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Light bodies in human pituitary adenomas

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Summary. Light bodies are large cytoplasmic granules originally described in the gonadotrophic cells of the rat pituitary gland. In order to determine whether similar bodies occur in the human anterior pituitary gland, 89 pituitary adenomas and periadenomatous tissue from 20 cases were examined by transmission electron microscopy. Double membrane bound bodies with filamentous internal structure identical to rodent light bodies were identified in 10 hormone-producing adenomas: 5 PRL, 1 PRL-GH, 2 GH, and 2 ACTH-producing tumours. No light bodies were found in the remaining 79 tumours nor in the pituitary cells in periadenomatous tissue from 20 cases. These results show that some human pituitary adenomas may contain light bodies identical to those seen in gonadotrophs of rat pituitary.

Key words: Human pituitary adenomas – Granules – Electron microscopy

Introduction

The term "light bodies" was introduced by Costoff (1973) to denote solitary large (700–1200 nm) amorphous granules of low-medium electron density in the gonadotrophic cells of the rat pituitary gland. Based on morphological and biochemical studies, it was established that these organelles do not represent typical hormone granules nor lysosomes, since they appear to be devoid of both hormones and acid phosphatase activity (Costoff 1973; Hymer and McShan 1963; Nakayama et al. 1970; Perdue and McShan 1962).

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Abbreviations. PRL: prolactin; GH: growth hormone; ACTH: adenocorticotropic hormone; FSH: follicle-stimulating hormone; LH: luteinizing hormone

In a recent study on rat pitiutaries, we noted that light bodies have a double-layered outer membrane and that the core has a finely filamentous appearance (Holck et al. 1987). Further, laminin and tubulin could be co-localized immunoelectronmicroscopically in the core. It was shown that the number of light bodies dropped dramatically following estrogen treatment which suppresses the hormone synthesis of gonadotrophic cells. In contrast, increased number of light bodies was seen following castration which stimulates hormone synthesis in these cells. Based on these observations, it was suggested that this unique organelle reflects the functional status of gonadotrophic cells in the rat pituitary.

Light bodies have so far not been described in the human pituitary gland. Thus we reviewed electron micrographs from 89 human pituitary adenomas to determine whether cytoplasmic organelles equivalent to rodent light bodies occur in normal human pituitary cells or human pituitary adenomas. We report that indeed morphologically similar granules were found in 10 hormone-producing adenomas. We conclude that the light bodies are not restricted to rat pituitary glands but also exist as distinct organelles in human anterior pituitary gland tumours.

Materials and methods

Eighty-nine pituitary adenomas (Holck et al. 1986) removed from 42 men and 38 women operated in the Department of Neurosurgery, Rigshospitalet, Copenhagen were examined by light and electron microscopy. Forty-three of the patients were hyperprolactinaemic and/or acromegalic, 9 had Cushing's disease and one had Nelson's syndrome. The remaining 27 patients had no obvious clinical or biochemical evidence of hormone hypersecretion and the tumours were removed primarily because of their space occupying nature. In addition, periadenomatous pituitary parenchyma from 20 patients was also examined.

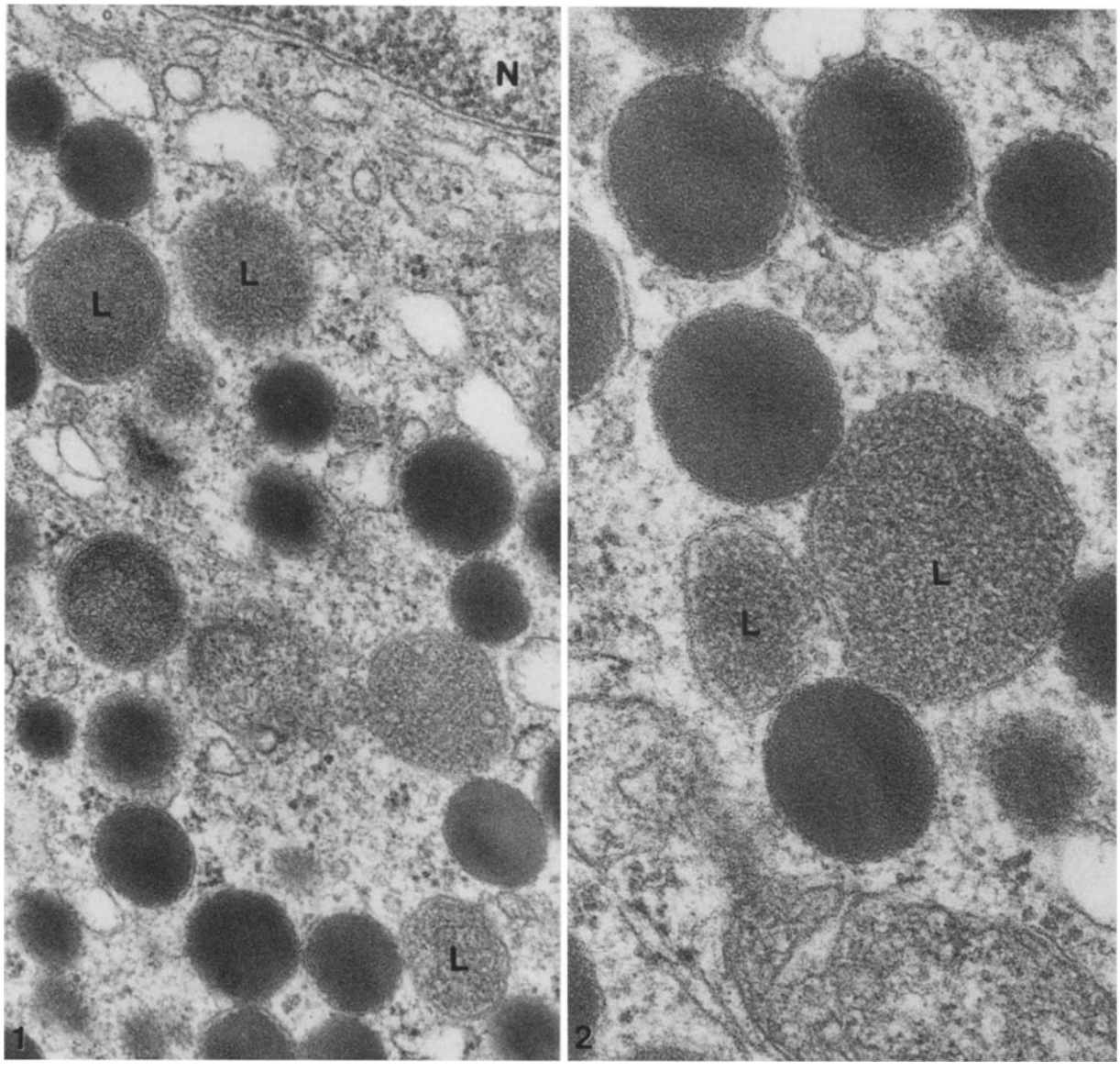

Fig. 1. An electron micrograph of a GH-producing human pituitary adenoma. Large electron-lucent light bodies are seen (*L*) among the smaller electron-dense secretory granules. Nucleus is indicated (*N*). ×42200

Fig. 2. Light bodies shown at higher magnification. The light bodies (*L*) exhibit a filamentous fine structure and an outer limiting double membrane. ×71250

Tissue specimens for electron microscopy were fixed in Karnovsky's fixative and processed using standard technique. Ultrathin sections were stained with uranyl acetate and lead citrate and examined with a Philips 201 electron microscope. Three to six blocks of tissues were examined in each case and at least 100 photos from every tumour, as well as 20–50 photos from every non-neoplastic specimen were examined.

Results

Review of electron micrographs from 89 human pituitary adenomas disclosed light bodies morphologically similar to that described in the rat pituitary in 10 cases. Light bodies were identified at low magnification by their large size (averaging 500 nm in diameter with a range of 300–1500 nm) and their electron-lucent appearance (Fig. 1). At higher magnification, a distinct filamentous substructure was discernible (Fig. 2). Most light bodies were surrounded by a complete or fragmented double membrane (Fig. 2). In the 10 positive cases studied, light bodies were present in 10–25% of the adenoma cells. The number of light bodies per cell in a given section varied but in general, 1–10 light bodies were recorded. The presence of light

bodies did not appear to correlate with the number, size and type of secretory granules in a given adenoma cell. Light body-positive cells were not found in areas with major autolytic or degenerative changes. The light bodies had no preferential location within the cytoplasm and had no apparent connection to the rough endoplasmic reticulum or the Golgi complex. In one GH-producing adenoma with typical fibrous bodies, light bodies were also seen, but no spatial relationship between these two structures could be identified. Exocytosis of light bodies was not observed.

All the light body-positive cases were hormone-producing adenomas. Thus 5 tumours were clinically diagnosed as PRL-producing, 1 PRL-GH-producing-, 2 GH-producing and 2 ACTH-producing. No light bodies were found in the remaining 79 tumours nor in the pituitary cells of periadenomatous tissue from 20 cases.

Discussion

This communication describes cytoplasmic granules in human pituitary adenomas indistinguishable from light bodies of gonadotrophic cells in rat pituitaries (Costoff 1973; Holck et al. 1987). Thus, we show that the light bodies are not limited to rat but may also occur in human pituitary gland. The diagnostic criteria include a large electron-lucent granule (300–1500 nm in diameter) with a filamentous fine structure and surrounded by a double membrane. It should be emphasized that these features are most readily distinguished after the tissue has been treated with tannic acid (Holck et al. 1987; Simionescu and Simionescu 1976).

We are not aware of any previous systematic attempts to study light bodies in human pituitary cells. The existence of organelles comparable to the light bodies might however be deduced from previous electron microscopic studies of human pituitaries and pituitary adenomas. Secretory granules of low to medium density, lying amidst more typical electron dense hormone granules might conceivably represent light bodies (Kovacs and Horvath 1975; Kovacs et al. 1980; Krieger et al. 1976). A recent description of some pituitary granules of low electron density, featuring a filamentous "change" (Challa et al. 1985), is not unlike the light bodies discussed here. Secretory granules with a crystalline texture (von Lawzewitsch et al. 1974) may similarly represent light bodies.

In the rat, light bodies have been reported in gonadotrophic cells only (Costoff 1973; Holck et al. 1987). One may therefore question whether the light body-bearing cells we observed represented a mixture of gonadotrophic cells forming either a minor neoplastic component or entrapped non-neoplastic elements. However, the general ultrastructure of light body-containing cells correspond to that of the prevailing tumour cells and did not resemble gonadotrophs. It thus appears that light bodies, at least in the human pituitary, occurred in adenomas producing GH, PRL or ACTH. Unfortunately, we did not have the opportunity to study the rare endocrine-active (FSH/LH) gonadotrophic adenomas. A final conclusion as to whether light bodies occurred specifically in those adenoma cells producing a given hormone will await immunoelectron microscopic studies. Also, it might be an interesting question to address whether light body-containing cells belong to those "pituitary stem cells" (Kovacs et al. 1977; Yoshimura et al. 1977) that conceivably give rise to adenomas.

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