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Oncocytic Bronchial Adenoma

Histological, Histochemical and Ultrastructural Study

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Summary. Benign adenomas derived from the bronchial mucous glands are uncommon. Probably the least common variety is the oncocytomatous adenoma, this case being the second known example. The tumour was situated in the right main bronchus in a man aged 75. An oncocytomatous adenoma should be clearly distinguished from the common oncocytomatous change which affects the normal bronchial mucous gland cells seen in adults. The eosinophilic, columnar tumour cells seen by light microscopy contained numerous and prominent mitochondria by electron microscopy and granules of serous secretion. Other tumour cells contained microfilaments and were perhaps of myoepithelial origin.

The true oncocytomatous mucous gland adenoma needs to be distinguished from an oncocytomatous bronchial carcinoid tumour the cells of which contain dense core granules of neurosecretory type.

The bronchial oncocytomatous adenoma appears to be a benign tumour with a close similarity to its counterpart occuring in the salivary glands.

Key words: Bronchial gland adenoma – Oncocytoma – Electron microscopy

Introduction

True bronchial adenomas, excluding carcinoids, mucoepidermoid carcinomas and adenoid cystic carcinomas, are rare. Rouzeau (1975) reviewed only 26 cases. Spencer (1977, 1979) described an oxyphilic variety of adenoma, of which we present a second example.

Case Report

A man aged 75 has been admitted for a pneumopathy of the left lower lobe. His history involved poliomyelitis at the age of 13, without any sequel and idiopathic pneumothorax at 60. X-rays showed old apical scars of tuberculous origin. Endoscopy revealed a nodule on the external wall

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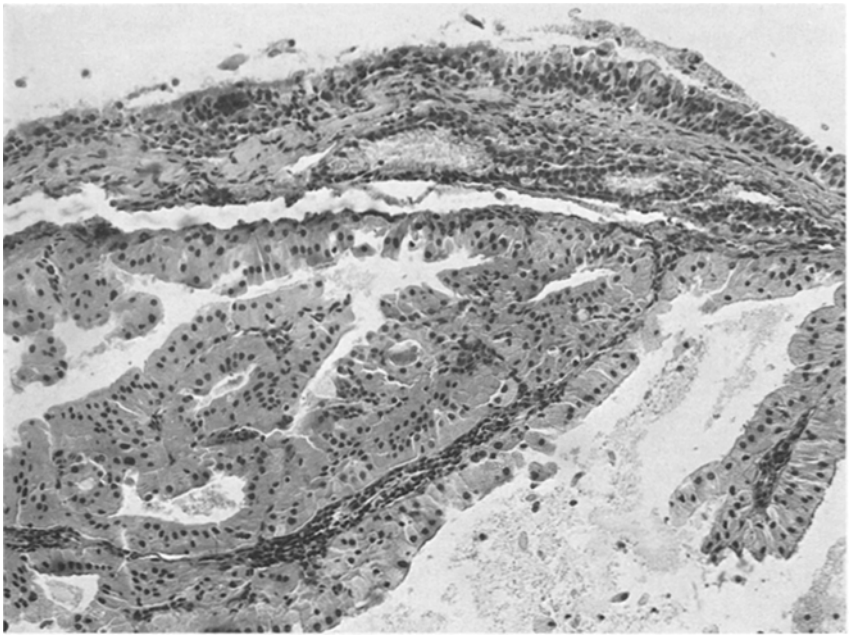

Fig. 1. A well limited microcystic and papillary tumour, covered with normal bronchial epithelium and a thin layer of lamina propria containing an excretory bronchial gland canal. H.E. ×150. L. 20799

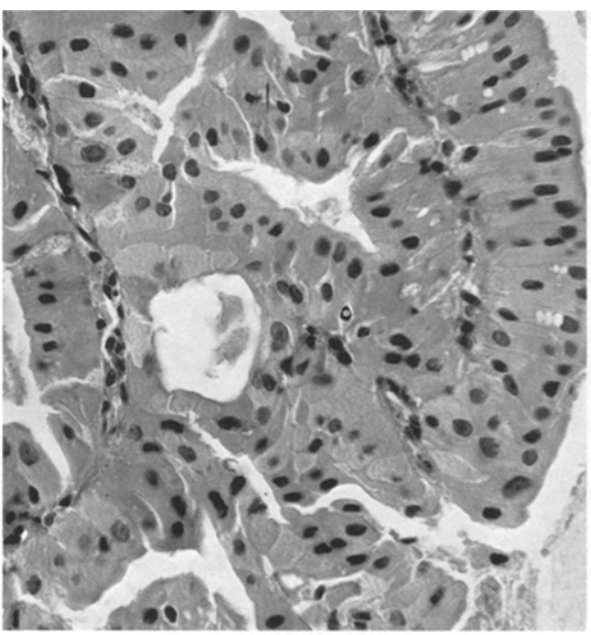

Fig. 2. The tumor cells are cylindrical. Their cytoplasm is granular and their nucleus small and regular. H.E. ×400. L. 20799

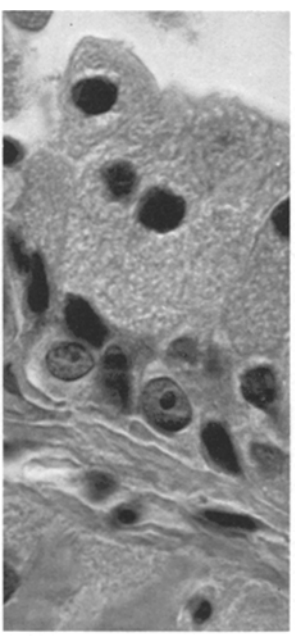

Fig. 3. Some small cells are found under the oxyphilic cells. They have a pale cytoplasm and a nucleus containing a nucleolus. H.E. ×1,200. L. 20799

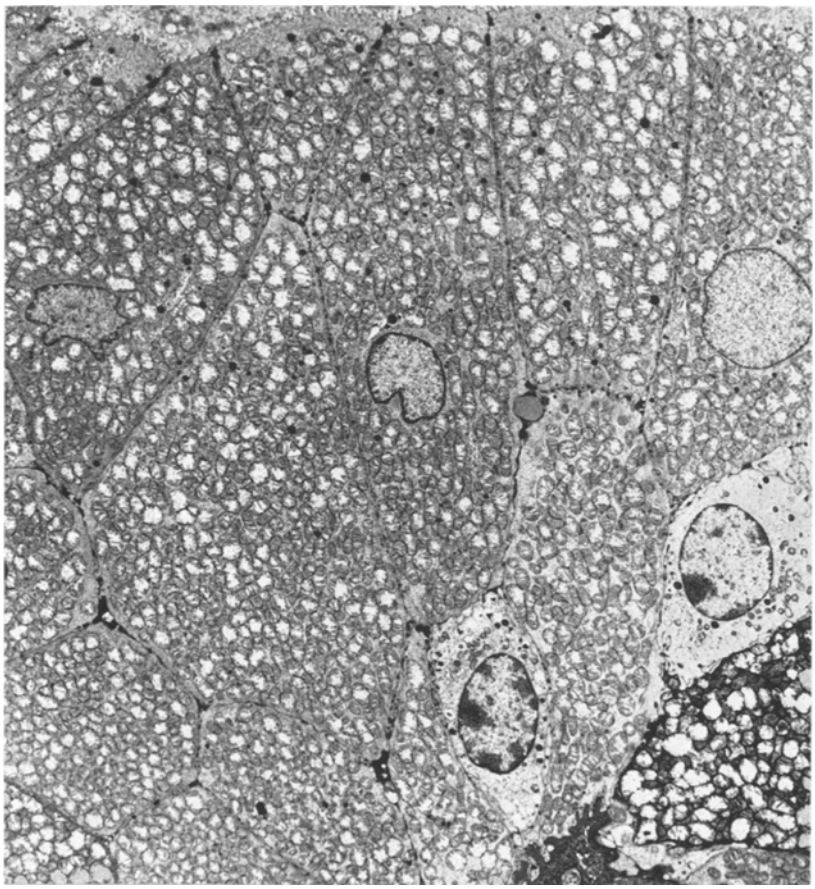

Fig. 4. Oxyphilic cells with geometric borders, in contact with a tumour lumen (upper part of the figure) and with two suprabasal "clear" cells. The oxyphilic cells appear filled with mitochondria. M.E. 218/77. IPS ×6,300

of the right main bronchus which was biopsied. Later, a second fibroscopic biopsy made for E.M. study completely removed the nodule. Two and a half years later the patient was well and fibroscopic checking showed a normal bronchus.

The first biopsy specimen was fixed in formalin and stained with H.E., P.A.S., Alcian blue, mucicarmine and according to the methods of Grimelius (1968) and Sevier and Munger (1965). The second biopsy specimen was fixed in glutaraldehyd.

Pathology

The nodule, 3 mm in diameter, protruded and was smooth and shiny, tan to pink in colour. Histological study revealed (Fig. 1) a well defined though not encapsulated tumour covered with a normal bronchial epithelium and a thin lamina propria containing a glandular excretory canal. The tumour was of microcystic and papillary structure. The main cells (Fig. 2), of cylindrical shape, were disposed along thin fibrovascular septa. These cells had a thinly

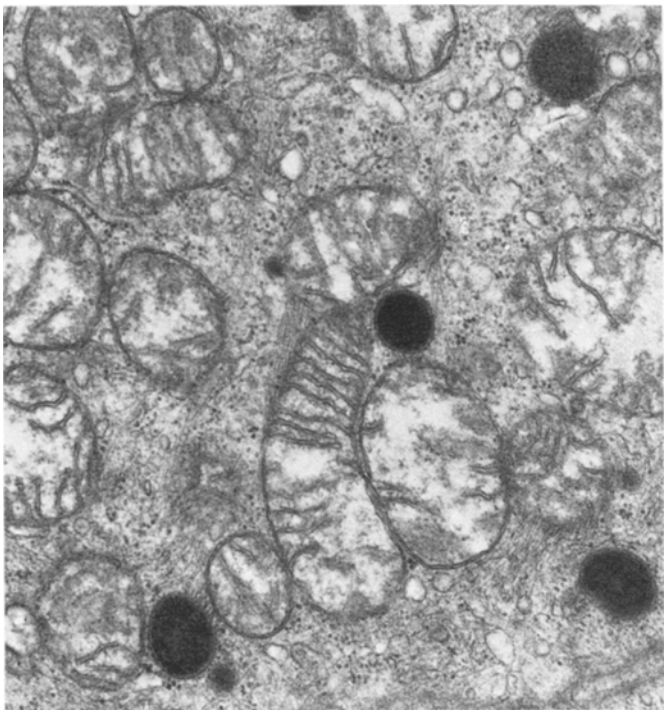

Fig. 5. Microfibrils converging on the membrane of the mitochondria of some of the oxyphilic cells. M.E. 218/77. ×29,000

granular and strongly eosinophilic cytoplasm. The small, basophilic nuclei were regularly disposed, showing no mitosis. Some of these cells contained small subnuclear vacuoles stained with PAS and mucicarmine. Rare cells, of smaller size, lay between the oxyphilic cells and the basal membrane (Fig. 3). They were polyedric, with a faint cytoplasm and a large nucleus of vesicular structure containing a big nucleolus. Occasionally transitional cells between the two preceding types were found, showing an elongated and eosinophilic cytoplasm. Finally some goblet cells contained vacuoles strongly stained by the PAS, mucicarmine and Alcian blue. These dyes also stained the microcavities of the tumour. No argyrophilic cells were found in the specimen.

Electron Microscopy

Here again, different cell-types were found. The main cells (Fig. 4) contained a round or indented nucleus with thin and marginated chromatin. The cytoplasm was characterised by extremely hyperplastic mitochondria. In general, the mitochondria were arranged parallel to the long axis of the cell. Some of them contained glycogen granules, others being apparently linked to the cytoplasm by microfibrils (Fig. 5). A thin layer of cytoplasm free of mitochondria was seen around the nucleus and under the cell membrane. It contained rare granules

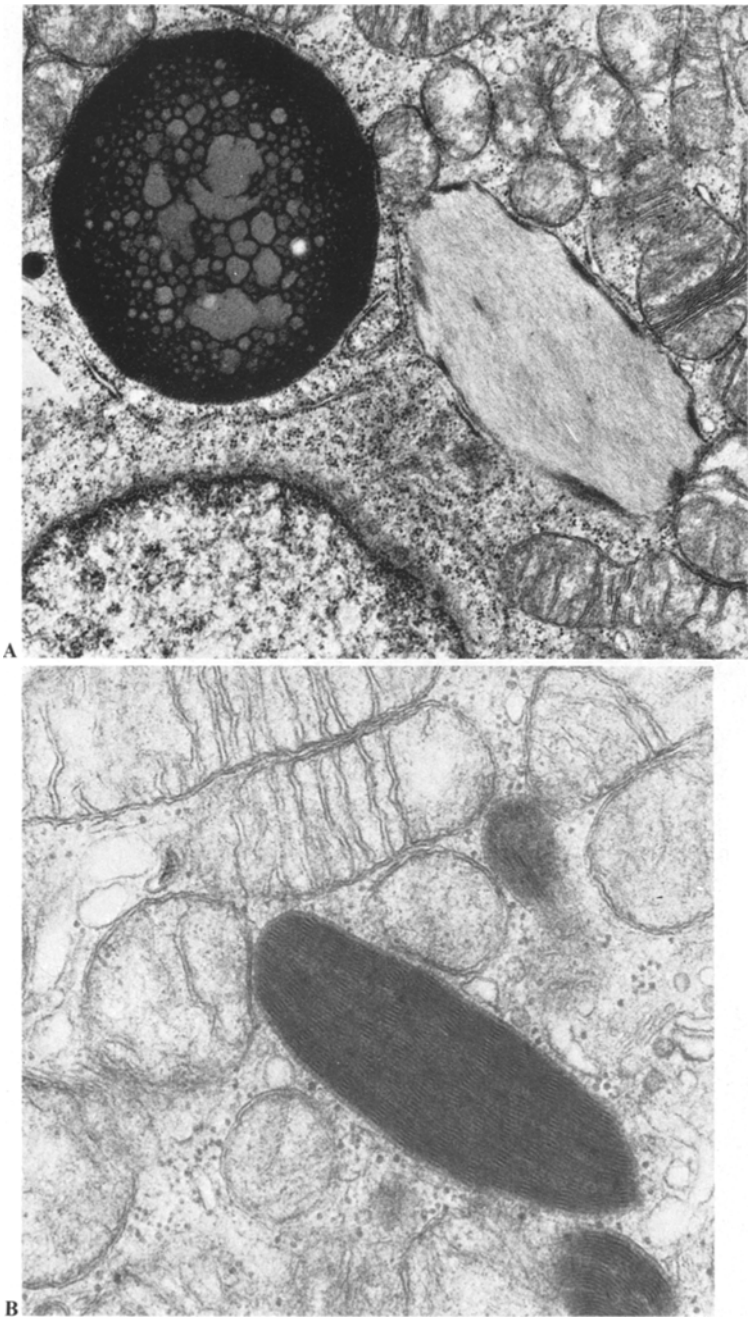

Fig. 6A, B. Oxyphilic cells containing unusual inclusions. **A** A lipopigment granule together with an oval inclusion. The inclusion is limited by a membrane and has a fibrillary content. **B** Oval or round inclusions, with a periodic fibrillary content. M.E. 218/77. IPS **A** ×35,000; **B** ×40,000

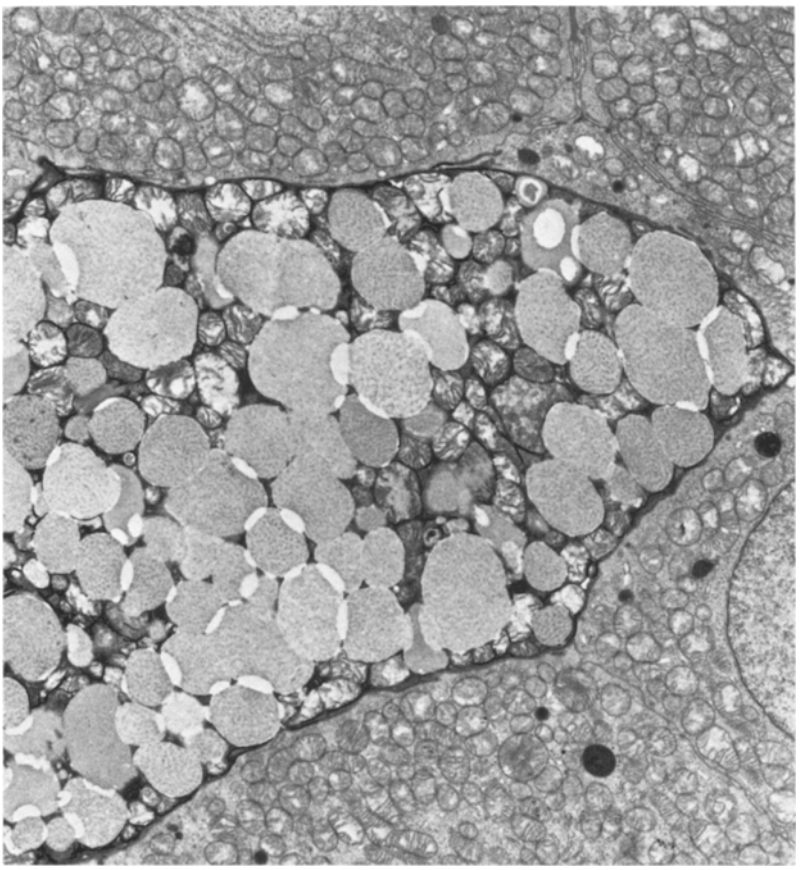

Fig. 7. A mucous cell containing spotted clear vacuoles is surrounded by oxyphilic cells. Its mitochondria are hyperplastic. M.E. 218/77. IPS ×6,300

of serous type, measuring from 300 to 1,000 n.m. in diameter. Other granules, strongly osmiophilic and sometimes vacuolated, measuring up to 2,300 n.m., had a lipopigment morphology (Fig. 6a). Two cells contained inclusions of irregular shape and size (Fig. 6a) with an inconspicuous membrane and a thinly fibrillar content. Other inclusions of rare occurrence (Fig. 6b) measuring from 440 to 700 n.m. were also limited by a membrane and had a periodic strongly osmiophilic fibrillary structure. The cytoplasm also contained free ribosomes, an ergastoplasm of moderate size and a supranuclear Golgi apparatus. Microfibrils were sometimes observed along the plasma membrane, oriented towards the desmosomes. The cell membrane showed apical and lateral digitations, the latter lying in intercellular spaces.

A second cell type, corresponding to the goblet cells contained numerous clear and spotted vacuoles, measuring from 1,200 to 2,300 n.m. (Fig. 7). The other part of the cytoplasm was filled with large mitochondria. A third cell type, lying under the former and above the basal membrane, had a flat plasma membrane with many desmosomes. The nucleus was larger than before, with a coarser marginated chromatin (Fig. 4). The cytoplasm looked clearer, due

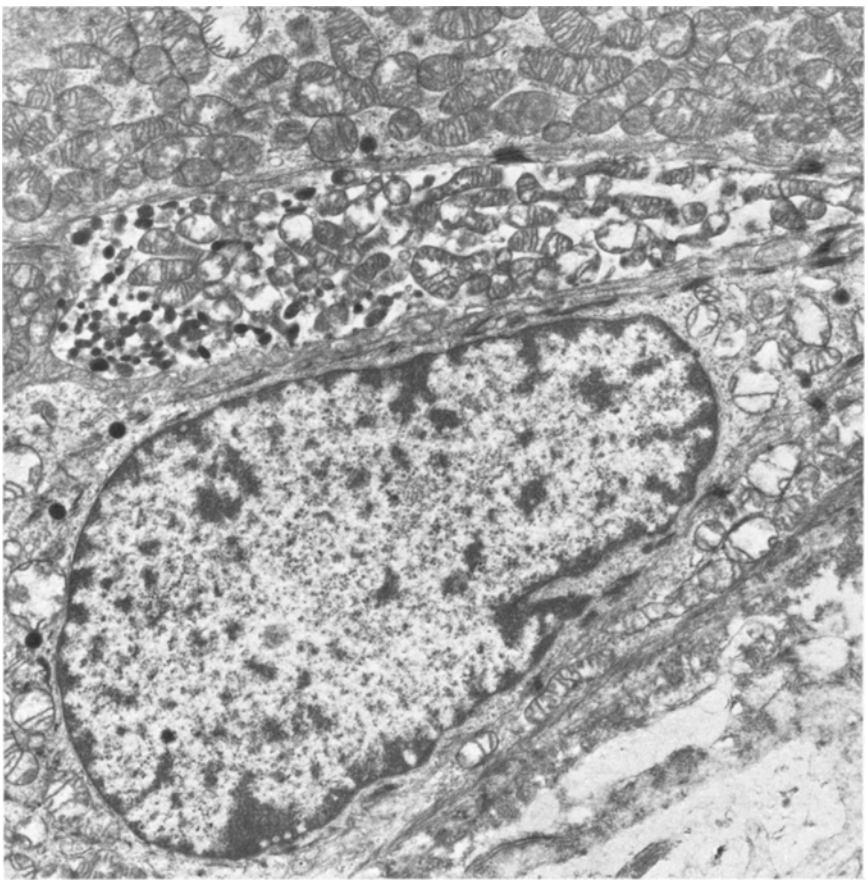

Fig. 8. A cell containing fibrillary arrays in its cytoplasm together with an apparently increased mass of mitochondria. M.E. 218/77. IPS ×8,000

to the scarcity of organelles in which mitochondria occurred in variable number. Very rare suprabasal cells, also provided with a clear cytoplasm, contained rather thick arrays of microfibrils measuring up to 3 n.m. in diameter apparently converging towards the base of the cell, though no converging on electron-dense regions on the plasma membrane have been observed so far. Other cells (Fig. 8) also containing these fibrils in their perinuclear cytoplasm showed hyperplastic mitochondria. We have also found a Kultschitzky cell, some lymphocytes and mastocytes in the tumour. In the vicinity of the lesion, a bronchial gland contained all the known cell types (Bensch et al. 1965; Meyrick and Reid 1970): serous, mucous, basal and myoepithelial.

Discussion

Our case is very similar to the one described by Spencer (1977, 1979). The two lesions were found in a main bronchus. They were of small size (2 to 3 mm) and were discovered haphazardly: at autopsy in Spencer's case, during a routine fibroscopy in our case. The patients were adult men. Groups of

oncocytes are often found in the bronchial glands. They appear in adult and old people: Matsuba et al. (1972) never observed them in patients under the age of 33 years. However, there is a major difference between these foci of oncocytic transformation and the lesion we describe. The focal oncocytic transformation is a cellular phenomenon which does not modify the glandular architecture. In the lesion we describe, the normal glandular architecture is destroyed.

Histology is sufficient to differentiate the oxyphilic cell adenoma from other tumours or pseudotumourous lesions composed of granular and eosinophilic cells: granular cell tumour; metastasis of oxyphilic cell carcinoma of the kidney or thyroid; malakoplakia (Walter, Warter and Roeslin 1978). The argyrophilia and, on electron microscopy, the presence of neurosecretory granules, lead to the diagnosis of oncocytomatous carcinoid. This diagnosis is easier when the tumour is incompletely oncocytomatous (Weiss and Ingram 1961). Due to the presence of dense core granules, the case described by Fechner and Bentinck (1973) may be considered as a typical oncocytomatous carcinoid (Walter, Warter and Morand 1978). The tumour reported by Santos-Briz et al. (1977) is similar to Fechner and Bentinck's case, as well as to the observation of Böck et al. (1977), in which the authors found high levels of serotonin together with dense core granules. Moreover, if the oxyphilic adenoma and carcinoid have mitochondrial hyperplasia, allowing us to call them oncocytomas (Hamperl 1962), they show a striking difference: in the oncocytomatous carcinoid (Walter, Warter and Morand 1978) the plasma membranes are parallel, with scanty or absent intercellular spaces. We have seen that in the case of the adenoma these spaces are well defined and contain interdigitations.

The oncocytic adenoma we describe is apparently composed of various cell types. The main cells show a mitochondrial hyperplasia that is so marked that no specific cytoplasmic organelles are to be found. Nevertheless, some of them contain serous granules. Some of the mitochondria contain glycogen granules, a feature reported in parotidic oncocytomas (Hübner et al. 1967; Tandler et al. 1970; Thackray and Lucas 1974) and in a case of Warthin's tumour (Tandler and Shipkey 1964). The presence of microfilaments perhaps linking the mitochondria to the cytoplasm appears in an oncocytic cyst of a salivary gland (Hübner et al., 1967). The two types of fibrillary and membrane-bound inclusions (Fig. 6A and B) have not been found in our review of the literature. Their exact significance is unknown. The tumour also contains rare goblet cells. Their mitochondria are hyperplastic though less developed than in the oncocytes and they possibly represent an intermediate stage in oncocytic transformation. The clear suprabasal cells are normally found in the bronchial glands. Some of them contain rather well developed microfibrils. Such arrays of microfibrils are also discovered in rare cells of elongated shape lying parallel to the oncocytes. These cells are very similar to the ones called myoepithelial by Askew et al. (1971) in a case of salivary oncocytoma. It seems impossible to agree with a myoepithelial nature for the cells we have described, which lack any convergence of the fibrils towards electron-dense regions on the plasma membrane. It should be remembered that some fibrils are normally present in serous glandular cells (Bensch et al. 1965). In any event the presence of myoepithelial cells in oncocytic and non oncocytic tumours of salivary glands is well documented (Hübner et al. 1967; Hübner 1971).

In conclusion, our ultrastructural study leads us to call the tumour an oncocytoma. It shows that the oncocytic transformation is not confined to one cellular type in a single lesion.

The rarity of the tumour is surprising if we compare it to the high frequence of foci of oncocytes in the bronchial glands of adults. This appears to be similar to what is known to happen in the salivary glands (Thackray and Lucas 1974).

As far as prognosis is concerned, the oncocytomas of salivary gland are benign and should be treated by limited resection (Blanck et al. 1970). The oncocytic bronchial gland adenoma seems to be an equally benign lesion.

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