Benign clear cell tumour of the lung – intermediate filament typing as a tool in differential diagnosis

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ABSTRACT: A case of a benign clear cell ("sugar") tumour of the lung in a 61-year-old woman is presented. Characteristic routine histological features are provided and problems concerning differential diagnosis are discussed. Immunohistochemical stainings for the intracytoplasmatic intermediate filament proteins keratin and vimentin in our patient suggest a mesenchymal origin for this rare pulmonary neoplasm, and provide useful diagnostic aid in inconclusive cases.

Eur Respir J. 1988, 1, 288–290.

In 1963, Liebow and Castleman first reported a peculiar solitary benign pulmonary tumour of unknown histogenesis, characterized by large glycogen-rich clear cells, closely resembling metastatic renal cell carcinoma [1]. In 1971, they published a more detailed report with clinical, radiological and histological features of this unusual lesion from twelve collected cases [2]. These primary pulmonary tumours, descriptively named benign 'clear cell' ('sugar') tumours of the lung, have been listed twenty times in world literature. The cells of origin of this tumour remain debatable. The following case report provides immunohistochemical data suggestive of mesenchymal histogenesis.

Case report

An asymptomatic 61-year-old woman was found to have a solitary peripheral nodule in the left lung on routine preoperative chest roentgenogram before cataract extraction. The coin lesion was well circumscribed, homogeneous and smoothly contoured and projected anteriorly in the left hilar region. A chest roentgenogram taken eight years before admission showed no visual lesion. Physical examination was within normal limits, except for a palpable mass in the left breast, showing benign fibroadenoma on excision biopsy.

Laboratory studies revealed no abnormalities. Further screening, including an intravenous pyelogram, gave no evidence of a primary tumour other than in the lung. The tumour could not be visualized bronchoscopically; brushings and washings were negative. On a selective bronchogram the lesion was located between the superior lingular and anterior segment of the left upper lobe, suggesting no relationship with the bronchial tree. A left thoracotomy was performed, revealing a well-demarcated soft tumour at the mediastinal surface of the upper lobe, directly underneath the pleura, but without involvement of this structure. Again, there was no evidence of involvement of a bronchus or major vessel. The mass could be 'shelled-out' easily, but frozen section was not conclusive about benignancy, so lobectomy was performed. The patient recovered uneventfully from the surgery.

Description of the tumour

Grossly, the tumour was ovoid, well-demarcated, measuring 3 cm in diameter, and grey-brown in colour. On cross-section the nodule appeared oedematous, pale and somewhat friable. Haemorrhage or necrosis were absent. Microscopically, there was a uniform pattern throughout the lesion, consisting of large round or polygonal cells with clear cytoplasm, supported by very little connective tissue, and surrounded by numerous delicate capillaries and some thin sinusoidal vessels, providing a rich blood supply. No fibrous capsule was seen between the tumour and surrounding lung tissue. Mitotic figures were virtually absent. Nuclei were quite polymorph but with prominent nuclear membranes and small nucleoli. The cytoplasm of the clear cells contained an abundant amount of periodic acid-Schiff (PAS-positive) diastase sensitive material, interpreted as glycogen (fig. 1). Reticulin stain revealed tiny fibres embracing individual cells only. Immunohistochemi-
Is renal cell (Grawitz) tumor a carcinosarcoma?

Renal cell carcinomas demonstrate differentiation from benign clear cell tumours. The addition, renal cell carcinomas do not contain the immense quantities of glycogen size even after simple enucleation [2].

'Grawitz' hypernephroid, or clear cell tumour of the kidney, are thick-walled arteriolar blood supply, large masses of cells by connective tissue (rather than individual cells). The clear cell carcinoma of the lung is a rare bronchogenic tumour with histological and biologic characteristics of malignancy: the cells are reactive for both cytokeratin and vimentin [3]. Membrane-bound glycogen particles seem to be one of the clinical survey with staining of intermediate filament proteins showed that the stain for keratin was negative in tumour cells, the only positive cells being the epithelial elements covering the alveolar spaces. Staining for vimentin was clearly positive in tumour cells.

Discussion

Benign peripheral lesions without relationship to larger vessels or bronchi, i.e. benign clear cell tumours of the lung, usually present silently as solitary coin lesions on routine chest roentenograms. Most patients reported in the literature were in the fifth to seventh decades of life. The radiologically homogeneous, smooth contoured, rounded or spherical lesions vary between 1 and 4 cm in diameter [2]. They usually grow very slowly, and they do not recur or metastasize even after simple enucleation [2].

Features which help to distinguish malignant clear cell tumours in the lung from benign 'sugar' tumours are thick-walled arteriolar blood supply, haemorrhage, necrosis, presence of fat and haemosiderine in tumour cells, multitude of mitoses, and bundling of large masses of cells by connective tissue (rather than scarce reticulum-fibres extending among the individual cells). The clear cell carcinoma of the lung is a rare bronchogenic tumour with histological and biological characteristics of malignancy: the cells are filled with PAS-positive material, which fails to stain for glycogen, making possible an unequivocal differentiation from benign clear cell tumours. The 'Grawitz' hypernephroid, or clear cell tumour of the kidney metastatic in the lung, stains with PAS, but does not contain the immense quantities of glycogen typical of the benign clear cell tumour of the lung. In addition, renal cell carcinomas demonstrate immunoreactivity for both cytokeratin and vimentin [3]. Membrane-bound glycogen particles seem to be one of the diagnostic ultrastructural features, distinguishing benign clear cell tumour from any other known tumour. Thus, electron microscopic study may be necessary for its definitive diagnosis, although possibly only in the unusual case with necrosis and haemorrhage, as reported by Sale and Kulander [4].

The histogenesis of the benign clear cell tumour of the lung is not yet fully clarified. In 1971, Becker and Sower reported ultrastructural characteristics, and noted membrane-bound, rossette, and monogranular forms of glycogen within the cells [5]. Electron microscopic observation of dense core vesicles of the neurosecretory type in 2 to 5% of cells made them conclude that these tumours were most likely derived from Kulchitsky cells, and thus histogenetically related to pulmonary carcinoids. Hoch et al. [6] stressed that membrane-bound electron-dense granules may not be 'neurosecretory' but glycogen-bound vesicles or lysosomes, and they interpreted the ultrastructural evidence as being suggestive of smooth muscle or pericytic origin. They also found the presence of intracytoplasmatic filaments tended to favour smooth muscle. Fukuda et al. recently suggested again that the benign clear cell tumour of the lung may be of vascular smooth muscle cell or pericytic origin, but electron microscopic observation revealed no intracytoplasmatic filaments, possibly due to the abundant glycogen obscuring their presence [7].

Immunohistochemical observations in our patient suggest a new tool in its differential diagnosis, whilst also giving information related to its histogenesis. The expression of intracytoplasmatic intermediate filament proteins is specific for a certain tissue type [8], for instance the presence of cytokeratins in a tumour is a strong indication of its epithelial origin. The combination of a negative stain for cytokeratin and a positive stain for vimentin in the tumour cells of our patient clearly supports the original hypothesis of mesenchymal histogenesis, presuming (peri)vascular smooth muscle cells [9] to be the ones of origin in benign 'sugar' tumours.

Acknowledgements: The authors thank R.H.U. Rammeloo for supplying prothrombectomy patient data.

References


RÉSUMÉ: Description d’un cas d’une tumeur bénigne à cellules claires du poumon, dont le diagnostic a reposé sur des aspects caractéristiques des coupes histologiques. À notre connaissance, il s’agit du premier cas avec des investigations immunohistochimiques pour filaments intermédiaires, qui sont suggestifs pour une origine mésenchymale de cette tumeur rare et qui sont important pour le diagnostic différentiel.