Acta Neurochirurgica 51, 195—201 (1980)

ACTA
NEUROCHIRURGICA

Division of Neuropathology and Department of Neurosurgery, University of Göttingen, Federal Republic of Germany

Ultrastructurally Abnormal Mitochondria in the Pituitary Oncocytoma*

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With 3 Figures

Summary

A pituitary adenoma in a 67-year-old man was characterized by abundant mitochondria and identified as an oncocytoma, which clinically and histologically appeared as a chromophobe adenoma. In addition to the numerous mitochondria within the neoplastic cells, structurally abnormal mitochondria were also present. Compared with other pituitary oncocytomas reported in the literature, abnormally structured mitochondria appear rare among the mitochondrial population of pituitary oncocytomas.

Introduction

Recently morphological aspects of pituitary adenomas have been greatly enlarged by regularly incorporating ultrastructural studies of the tumour tissue (Hachmeister 1973, Landolt 1975, Saeger 1977). The diagnosis of pituitary oncocytoma depends entirely on electron microscopic investigation (Saeger 1977). Oncocytomas develop in various exocrine and endocrine glandular tissues such as the parotid, the parathyroids, and the thyroid. Occurrence of this type of tumour among pituitary neoplasms is, therefore, not surprising. Electron microscopy of pituitary oncocytomas not only reveals innumerable mitochondria but occasionally also quite abnormally structured mitochondria, as presented in the following observation.

* This paper is dedicated to Hans Orthner, M.D., on the occasion of his 65th birthday.

0001-6268/80/0051/0195/$ 01.40

Material and Methods

Pituitary tumour tissue was removed and fixed for electron microscopy according to regular techniques from a 67-year-old male whose symptomatology consisted of almost complete amaurosis on the left, a temporal visual field defect on the right, a radiologically enlarged sella turcica, and a large suprasellar mass shown by computer tomography, suggesting a pituitary adenoma, which was confirmed at surgery.

Results

Light microscopic studies established the diagnosis of a chromophobe adenoma (Fig. 1, inset). Toluidine blue-stained thick sections revealed many organelles within neoplastic cells. On electron microscopy the neoplastic cells consisted of two types. One population contained numerous mitochondria. Many were severely swollen and their cristae were disrupted. Others appeared regular (Fig. 1). The entire mitochondrial population of each cell showed either matrical swelling or a normal matrix. In addition to swollen and non-swollen mitochondria abnormally structured mitochondria were encountered (Fig. 2). Some were circular in shape (Fig. 2 a), or contained smaller mitochondria (Fig. 2 b), or appeared rather elongated (Fig. 2 c). Others were filled with singular homogeneously electron-dense spheroid inclusions of various sizes (Fig. 2 d). Occasionally mitochondrial membranes formed an extensive chiefly circularly arranged feltwork (Fig. 3). Electron-dense granules were loosely scattered among the mitochondria (Fig. 1). The second type of cells (Fig. 1) contained rather scant amounts of mitochondria, and chiefly harboured a finely granular cytosol and a few electron-dense granules. Granules and mitochondria abnormal as to size, shape, and internal features were not encountered in fibroblasts or mural cells of the vasculature.

Comment

The oncocytoma is defined as a neoplasm enriched by numerous mitochondria. Compared to the ultrastructure and quantity of mitochondria in non-oncocytic pituitary adenomas of various kinds, the number of mitochondria appeared clearly increased in our tumour and, therefore, it conforms to the oncocytomas of the pituitary previously described (Landolt 1975, Saeger 1977). As other types of pituitary tumours, eosinophilic, basophilic, or chromophobic, represent neoplastic counterparts of different individual cell types of the normal pituitary gland, so do oncocytes exist in normal human pituitary gland (Paiz and Hennigar 1970, Kovacs *et al.* 1974), and they are possibly the source of neoplastic oncocytes. Oncocytes seem

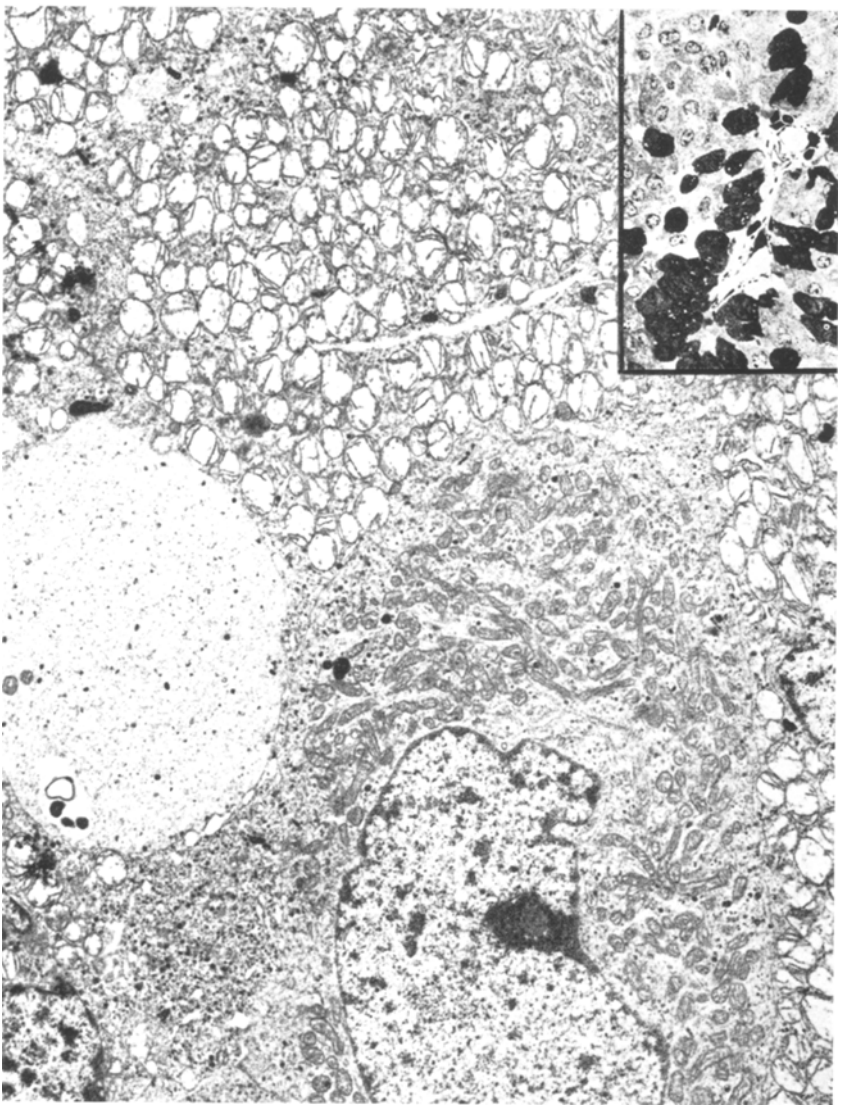

Fig. 1. Three types of neoplastic cells are apparent: two containing large amounts of mitochondria, with swollen mitochondria in one cell and normal mitochondria in another, and a third cell almost completely devoid of mitochondria. ×6,650. Inset: Toluidine-blue stained 1 μm thick section also reveals compact and clear cells. ×275

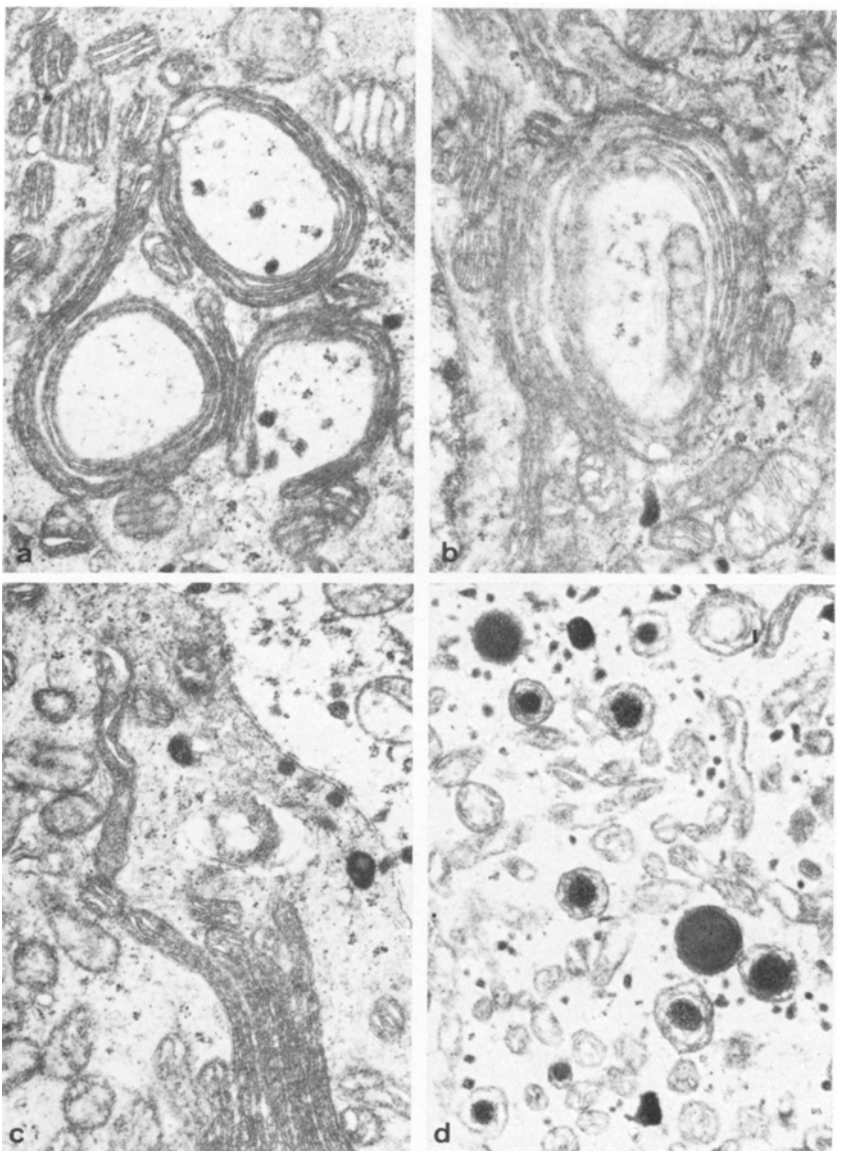

Fig. 2. A set of structurally abnormal mitochondria shows: a) circular mitochondria; ×22,000; b) circular mitochondrial membranes surrounding a central mitochondrion; ×13,475; c) slender, elongated mitochondria; ×23,000; and d) mitochondria bearing electron dense inclusions; ×17,150

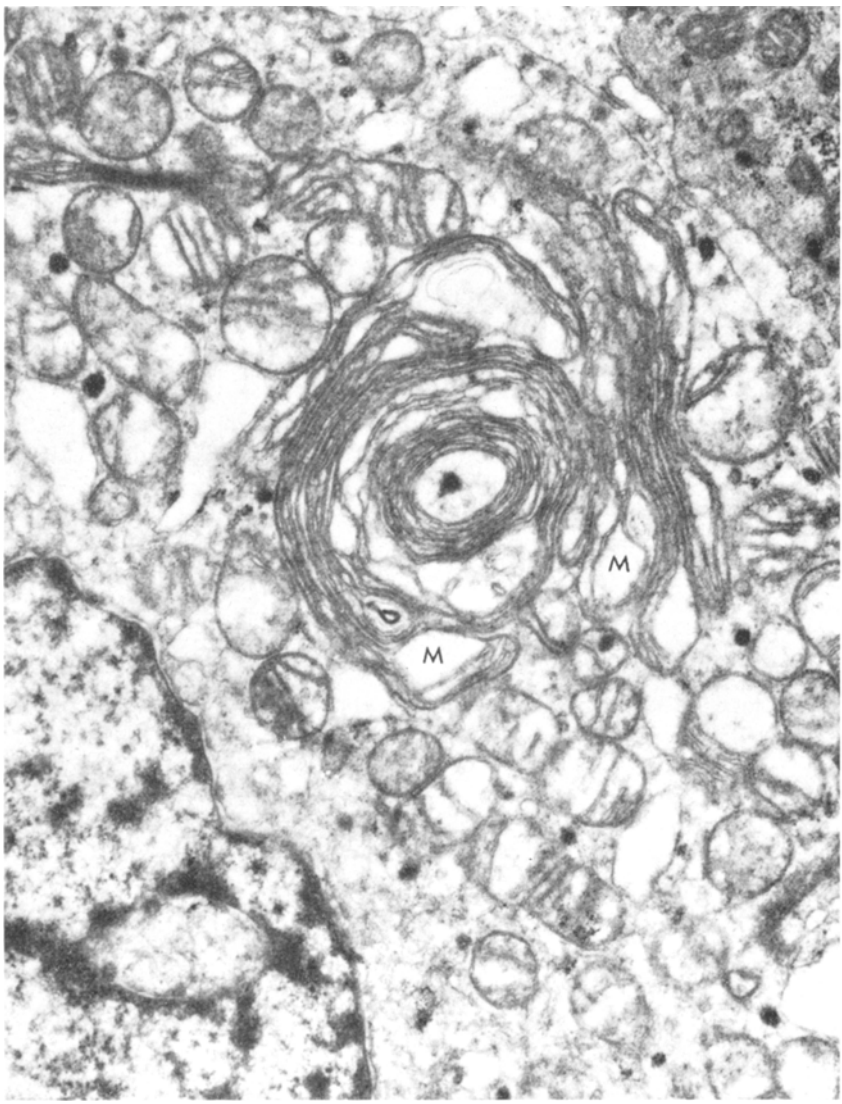

Fig. 3. An elaborate feltwork of membranes originates from swollen mitochondria (*M*). ×24,000

to indicate a certain metabolic stage of the corresponding glandular cells as shown by the presence of transitional forms between oncocytic and non-oncocytic cells in normal pituitary glands (Kovacs *et al.* 1974) and the presence of secretory granules within oncocytes. These findings point to the capability of various types of pituitary epithelial cells to be transformed into oncocytes (Kovacs *et al.* 1974). Therefore, the existence of oncocytomas of the pituitary analogous to other pituitary neoplasms derived from preexisting pituitary cell types does not come as a surprise. Whether transformation of non-oncocytic cells to oncocytes occurs before neoplastic derangement of pituitary cells or thereafter, or both, is not yet clear (Kovacs and Horvath 1973, Roy 1978). The presence of secretory granules in many neoplastic oncocytes in our tumour emphasizes the close relation to or derivation from non-oncocytic pituitary cells.

The two populations of oncocytic cells containing swollen mitochondria or non-swollen mitochondria seem to be a regular feature of pituitary oncocytomas as depicted by Horvath and Kovacs (1976), Saeger (1977), and Roy (1978). The presence of swollen electron-lucent mitochondria—as also seen in our tumour—seems to be more the rule (Saeger 1977, Gjerris *et al.* 1978, Roy 1978) than the exception, indicating a particular state of metabolic activity or necrobiosis (Saeger 1977) rather than anoxic or laboratory artifacts as such swelling of mitochondria may often suggest.

Structural abnormalities of mitochondria in pituitary oncocytomas, particularly inclusions, have rarely been reported (Landolt and Oswald 1973, Gjerris *et al.* 1978). These abnormally structured mitochondria may reflect a particular metabolic state or damage, perhaps of a reversible nature, since structurally abnormal mitochondria have been produced experimentally in striated muscle fibres under ischaemic (Karpati *et al.* 1974, Heffner and Barron 1978) conditions. If hypoxia had found its morphological expression in our pituitary oncocytoma, acute hypoxia might be reflected in the swelling of mitochondria, chronic hypoxia in abnormal ultrastructure of mitochondria. Ultrastructural abnormalities of mitochondria in oncocytomas are, therefore, not unusual.

The presence of cells devoid of mitochondria and of cytoplasmic granules in oncocytic and non-oncocytic tumour cells suggests either a mixed tumour or a transitional type of tumour, possibly primarily granular, but finally having developed into an oncocytic type.

References

Gjerris, A., Lindholm, J., Riishede, J., Pituitary oncocytic tumor with Cushing's disease. Cancer *42* (1978), 1818—1822.

Hachmeister, U., Ultrastructural aspects of anterior pituitary tumors. In: Modern aspects of neurosurgery (Kuhlendahl, H., Brock, M., Le Vay, D., Weston, T. J., eds.), Vol. 4, pp. 108—115. Proceedings of the German Society of Neurosurgery. Amsterdam: Excerpta Medica. 1973.

Heffner, R. R., Barron, S. A., The early effects of ischemia upon skeletal muscle mitochondria. J. Neurol. Sci. *38* (1978), 295—315.

Horvath, E., Kovacs, K., Ultrastructural classification of pituitary adenomas. J. Canad. Sci. neurol. *3* (1976), 9—21.

Karpati, G., Carpenter, S., Melmed, C., Eisen, A. A., Experimental ischemic myopathy. J. neurol. Sci. *23* (1974), 129—161.

Kovacs, K., Horvath, E., Pituitary "chromophobe" adenoma composed of oncocytes. A light and electron microscopic study. Arch. Path. *95* (1973), 235—239.

— — Bilbao, J. M., Oncocytes in the anterior lobe of the human pituitary gland. A light and electron microscopic study. Acta neuropath. *27* (1974), 43—54.

Landolt, A. M., Ultrastructure of human sella tumours. Correlation of clinical findings and morphology. Acta neurochir. (Wien), Suppl. *22* (1975), 1—167.

— Oswald, U. W., Histology and ultrastructure of an oncocytic adenoma of the human pituitary. Cancer *31* (1973), 1099—1105.

Paiz, C., Hennigar, G. R., Electron microscopy and histochemical correlation of human anterior pituitary cells. Amer. J. Path. *59* (1970), 43—74.

Roy, S., Ultrastructure of oncocytic adenoma of the human pituitary gland. Acta neuropath. (Berl.) *41* (1978), 169—171.

Saeger, W., Die Hypophysentumoren. Pituitary tumors. In: Progress in Pathology (Büngeler, W., Eder, M., Lennert, K., Peters, G., Sandritter, W., Seifert, G., eds.), Vol. 107. Stuttgart-New York: G. Fischer. 1977.

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