Pleomorphic adenoma of the bronchus

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Abstract
An example of pleomorphic adenoma of the bronchus is described in a 27 year old male student who was referred for evaluation of a coin lesion identified incidentally on chest x ray. The tumour exhibited the classic histological, immunohistochemical and ultrastructural features of this rare entity but, in addition, contained mature and immature adipose tissue in the stroma and showed transition, in its superficial portion, between ostensibly normal bronchial mucus glands and tumour tubules. Neither of these features has been commented upon previously.

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Keywords: bronchus, pleomorphic adenoma, adipose tissue, mucus glands.

Methods
Tissue blocks were fixed in 10% buffered formalin, routinely processed and embedded in paraffin wax. Sections were stained with haematoxylin and eosin, alcin blue (pH 2.5) and periodic acid Schiff (PAS) after diastase pretreatment. Sequential sections were stained for keratin (AE1/AE3; ICN, Costa Mesa, California, USA), S100 protein and epithelial membrane antigen (EMA) (Dako, Glostrup, Denmark) and smooth muscle actin (Enzo Diagnostics, New York, USA). Further tissue blocks were fixed in 3% glutaraldehyde and examined by electron microscopy.

MICROSCOPY
On its bronchial aspect, the lesion was covered by normal respiratory epithelium. Within the lung, however, it was separated from normal parenchyma by a dense fibrous capsule of variable thickness. Peribronchial adipose tissue was present at the resection margin of the lobectomy specimen but not in the immediate vicinity of the tumour. The mass was roughly spherical and, at its centre, had a stellate, peripheral area, radiating from which were irregular, solid islands of polygonal epithelial cells with moderate amounts of eosinophilic cytoplasm, and scattered cells, either singly or in groups, in which the cytoplasm had a more hyaline, glassy appearance. The stroma between the cellular areas contained spindle shaped and stellate cells set in a variably myxoid, hyaline or focally chondroid matrix. Zones of adipose tissue were easily identifiable in the stroma (figure, panel A), some of which contained lipoblasts (figure, panel B). In both the cellular and myxoid areas there were well formed tubular structures, many of which were lined by distinct epithelial and myoepithelial layers. Squamous metaplasia was identified in

the mucus cells of the superficial zone of the tumour.

The cells lining the tubules and most of the solid epithelial islands stained positively for keratin, whereas only the luminal aspect of these cells stained with antibody to EMA. S100 protein and smooth muscle actin were demonstrable in myoepithelial cells around tubules and also in single cells, or groups of cells, in solid epithelial zones, corresponding to the cells with hyaline cytoplasm noted on staining with haematoxylin and eosin. The peritubular distribution of myoepithelial cells was very variable, ranging from scattered peripheral cells in those glands with mucin secreting epithelium to continuous runs of such cells enclosing classic tumour tubules. Other tubules showed completely haphazard distribution of myoepithelial cells, in solid clumps or even lying inside the epithelial cell layer. Adipocytes stained strongly for S100 protein but not for actin or EMA.

ELECTRON MICROSCOPY

Epithelial cells lining tubules varied from cuboidal to columnar, the former often containing little mucin and the latter numerous mucin vacuoles. Both of these cell types demonstrated poorly formed, stubby microvilli on the luminal surface. Tight junctions were evident at the luminal aspects of epithelial cells and, elsewhere, desmosomes were plentiful between epithelial and myoepithelial cells. These latter cells, with cytoplasmic aggregates of thin filaments and overlapping dense bodies, were not only related to tubular structures but were also present isolated in the myxoid stroma. Flattened epithelial cells containing bundles of tonofilaments were readily identified. Adipocytes were ultrastructurally unremarkable and, in particular, myofilaments were not identified in the cytoplasm, nor were such filaments observed in cells which had the morphology of lipoblasts (figure, panel B).

Discussion

Pleomorphic adenoma of the bronchus is extremely uncommon, with approximately 20 verifiable cases documented to date. At 27 years of age, the case presented here is the youngest on record, previous cases falling within the age range of 35–74 years. About one third of all cases come to light incidentally, as in the case reported here.

The histological and ultrastructural features of pleomorphic adenoma of the bronchus, as seen in this case, are identical with those of lesions arising in salivary gland. Features, however, which have not been annotated previously, include the presence of adipose tissue within the stroma and the apparent continuity of the tumour tubules with glandular structures which resemble normal mucus glands, towards the bronchial luminal surface. This latter phenomenon is consonant with the hypothesis that pleomorphic adenoma arises from cells of the intercalated duct but we have been unable to find reference to this spatial juxtaposition in other reports of this condition.
Adipose tissue in salivary pleomorphic adenomas is well recognised although its derivation remains unclear. There are three possible explanations for its presence: first, that it is the result of the incorporation of pre-existing stromal fat of the organ in which the tumour has arisen; second, that it represents adipose differentiation of mesenchymal cells in a true biphasic tumour; or, third, that it is caused by adipose metaplasia of primordial myoepithelial cells. While the first possibility might be invoked for pleomorphic adenomas arising in fatty organs such as breast, salivary gland or skin, it seems less likely in the context of the lung where fat is, at best, sparse and which, in this case, was not evident immediately adjacent to the tumour. If one believes, as the weight of evidence tends to suggest, that pleomorphic adenoma “is not a true mixed tumour but is of solely epithelial origin, and that the connective tissue appearances are secondary” then the second postulate seems unsafe. If, as we believe, the third suggestion is true (and the presence of cells (figure, panel B) with the morphological characteristics of lipoblasts argues that this might be so, absence of myofilaments on electron microscopy notwithstanding) then adipose metaplasia might be added to the list of morphologies that modified myoepithelial cells can adopt.

Because so few cases of pleomorphic adenoma of the bronchus have been documented it is difficult to assess their prognosis. Undoubted malignant variants have been described which, in addition to the generally accepted histological features of malignancy, such as necrosis and high mitotic rate, tend to be larger than their benign counterparts.

In the salivary gland pleomorphic adenomas are notorious for their tendency to recur, principally because of their gross morphology and the difficulty in achieving adequate excision in surgically complicated terrain. Genuine recurrence of a benign pleomorphic adenoma of the bronchus, however, has been recorded only once and in that instance it is unclear if adequate resection of the primary tumour was achieved. The “recurrence” documented by Sakamoto et al. is difficult to accept as such, principally because it was found in the periphery of the opposite lung, nine years after initial lobectomy. The possibility that this predominantly chondroid tumour might have represented asynchronous metastases from an undetected low grade mesenchymal tumour elsewhere was not entertained.

It would appear logical, therefore, that benign pleomorphic adenomas of the bronchus should not recur if, as in this case, an adequate resection margin can be obtained.

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Detection by PCR of *Toxoplasma gondii* in blood in the diagnosis of cerebral toxoplasmosis in patients with AIDS

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Abstract

The polymerase chain reaction (PCR) for amplification of *Toxoplasma gondii* DNA was performed prospectively in the blood of 19 patients with AIDS and cerebral toxoplasmosis. The B1 gene and TGR1E sequence were used as targets and results were confirmed by hybridisation. Controls consisted of 24 HIV infected patients with tissue culture proven *T. gondii* para-sitaemia and 57 HIV infected patients without toxoplasmosis. PCR was positive with both targets in 20 of 24 samples (84%) from patients with parasitaemia. Three of 57 samples (5%) from patients without toxoplasmosis were PCR positive with either target, but none was positive with both targets. Only three of the 19 patients (16%) with cerebral toxoplasmosis had a positive PCR with both targets before the