedded tissue sectioned at 4 μm. Sources of primary antibodies and *Ulex europaeus* lectin (UEA-1) used and their working dilution's are summarized in Table 1. Appropriate controls were made in every case.

For electron microscopic examination, small fragments of the tumour obtained immediately after surgery were fixed in 2% glutaraldehyde in 0.1 M cacodylate buffer, pH 7.3, and post-fixed in 1% osmium tetroxide in the same buffer and in 0.5% uranyl acetate in distilled water. They were embedded in a Epon-Araldite mixture [15] and appropriate areas, selected from 1 μm toluidine blue stained sections, were thin-sectioned, sequentially stained with uranyl acetate and lead citrate, and observed in a CM 10 Philips electron microscope.

Table 1 Immunostaining results (– negative, + occasionally positive, ++ most cells positive, +++ strongly positive, *UCHL* University College Hospital London)

Antigen	Source of antiserum	Working dilution	Cell types	
			Epithelial lining	Interstitial stroma
Cytokeratin (CK1)	Dako A/S,Glostrup,Denmark	1:10	+++	–
Cytokeratin (CAM5.2)	UCHL, London, Great Britain	1:10	+++	–
Epithelial membrane antigen (EMA)	Dako A/S,Glostrup,Denmark	1:20	+++	–
Carcinoembryonic antigen (CEA)	Dako A/S,Glostrup,Denmark	1:1500	++	–
Desmin	Dako A/S,Glostrup,Denmark	1:5	–	+
Vimentin	Dako A/S,Glostrup,Denmark	1:800	–	+++
FVIII	Dako A/S,Glostrup,Denmark	1:10	–	–
CD68 (KP1)	Dako A/S,Glostrup,Denmark	1:40	–	–
Cyclin (PCNA)	Dako A/S,Glostrup,Denmark	1:300	–/+	+
Ulex europaeus lectin (UEA-1)	Dako A/S,Glostrup,Denmark	1:100	–	–
Estrogen receptor (ES)	Immunotech	1:10	–	–
Progesterone receptor (PS)	Abbott	1:80	–	–

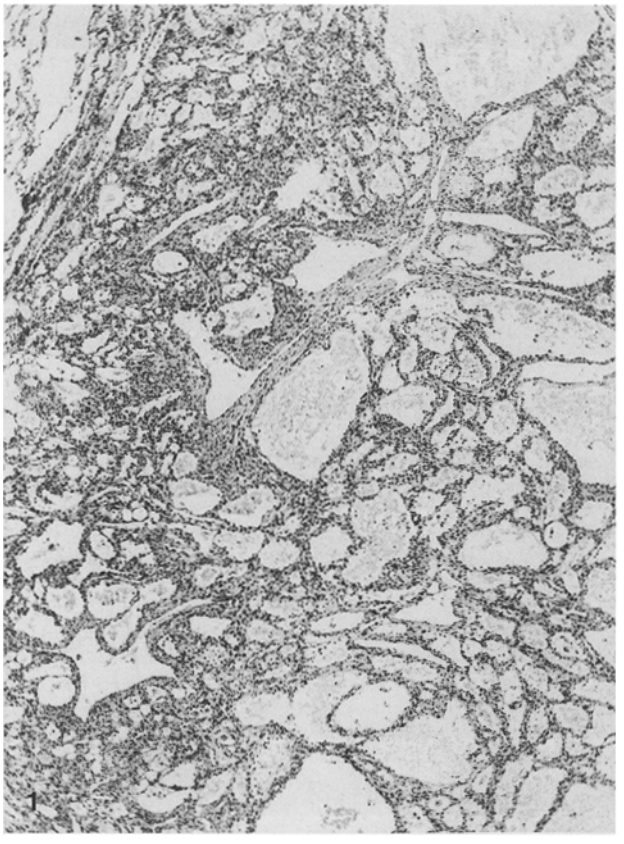
For DNA cytometry, fresh tumour samples were frozen and stored at –80°C and treated according to a modification of the method of Thornthwaite et al. [25]. The specimens were mechanically disaggregated with scalpels and the cell suspension obtained was filtered, counted and incubated with propidium iodide 50 µg/ml in TRIS-magnesium chloride buffer for 1 h at room temperature, treated with RNase A 1 mg/ml in phosphate-buffered saline and 0.5% Nonidet P40. After filtration through a 55 µm nylon mesh, the stained nuclei were analysed using an EPICS Profile II flow cytometer (Coulter Electronics, Hialeah, Fla.) equipped with a 488 nm argon laser. At least 10,000 cell nuclei were collected for each sample. Cell cycle analysis was performed using the Multicycle Software Program (Phoenix Flow Systems, San Diego, Calif.) based upon the polynomial S-phase algorithm developed by Dean and Jett [7] with an iterative, nonlinear least squares fit performed by the method of Marquardt [11].

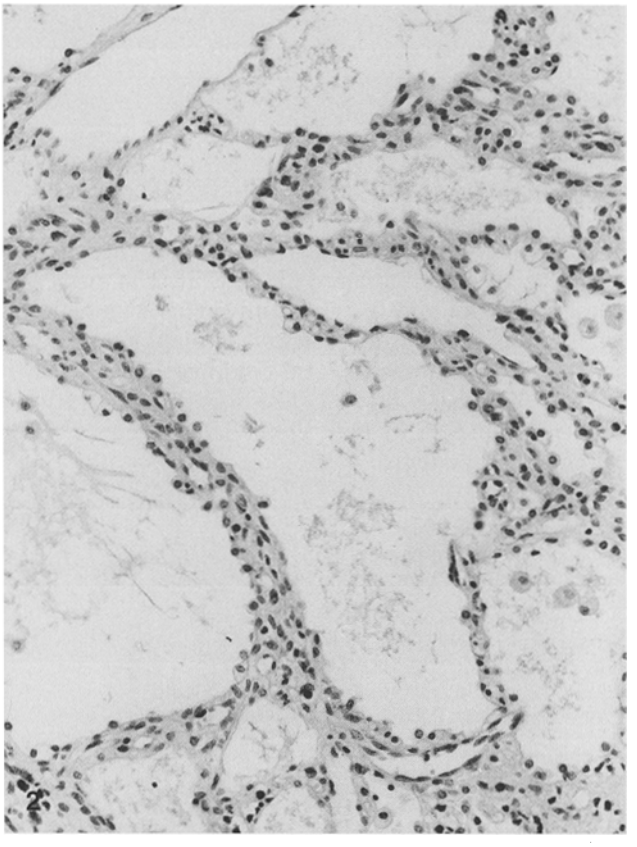
Fig. 1 Low magnification showing sharp demarcation from the adjacent lung parenchyma (*upper left corner*) and cystic spaces larger in the central area of the tumour (*right*) H&E, ×90

Fig. 2 Cystic spaces with intraluminal proteinaceous material and alveolar macrophages. H&E, ×220

Results

The resected lung segment contained a well defined tumour mass measuring 60×45×40 mm, subpleurally locat-





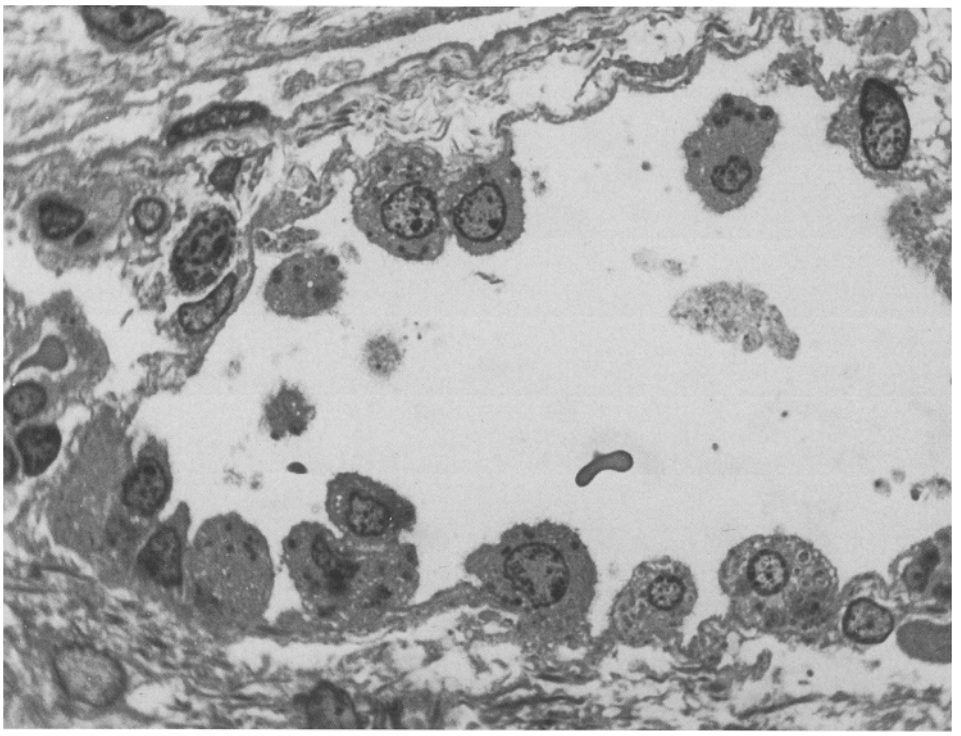


Fig. 3 Epithelial lining cells with a hobnail appearance, resembling type II pneumocytes. Semi-thin section, ×1,100

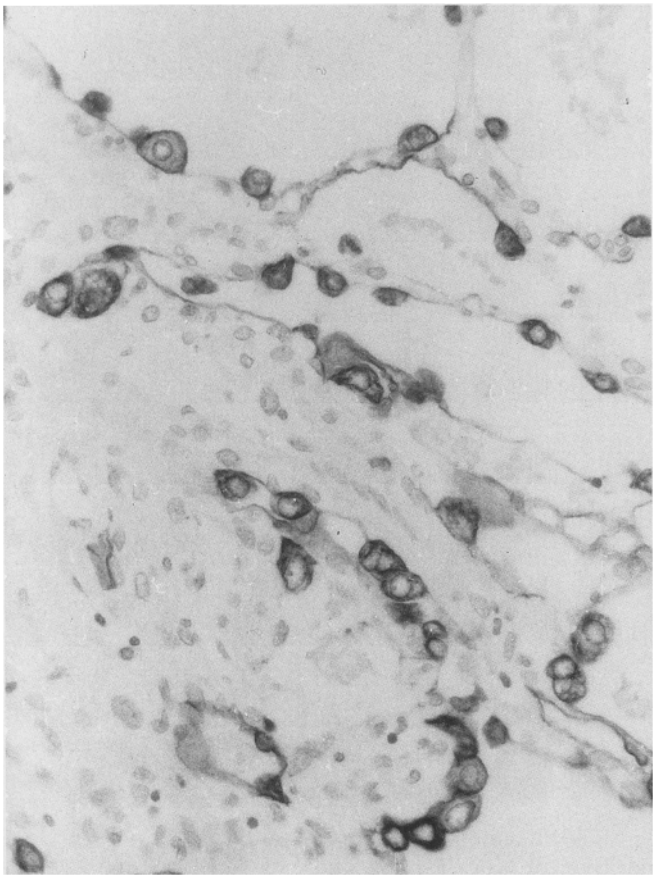


Fig. 4 Epithelial lining cells exhibiting strong positivity for low molecular weight keratin. CAM5.2, ×900

ed, that easily shelled-out from the adjacent pulmonary parenchyma. The cut surface was soft and spongy with a homogeneous pink-grey microcystic appearance. No relation with adjacent bronchial or vascular structures were observed and the remaining lung tissue was unremarkable.

On light microscopy the tumour was well demarcated and consisted of multiple cystic spaces of variable size, larger in the central areas, and smaller at the periphery of the lesion (Fig. 1). The spaces were lined by plump cells with a hobnail appearance, resembling reactive type II pneumocytes (Figs. 2, 3), and occasionally contained intraluminal PAS+ granular proteinaceous debris and foamy alveolar macrophages. The intervening septa varied in thickness and were composed of spindle and stellate cells in a myxoid stroma, with a variable inflammatory cell infiltrate of lymphocytes, eosinophils, plasma cells and occasional mast cells. The septa were richly vascularized with numerous vessels ranging in size from small-to-large ectatic capillaries. Foci of interstitial haemorrhage and haemosiderosis were also observed. Mitotic activity was inconspicuous and no atypical features were noted.

Immunohistochemical findings are shown in Table 1. The type II pneumocyte lining cells exhibited strong staining with low molecular weight keratins (CAM5.2; Fig. 4) and epithelial membrane antigen and were negative for high molecular weight keratins (CK1). Carcinoembryonic antigen cytoplasmic positivity was also present. None of the cells in the interstitium stained for the above cited antibodies, but were strongly positive for vimentin with occasional cells positive for desmin. Staining for factor VIII related antigen and UEA-1 was observed

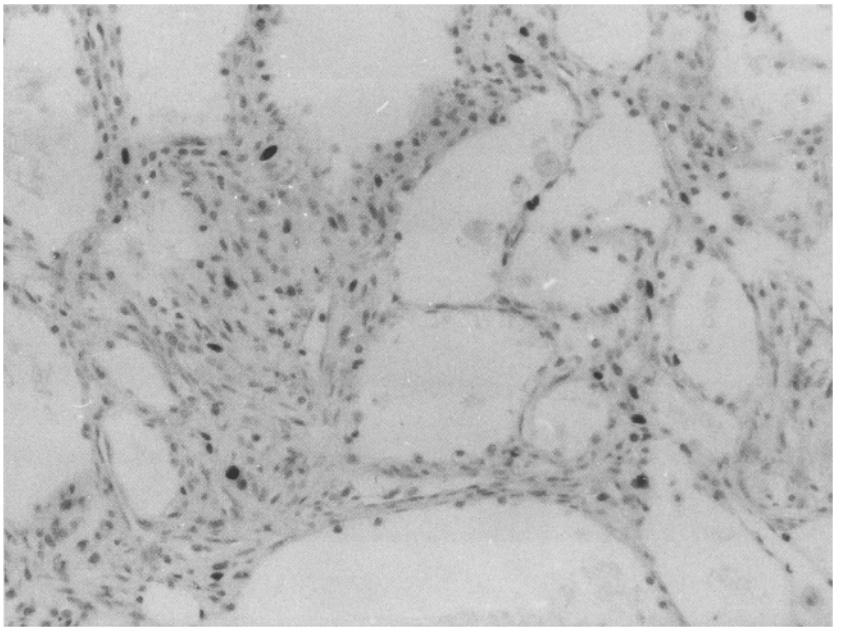


Fig. 5 Proliferating cell nuclear antigen stained mesenchymal cells and occasional epithelial lining cells nuclei. ×220

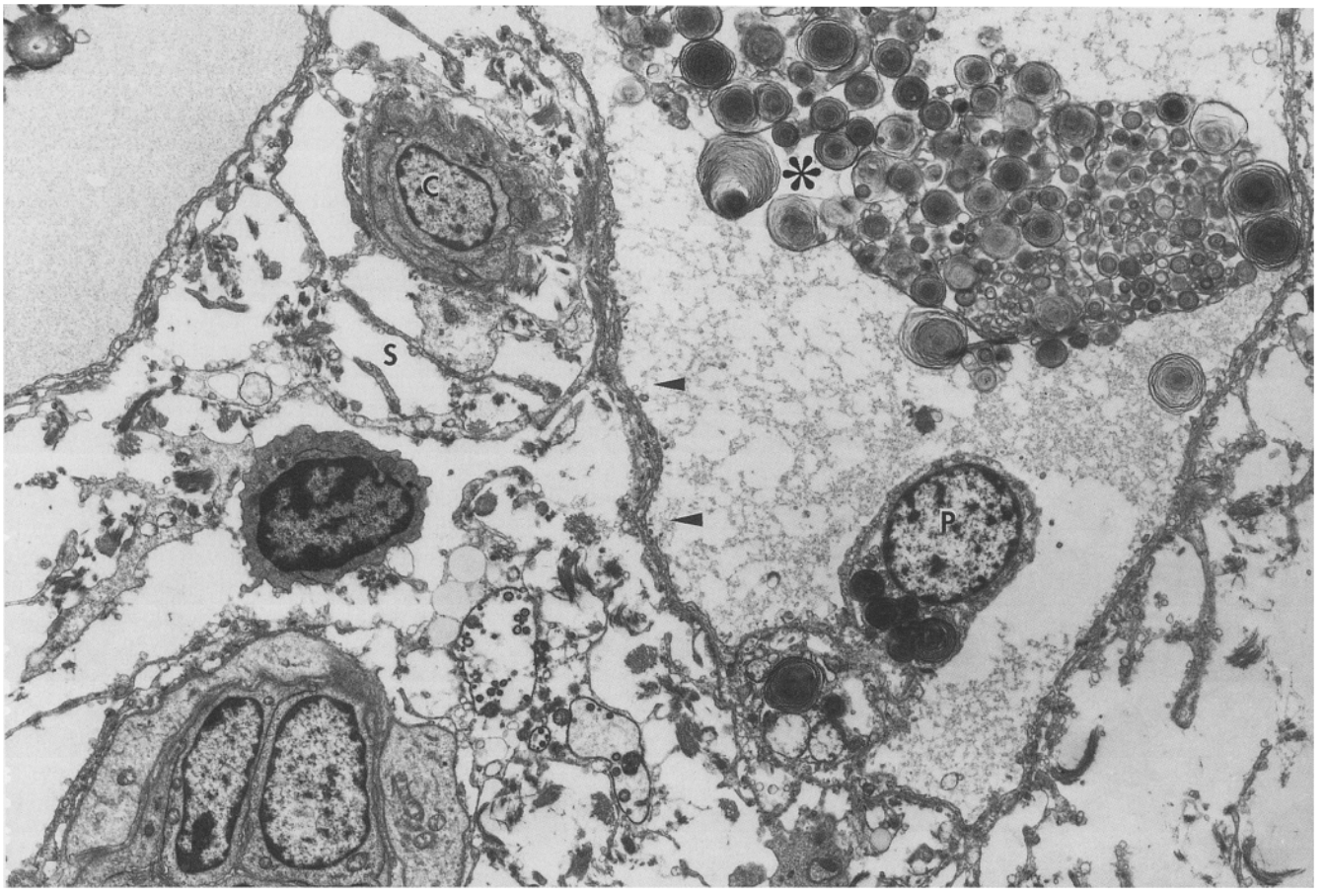


Fig. 6 Cystic space lined by flattened cells (*arrowheads*) and type II pneumocyte like cells (*P*) with intraluminal lamellar bodies (*), separated by septa (*S*) with capillaries (*C*). ×3,800

only in the endothelial cells. Alveolar macrophages were positive for KP1. Proliferating cell nuclear antigen positive nuclei were noted mainly in cells of the interstitial stroma although some epithelial type II pneumocyte lining cells were also stained (Fig. 5). No positivity for hormone receptors was documented on tumour cells.

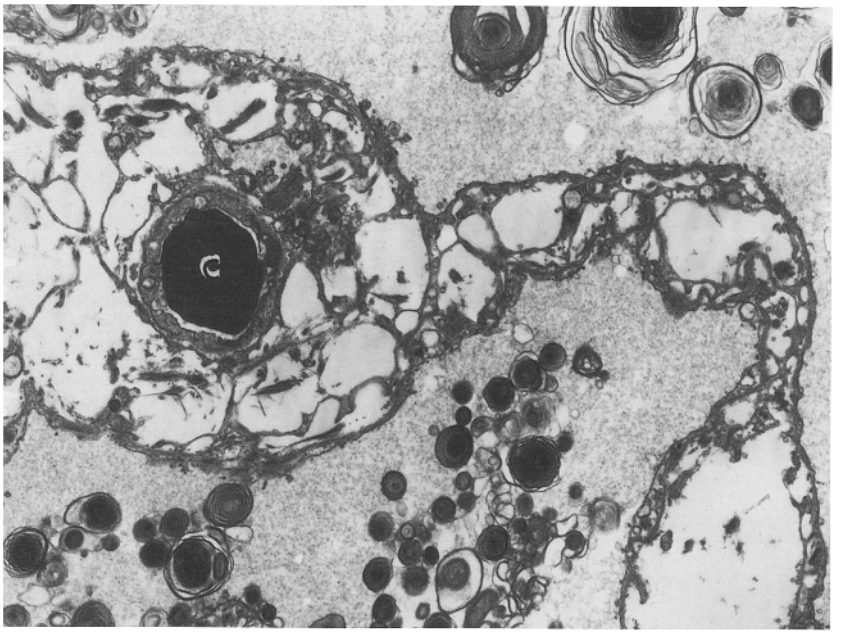


Fig. 7 Septa with central capillary (*C*) showing the edematous appearance due to irregular branching of thin processes from the interstitial cells. ×3,400

Electron microscopically the lining of the cysts was composed of two cell types (Fig. 6). The first consisted of very flattened cells, sometimes reduced to a very thin layer of cytoplasm. Nuclei had a smooth contour. Cytoplasmic organelles were scarce and limited to small mitochondria, some polyribosomes and electron lucent small vesicles. The second cell type consisted of large bulging cells with regular nuclei, peripherally marginated heterochromatin and small dense nucleoli. The cytoplasm was rich in organelles and contained conspicuous lamellar inclusions up to 4 μm in diameter, frequently accumulated at the apical pole. Short microvilli were seen in the apical area, as well as occasional digitiform expansions in the basal surface of the cells. Bulging and flattened cells showed tight junctions, and a continuous basal lamina, 17–23 nm in thickness.

In the lumen of the cystic spaces, besides low-electron-dense fibrillar and flocculent material, we found compact groups of concentric irregular lamellar structures up to 2.5 μm in diameter, similar to those found in the cytoplasm of the bulging cells of the cyst walls. In some places the inclusions were more regular with dense layers with periodicity of 18–22 nm.

The septa (Fig. 7) had variable widths, from as little as 1.5 μm to large multicellular areas, with many electron-lucent areas and contained scattered inflammatory cells, interstitial cells and capillaries. The interstitial cells had elongated smooth nuclei with dispersed heterochromatin and small dense nucleoli, and cytoplasm containing dilated rough endoplamic reticulum cisternae, free ribosomes, round mitochondria with clear matrix and lipid droplets. No basal lamina was observed. Thin intermixing irregular cell projections created the spongy mesh-network appearance of the septa. Cell processes from different cells contacted, with occasional differentiation of subplasmalemmal densities. In areas approaching the cyst walls these processes developed small "feet", that touched the distal face of the basal membrane of the lining cells. In the electron-lucent spongy cavities thin (0.15–0.20 μm) discrete and randomly orientated bundles of collagen fibrils were seen.

Capillaries present in the septa had, in most cases, thick endothelial cells, with virtual or narrow lumina. No Weibel-Palade bodies were observed. The basal lamina was frequently reduplicated. Pericytic cells, when present, showed cytoplasmic thin projections that intermixed with those of interstitial cells.

On flow cytometry the lesion showed a diploid population of tumour cells with a S-phase fraction of 4.2% (coefficient of variation: 3.71%).

Discussion

Alveolar adenoma is a distinctly uncommon lung lesion. Table 2 summarizes the clinical findings of the nine cases reported to date, including the present case.

The rarity of this lesion and the fact that most of the reported cases came from consultation files has not previously allowed a definitive study of this entity, particularly in terms of histogenesis and also in respect to its relationship with other pulmonary lesions.

We think that alveolar adenoma is undoubtedly a neoplastic lesion. It is a solitary mass of sharply demarcated alveolar structures, reproducing the normal alveolar architecture, growing in a centrifugal-like fashion with compression of the adjacent lung tissue in a way similar to that observed in thyroid and parathyroid adenomas. Its focal nature and clinical aspects exclude a reactive process. The demonstration of a translocation der (16) t (10; 16) (q23; 24) in 19% of the cells points to a clonal origin, as reported in another publication [21]. Furthermore,

Table 2 Clinical summary of the reported cases of alveolar adenoma (*M* male, *F* female, *LLL* left lower lobe, *RML* right medium lobe, *RUL* right upper lobe, *RLL* right lower lobe, *LUL* left upper lobe, *LIN* lingula, *ANED* alive with no evidence of disease, *LOST* lost to follow-up)

Case no.	Age	Sex	Presenting symptoms	Radiology	Location	Treatment	Size (cm)	Follow-up	Reference
1	45	F	Asymptomatic	Solitary peripheral nodule	LLL	Wedge biopsy	2.0	ANED, 13 months	[28]
2	74	F	Weakness, rash	Solitary peripheral nodule	RML	Lobectomy	2.5	ANED, 120 months	[28]
3	54	F	Asymptomatic	Solitary peripheral nodule	RUL	Lobectomy	2.5	ANED, 12 months	[28]
4	58	M	Asymptomatic acromegaly	Solitary peripheral nodule	LLL	Wedge biopsy	1.5	ANED, 56 months	[28]
5	64	M	Unknown	Solitary peripheral nodule	RUL	Lobectomy	1.2	LOST	[28]
6	59	F	Asymptomatic	Solitary peripheral nodule	RUL	Lobectomy	1.3	ANED, 13 months	[28]
7	60	F	Asymptomatic aortic stenosis	Solitary peripheral nodule	LIN	Wedge biopsy	unknown	ANED	[2]
8	67	F	Asymptomatic	Solitary peripheral nodule	RML	Enucleation	2.8	ANED, 3 months	[22]
9	60	F	Asymptomatic	Solitary peripheral nodule	LUL	Lobectomy	2.0	ANED, 24 months	[23]
10	55	F	Asymptomatic	Solitary peripheral nodule	RLL	Atypical segmentectomy	4.0	ANED, 32 months	Present case

none of the malformative or hamartomatous lesions described so far in the lung [6, 10] shares any clinical or morphological characteristic with alveolar adenoma other than of a pulmonary mass.

The biological behaviour of alveolar adenoma in the cases reported has been that of a benign lesion. No recurrences or metastases have been observed. In addition to the absence of histological characteristics of malignancy (such as infiltrative growth, atypia, mitotic activity and necrosis) the finding of a DNA diploid pattern and low S-phase value in our case, also favour this interpretation, in spite of the short follow-up period of the cases reported.

We do not share Dail and Hammar's [6] interpretation that the epithelial structures in alveolar adenoma are entrapped. Based on the pathological features of alveolar adenoma we think the epithelial lined spaces are an integral part of the tumour. Entrapped normal structures are usually observed only in the peripheral areas in a growing lesion. That is not the case in alveolar adenoma where these spaces are randomly present. Compression of the central cystic areas is not observed, as would be expected for entrapped alveolar spaces. In fact it is the peculiar multicystic pattern that helps us to recognize alveolar adenoma as a distinct entity. In addition, the characteristic "shelling out" demarcation from the adjacent lung tissue would be most unlikely for a neoplasm entrapping normal alveoli.

The cellular origin of this tumour remains to be elucidated. Although we were unable to find a definitive candidate, we share the view of Semeraro and Gibbs [22] that the cell of origin in alveolar adenoma is probably a primitive mesenchymal cell that has the capacity to differentiate toward a type II pneumocyte lineage. An alternative view would be to consider this lesion to be a benign mixed epithelial-mesenchyme tumour as proposed by some authors for sclerosing haemangioma of the lung [4, 18].

Many other pulmonary lesions are histogenetically related to alveolar epithelial cells, particularly the type II pneumocyte [6, 24]. Of the different entities presumed to be derived from these cells, bronchioloalveolar carcinoma is the clinically most relevant lesion [3, 5]. In contrast to bronchioloalveolar carcinoma, alveolar adenoma is well circumscribed, lacks the typical lepidic infiltrative growth pattern, and shows absence of the cytological characteristics of malignancy. These combined features also differentiate alveolar adenoma from other alveolar lesions assumed to be precursors of bronchioloalveolar carcinoma, such as atypical adenomatous hyperplasia of the lung [16, 17, 27], bronchioloalveolar adenomas [13] and others [26], all of them sharing with bronchioloalveolar carcinoma the infiltrative and lepidic growth pattern, cytological atypia, multifocality and the typical intranuclear inclusions observed by electron microscopy. Further, the cytogenetic findings in our case are distinct from the ones so far published in malignant lung neoplasms [14].

Another uncommon lesion, papillary adenoma of type II pneumocyte [19], shares a benign behaviour with alveolar adenoma. However, although it lacks nuclear atypia, the limited invasive potential, the prominent papillary architecture, the presence of cells with Clara cell differentiation, and intranuclear inclusions, are more akin to bronchioloalveolar carcinoma.

Sclerosing haemangioma of the lung [9] is the lesion that most closely recapitulates alveolar adenoma. This has led Semeraro and Gibbs [22] to hypothesize that alveolar adenoma represents a histological variant of sclerosing haemangioma. The similarity between both lesions is remarkable (Table 3). If one puts aside the more polymorphic histological appearance and the presence of

Table 3 Comparison between clinical and morphological findings of the reported cases of alveolar adenoma including the present one, and sclerosing haemangioma of the lung (*KER* keratin, *EMA* epithelial membrane antigen, *CEA* carcinoembrionic antigen, *FVIII* factor VIII related antigen, *SAP* surfactant apoprotein, *UEA* Ulex europaeus lectin, *VIM* vimentin, *ACT* actin, *DES* desmin, *ER* oestrogen receptor, *PR* progesterone receptor)

	Alveolar adenoma	Sclerosing haemangioma
Age range, years (median)	45-54 (59)	7-83 (45)
F/M ratio (F%)	4.0 80%	4.6 82%
Symptoms	Asymptomatic (80%)	Asymptomatic (50-90%)
Radiology	Solitary peripheral and subpleural mass	Solitary peripheral and subpleural mass
Size range, cm (median)	1.2-4.0 (2.0)	0.4-8.2 (2.8)
Gross findings	Well circumscribed, "shells-out" from the adjacent normal lung	Well circunscribed, "shells-out" from the adjacent normal lung
Architectural pattern	Multicystic sclerotic or mixed	Solid, papillary, cystic,
Lining cells	Type II pneumocyte differentiation	Type II pneumocyte differentiation
Interstitial cells	Similar to normal alveolar interstitial cells	Polygonal clear cells present in solid and papillary areas and inconspicuous in the sclerotic and cystic areas
Inflammatory cells	Present	Present
Electron microscopy	Type II pneumocyte differentiation of lining cells	Type II pneumocyte differentiation of the lining cells
Immunocytochemistry		
Lining cells:	KER(+), EMA(+), CEA(+) FVIII(−), UEA(−)	SAP(+), KER(+),EMA(+),CEA(+) FVIII(−), UEA(−),CD34(−)
Interstitial cells	VIM(+),ACT(±),DES(±)	VIM(+),ACT(±),HMB45(−)
Hormonal receptors	ER(−), PR(−)	ER(±), PR(±)[1,20]
DNA cytometry	Diploid	Diploid [12]
Karyotype	der(16)t(10;16)(q23,24)[21]	No studies reported
Follow-up	Benign tumour, all cases alive and well	Benign tumour, although disputable metastasis reported in two cases [6]

the epithelioid-looking septal cells in sclerosing haemangioma, no major differences emerge either in clinical or morphological grounds between both entities. Perhaps alveolar adenoma and sclerosing hemangioma represent different morphological aspects of the same process, although no case has been reported showing a combination of the two tumour patterns. Until further characterization of both entities is made the problem of their histogenesis will remain. We are unaware of any report on the cytogenetics on sclerosing haemangioma of the lung but it would be of interest to know if similar chromosomal alterations are present in the two lesions.

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References

1. Aihara T, Nakajima T (1993) Sclerosing hemangioma of the lung: pathological study and enzyme immunoassay for estrogen and progesterone receptors. Acta Pathol Jpn 43:507–515
2. Al-Hilli F (1987) Lymphangioma (or alveolar adenoma?) of the lung. Histopathology 11:979–980
3. Axiotis CA, Jennins TA (1988) Observations on bronchioloalveolar carcinoma with special emphasis on localized lesions. A clinicopathological, ultrastructural, and immunohistochemical study of 11 cases. Am J Surg Pathol 12:918–931
4. Chan KW, Gibbs AR, Lio WS, Newman GR (1982) Benign sclerosing pneumocytoma of the lung (sclerosing hemangioma). Thorax 37:404–412
5. Clayton F (1988) The spectrum and significance of bronchioloalveolar carcinomas. Pathol Annu 23:361–394
6. Dail DH, Hammar SP (1994) Pulmonary pathology, 2nd edn. Springer, New York Berlin Heidelberg
7. Dean P, Jett J (1974) Mathematical analysis of DNA distribution derived from flow micro-fluorometry. J Cell Biol 60:523–527
8. Hsu SM, Raine L, Fanger H (1981) The use of avidin-biotin-peroxidase complex (ABC) in immunoperoxidase techniques. A comparison between ABC and unlabeled antibody PAP procedures. J Histochem Cytochem 29:577–580
9. Katzenstein AL, Gmelich JT, Carrington CB (1980) Sclerosing hemangioma of the lung. A clinicopathologic study of 51 cases. Am J Surg Pathol 4:343–356
10. Mackay B, Lukeman JM, Ordónez NG (1991) Tumors of the lung. In: Bennington JL (ed) Major problems in pathology, vol 24. Saunders, Philadelphia
11. Marquardt DW (1963) An algorithm for least-square estimation of nonlinear parameters. Soc Ind Appl Math 11:431–441
12. Matsuki Y, Ihara N, Satoh Y, Kokai Y, Takanashi R (1993) Flow cytometric analysis of the DNA content of sclerosing hemangioma of the lung. Rinsho Byori 41:227–229
13. Miller RR (1990) Bronchioloalveolar cell adenomas. Am J Surg Pathol 14:904–912

14. Mitelman F, Johansson B, Mertens F (1994) Catalog of chromosome aberrations in cancer, 5th edn. Wiley-Liss, New York
15. Mollenhauer HH (1964) Plastic embedding mixtures for use in electron microscopy. Stain Technol 39:107–112
16. Mori M, Chiba R, Takahashi T (1993) Atypical adenomatous hyperplasia of the lung and its differentiation from adenocarcinoma. Characterization of atypical cells by morphometry and multivariate cluster analysis. Cancer 72:2331–2340
17. Nakamishi K (1990) Alveolar epithelial hyperplasia and adenocarcinoma of the lung. Arch Pathol Lab Med 114:363–368
18. Ng WL, Ma L (1983) Is sclerosing hemangioma of lung an alveolar mixed tumor? Pathology 15:205–211
19. Noguchi M, Kodama T, Shimosato Y, Koide T, Naruke T, Singh G, et al (1986) Papillary adenoma of type 2 pneumocytes. Am J Surg Pathol 10:134–139
20. Ohori NP, Yousem SA, Sonmez-Alpan E, Colby TV (1991) Estrogen and progesterone receptors in lymphangioleiomyomatosis, epithelioid hemangioendothelioma, and sclerosing hemangioma of the lung. Am J Clin Pathol 96:529–535
21. Roque L, Oliveira P, Martins C, Carvalho C, Serpa A, Soares J (1996) A non-balanced translocation (10;16) demonstrated by FISH analysis in a case of alveolar adenoma of the lung. Cancer Genet Cytogenet 89:34–37
22. Semerabo D, Gibbs AR (1989) Pulmonary adenoma: a variant of sclerosing haemangioma of lung? J Clin Pathol 42:1222–1223
23. Siebenmann RE, Odermatt B, Hegglin J, Binswanger RO (1990) Das Alveolarzelladenom. Ein neu erkannter gutartiger Lungentumor. Pathologe 11:48–54
24. Singh G, Katyal S, Ordonez NG, Dail DH, Negishi Y, Weedn VW, Marcus PB, et al (1984) Type II pneumocytes in pulmonary tumors. Implications for histogenesis. Arch Pathol Lab Med 108:44–48
25. Thornthwaite JT, Sugarbaker EV, Temple WJ (1980) Preparation of tissues for DNA flow cytometric analysis. Cytometry 1:229–237
26. Travis WD, Linnoila RI, Horowitz M, Becker RL Jr, Pass H, Ozols R, et al (1988) Pulmonary nodules resembling bronchioloalveolar carcinoma in adolescent cancer patients. Mod Pathol 1:372–377
27. Weng S, Tsuchiya E, Satoh Y, Kitagawa T, Nakagawa K, Sugano H (1990) Multiple atypical adenomatous hyperplasia of type II pneumocytes and bronchiolo-alveolar carcinoma. Histopathology 16:101–103
28. Yousem SA, Hochholzer L (1986) Alveolar adenoma. Hum Pathol 17:1066–1071