

## CASE REPORT

# Alveolar adenoma of the lung: a clinicopathological description of a case of this very unusual tumour

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*J Clin Pathol* 2005;58:1211–1214. doi: 10.1136/jcp.2004.020800

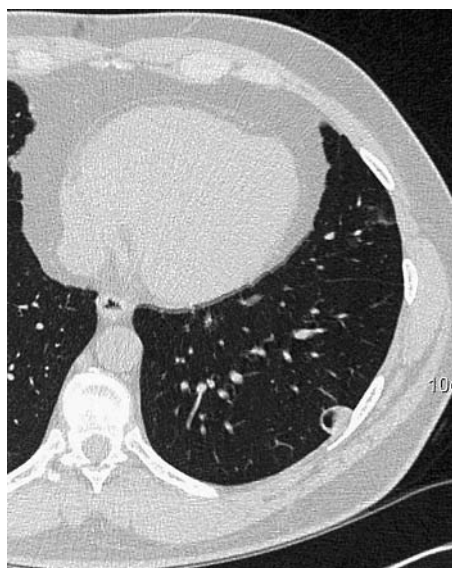
Alveolar adenomas are extremely rare, and are probably benign lung tumours of unknown histogenesis. This report describes a case of alveolar adenoma in a 43 year old white man, who presented with pleuritic chest pain. A chest x ray and computerised tomography scan demonstrated a solitary left lower lobe lung nodule. Although a positron emission tomography scan seemed to document the benign nature of the lesion, a thorascopic wedge resection was performed to alleviate the symptoms and verify the diagnosis. Histologically, the lesion was well demarcated, dominated by large and small cysts with no normal lung parenchyma. The interstitial cellular component consisted of both epithelioid and vaguely spindle shaped cells. The cystic cell linings were mostly indistinct, although areas of cuboidal epithelial cells were seen. Multiple histochemical and immunohistochemical tests were performed. There were no histological signs of malignancy and the patient is doing well one and a half years postoperatively.

Alveolar adenoma is a pulmonary tumour of uncertain histogenesis. It was first described by Yousem and Hochholzer in 1986 and is sometimes referred to as “Yousem’s tumour”.<sup>1</sup> The only cumulative study is an analysis of 17 cases undertaken by Burke *et al* in 1999.<sup>2</sup> Full knowledge and understanding of these tumours is hampered by the fact that very few cases have been reported in the literature. Most authors agree that histologically these tumours are benign and recurrence has never been reported after resection.<sup>1–3</sup> Some authors have suggested that alveolar adenomas of the lung may represent the benign counterpart of bronchioloalveolar carcinoma.<sup>4</sup> Our case study adds to the current literature a patient with a full clinical evaluation—including for the first time to our knowledge a preoperative positron emission tomography (PET) scan—the description of gross, histological, histochemical, and immunohistochemical findings, and a one and a half year follow up after resection.

“Most authors agree that histologically these tumours are benign and recurrence has never been reported after resection”

### CASE REPORT

A 43 year old otherwise healthy white man presented with complaints of left sided pleuritic chest pain of a few weeks duration. The patient was a non-smoker, but had possibly been exposed to hazardous chemicals during military service. A physical examination was unremarkable. A chest roentgenogram revealed a left lower lobe nodule approximately 1–2 cm in diameter. A computerised tomography (CT) scan



**Figure 1** Computerised tomography scan of the chest showing a small posterolateral lung lesion in the lower lobe of the left lung.

verified the finding of a well circumscribed pleural based left lower lobe nodule, with no other abnormal findings (fig 1). The patient underwent a fluorine-18-fluorodeoxyglucose PET scan, which showed no signs of malignant or infectious processes in relation to the nodule (fig 2). Because of the patient’s continuous symptoms and concern for possible malignancy, the nodule was surgically removed. The patient underwent video assisted thorascopic surgery with a wedge resection of the nodule in the left lower lobe, lymph node sampling, and a lung biopsy. His recovery was uneventful, and 18 months later there is no sign of recurrence.

### PATHOLOGICAL FINDINGS

The lung specimen showed a pleural based nodule measuring 1.1 × 0.7 × 0.6 cm in diameter. The overlying visceral pleura had whitish/tan discolouration, but otherwise showed minimal reaction. On fresh cut, the tumour was macroscopically found to be “encapsulated” with a section surface that was soft, almost gelatinous, tan, and glistening. The tumour almost shelled out from the surrounding lung parenchyma. On closer examination, the cut surface was seen to be multicystic with small focal areas of haemorrhage. Cultures were obtained and were negative for fungi and tuberculosis.

Histologically, the periphery of the tumour was reasonably well circumscribed. The most prominent features were multiple cystic spaces that appeared to become larger towards

**Abbreviations:** CK, cytokeratin; CT, computerised tomography; PET, positron emission tomography



**Figure 2** Coronal section from the fluorine-18-fluorodeoxyglucose positron emission tomography scan through the area of the lung containing the tumour shows no isotope uptake.

the centre of the lesion (fig 3). Most of the cysts contained proteinous granular eosinophilic material, generally acellular. The cystic spaces were separated by delicate myxoid stroma and the cysts had an indistinct lining, but occasionally flattened cuboidal epithelial cells were present. The cells between the cysts were both epithelioid and vaguely spindle shaped, forming short fascicles. Many inflammatory cells were present (mainly plasma cells) and lymphoid aggregates were readily identifiable (fig 4).

On high magnification, a consistently high chromatin density was noted in the stromal cells and clear or vacuolated cytoplasm of the epithelial cells lining the cystic spaces. The spindle shaped cells of the stroma had a pale, bubbly, vacuolation reminiscent of the smooth muscle cells of a lymphangioliomyomatosis. Mitoses were very rarely seen.

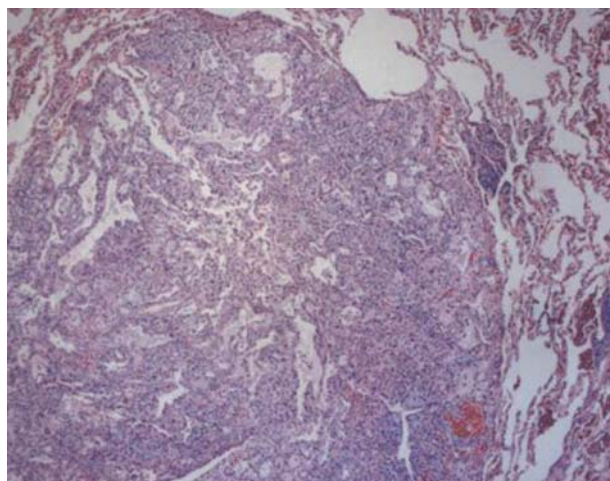
### IMMUNOHISTOCHEMICAL AND HISTOCHEMICAL FINDINGS

The acellular material within the cystic spaces was noted to be periodic acid Schiff positive. The mucicarmine stain was negative. The cells lining the cysts were found to be positive for cytokeratin (CK) AE1/AE3, CK7, CK20, and thyroid transcription factor 1 (fig 5). The stromal cells were negative for these markers.

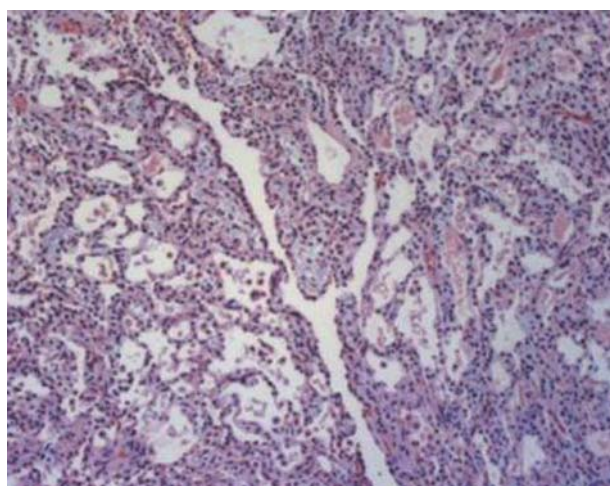
### DISCUSSION

Alveolar adenomas are extremely rare pulmonary neoplasms. The exact number of reported cases is difficult to ascertain because these tumours are often confused with other rare lung tumours. Using strict criteria of histology, histochemistry, and immunohistochemical studies, as defined by Burke *et al* in 1999, less than 25 cases of true alveolar adenoma have been reported.<sup>1-14</sup>

These tumours have been reported in all major geographical areas of the world and have been found in all races.<sup>1-14</sup> Most patients are middle aged to elderly, with a slight female predominance. These tumours are most often an incidental finding on a radiological examination, and when symptoms have been reported, they are either unrelated to the lesion or



**Figure 3** The tumour is well circumscribed and multicystic (haematoxylin and eosin stain; original magnification,  $\times 40$ ).

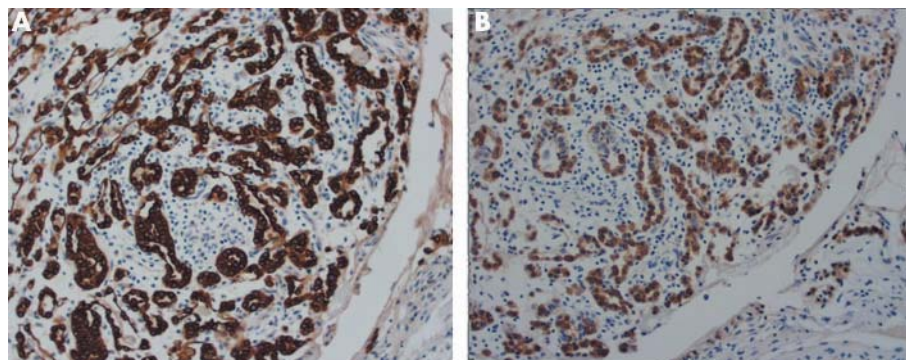


**Figure 4** The variably sized cystic spaces are lined by flattened cells and contain eosinophilic granular material and some macrophages. The interstitium contains a myxoid matrix (haematoxylin and eosin stain; original magnification,  $\times 100$ ).

pleuritic in nature. A few studies have specifically looked at the findings of chest CT and magnetic resonance imaging scans, and have found that these lesions have characteristics consistent with benign nodules, but are otherwise non-specific.<sup>6,7</sup> This is the first time a PET scan has been performed on a patient with alveolar adenoma and it was consistent with a benign process. Transbronchial biopsies, bronchial washings, and fine needle transcutaneous CT guided biopsies have been non-diagnostic in these cases.<sup>1-14</sup> In most instances, these tumours have been surgically excised using a simple wedge resection of the lung. Frozen sections, when reported, have either been inconclusive or suspicious of alveolar adenoma, without being diagnostic. The growth potential of alveolar adenomas is unknown. Most have been stable over a short period of time, but at least one case showed 20% growth during an eight month follow up.<sup>3</sup> In another, a "progressive enlargement" was noted over a period of one year.<sup>1</sup>

Macroscopic findings of previously reported cases have been consistent and similar to our own.<sup>1-14</sup>

In contrast, the histopathology is quite variable with the exception of being well demarcated and multicystic.



**Figure 5** Immunohistochemical staining showing positivity for (A) cytokeratin 7 (CK7) and (B) CK20 in the epithelial cells lining the cysts.

Microscopically, the cystic spaces dominate the picture, with the larger cysts usually concentrated in the middle of the tumour. The alveolar lumina usually contain few histiocytes, erythrocytes, and periodic acid Schiff positive granular material, as was seen in our case. The cysts are lined with a single layer of epithelial cells, with most of them being cuboidal or “hob nailed” in appearance. The cytoplasm is described as eosinophilic, finely vacuolated, or foamy. From the microscopic appearance and immunohistochemical studies, most authors agree that the epithelial component of this tumour is derived from type 2 pneumocytes.<sup>1–14</sup>

The interstitial component varies from sparse to exuberant. It usually contains collagen fibrils and prominent spindle or oval shaped cells. Ultrastructurally, these cells resemble fibroblasts or modified smooth muscle cells. Most reported cases have shown mild to moderate numbers of interstitial lymphocytes, plasma cells, and eosinophils, occasionally in clusters. A well developed, fine capillary network traverses the interstitial mesenchyme, but no large blood cells or bronchioles are identified in these lesions.<sup>1–13</sup>

“From the microscopic appearance and immunohistochemical studies, most authors agree that the epithelial component of this tumour is derived from type 2 pneumocytes”

Immunohistochemical studies have consistently shown that the epithelial cells are positive for thyroid transcription factor 1 and almost all are CK positive. Although most reports do not specify the subgroup of cytokeratins tested, antibodies against AE1/AE3, CK1, CK7, CK18, and CK19 have been found to be positive in these tumours.<sup>2–4</sup> To the best of our knowledge, this is the first time that a CK20 positive alveolar adenoma has been reported. Köppl *et al* specifically tested for apoprotein B and C of human surfactant and found them to be positive, again confirming the theory that the epithelial cells are derived from type 2 pneumocytes.<sup>5</sup> Immunohistochemical studies from several case reports have also verified that the interstitial cellular component of these tumours is made up of fibroblasts or fibroblast-like cells.<sup>2</sup>

Although most authors agree that alveolar adenomas are neoplastic in nature, some debate exists as to whether the epithelial or interstitial component of these tumours proliferates. In a recent study, Cavazza *et al* used microsatellite instability analysis to show that the stromal and epithelial components are genetically unrelated.<sup>14</sup> This again confirms the apparent dual nature of these lesions. Morphologically, these tumours are very bland with rare mitoses. However, too few cases have been reported to verify their benign nature. Although rapid growth has occasionally been reported, no recurrence after resections has been seen.<sup>1–14</sup> Roque *et al*

### Take home messages

- We report a very rare case of alveolar adenoma of the lung, which was immunohistochemically distinct from previously reported cases in that it was positive for cytokeratin 20
- This is the first time that an alveolar adenoma has been evaluated using positron emission tomography

reported a non-balanced translocation demonstrated by fluorescence in situ hybridisation analysis on a single case of alveolar adenoma. This chromosomal abnormality is of unknown importance.<sup>11</sup>

In conclusion, we report a rare case of alveolar adenoma of the lung. Immunohistochemically, it differed from previous reports because it was positive for CK20. Clinically, this is the first time that an alveolar adenoma has been evaluated using a PET scan.

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Accepted for publication 11 March 2005

### REFERENCES

- 1 Yousem SA, Hochholzer L. Alveolar adenoma. *Hum Pathol* 1986;**17**:1066–71.
- 2 Burke LM, Rush WJ, Khoor A, *et al*. Alveolar adenoma: a histochemical, immunohistochemical, and ultrastructural analysis of 17 cases. *Hum Pathol* 1999;**30**:158–67.
- 3 Cakan A, Samacilar O, Nart D, *et al*. Alveolar adenoma: an unusual lung tumour. *Interactive Cardiovascular and Thoracic Surgery* 2003;**2**:345–7.
- 4 Böhm J, Fellbaum C, Bautz W, *et al*. Pulmonary nodule by an alveolar adenoma of the lung. *Virchows Arch* 1997;**430**:181–4.
- 5 Köppl H, Freudenberg N, Berwanger I, *et al*. Alveoläres Adenom der Lunge. *Pathologe* 1996;**17**:150–3.
- 6 Fujimoto K, Muller NL, Sadohara J, *et al*. Alveolar adenoma of the lung: computed tomography and magnetic resonance imaging findings. *J Thorac Imaging* 2002;**17**:163–6.
- 7 Nussle K, Kolokythas O, Karhausen J, *et al*. Alveolar cell adenoma of the lung. *Röntgenpraxis* 1997;**50**:29–30.
- 8 Oliveira P, Moura Nunes JF, Clode AL, *et al*. Alveolar adenoma of the lung: further characterization of this uncommon tumour. *Virchows Arch* 1996;**429**:101–8.

- 9 **Haskovcova I**, Povysil C, Paiko P. Alveolar adenoma of the lung (case report). *Cesk Patol* 1997;**33**:49–52.
- 10 **Siebenmann RE**, Odermatt B, Hegglin J, *et al*. Alveolar cell adenoma. A newly defined benign lung tumor. *Pathologe* 1990;**11**:48–54.
- 11 **Roque L**, Oliveira P, Martins C, *et al*. A nonbalanced translocation (10;16) demonstrated by FISH analysis in a case of alveolar adenoma of the lung. *Cancer Genet Cytogenet* 1996;**89**:34–7.
- 12 **Papla B**, Malinowski E. Alveolar adenoma of the lung—a report of two cases. *Pol J Pathol* 2003;**54**:147–52.
- 13 **Menet E**, Etchandy-Laclau K, Corbi P, *et al*. Alveolar adenoma: a rare peripheral pulmonary tumor. *Ann Pathol* 1999;**19**:325–8.
- 14 **Cavazza A**, Paci M, De Marco L, *et al*. Alveolar adenoma of the lung: a clinicopathologic, immunohistochemical and molecular study of an unusual case. *Int J Surg Pathol* 2004;**12**:155–9.

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