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*Case report*

# Oncocytic adenocarcinoma of the ovary

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**Summary.** A case of ovarian adenocarcinoma mainly composed of oncocytes was studied by light and electron microscopy. Oncocytes, characterized by granular and eosinophilic cytoplasm by light microscopy possessed numerous mitochondria at the ultrastructural level. These oncocytes were classified into two types: typical and condensed oncocytes. Typical oncocytes seemed to be active, whereas condensed oncocytes were thought to be involved in a degenerative process. The two types of cells showed a close similarity to oncocytes in other organs (e.g., thyroid, parathyroid and salivary glands). This appears to be the first report of an ovarian oncocytic tumor.

**Key words:** Oncocyte – Adenocarcinoma – Ovary

The oncocyte is a histologically distinctive cell type characterized by granular and eosinophilic cytoplasm under light microscopy (Hamperl 1962). Electron microscopic investigations show that oncocytes have numerous mitochondria which occupy most of the cytoplasm, and the authors of these reports have proposed an ultrastructural criterion, mitochondrial hyperplasia, for diagnosing oncocytes and oncocytic tumors (Tandler et al. 1970; Askew et al. 1971; Fechner and Bentinck 1973). The cells, which were believed to be developed from metaplasia of epithelial cells, have been observed in several organs such as the salivary, thyroid and parathyroid glands (Tremblay 1969). Tumors composed of oncocytes are also known to develop in certain other organs (Hamperl 1962; Walter et al. 1978; Yu et al. 1980; Warter et al. 1981). These tumors are rare and generally possess a benign character, but some malignant ones have also been reported (Sidhu and Waldo 1975; Meijer and Hoitsma 1982).

To the authors' knowledge, ovarian adenocarcinoma with oncocytic change has not been reported in the literature. This is the first report to describe the light and electron microscopic features of a case of ovarian adenocarcinoma in which numerous tumor cells showed an oncocytic change.

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## Case report

A 39-year-old Japanese housewife (gravida 4, para 1) visited the Department of Obstetrics and Gynecology, Tohsei Hospital (Seto, Japan) on June 18, 1981 with complaints of lower abdominal pain for 6 months. Physical examination revealed a lower abdominal tumor, and ultrasonographic examination revealed a cystic ovarian tumor with partially solid character. Laboratory data showed no abnormal findings. Under the diagnosis of ovarian cancer, a laparotomy was performed on July 9, 1981. Left ovarian tumor was found in the lower abdomen with no evidence of metastasis.Trans-abdominal hysterectomy and bilateral salpingo-oophorectomy were performed. Follow-up studies have been conducted for 13 months and the patient had no signs of recurrence as of August, 1982.

## Materials and methods

For light microscopy, tumor tissues were fixed in 10% formalin and divided into five segments. Then three tissue samples were taken from each segment. Sections prepared under the general procedure were stained with hematoxylin and eosin, PAS, Alcian blue (pH 1 and 2.5), mucicarmine, PTAH and Grimelius method. For electron microscopy, tumor tissues were fixed in 2.5% glutaraldehyde and 2% paraformaldehyde, postfixed in 1% $OsO_4$, dehydrated in graded ethanol and embedded in Epon 812. Ultrathin sections cut on an LKB Ultrotome Type 4801A were double stained with uranyl acetate and lead, and examined in a Hitachi HU-12 electron microscope.

## Results

### *Gross findings*

A tumor developed from left ovary was well encapsulated and measured $15 \times 12 \times 9$ cm (Fig. 1). The cut surface showed a large monocystic appearance with partially solid proliferation. Cystic fluid was serous and yellow

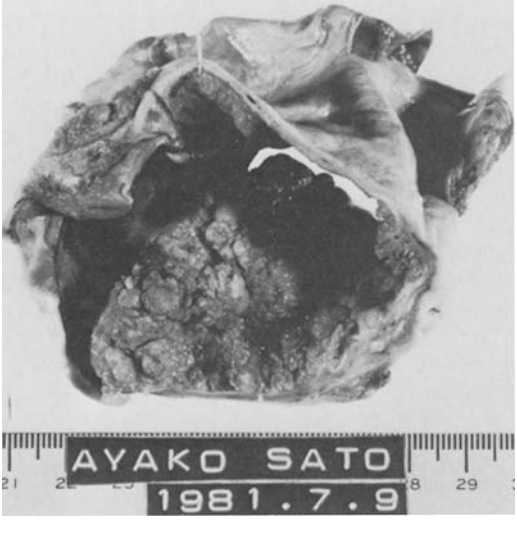


**Fig. 1.** Cut surface of the cystic left-sided ovarian tumor with partial solid proliferation

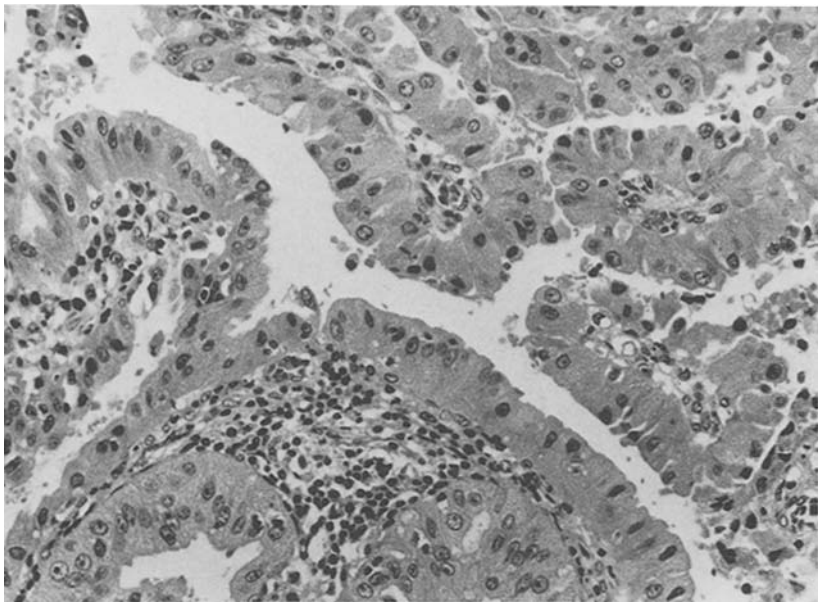

**Fig. 2.** Light micrograph of the oncocytic tumor cells showing papillary proliferation. Prominent stromal infiltration of plasma cells and eosinophils is also shown. H&E. ×400

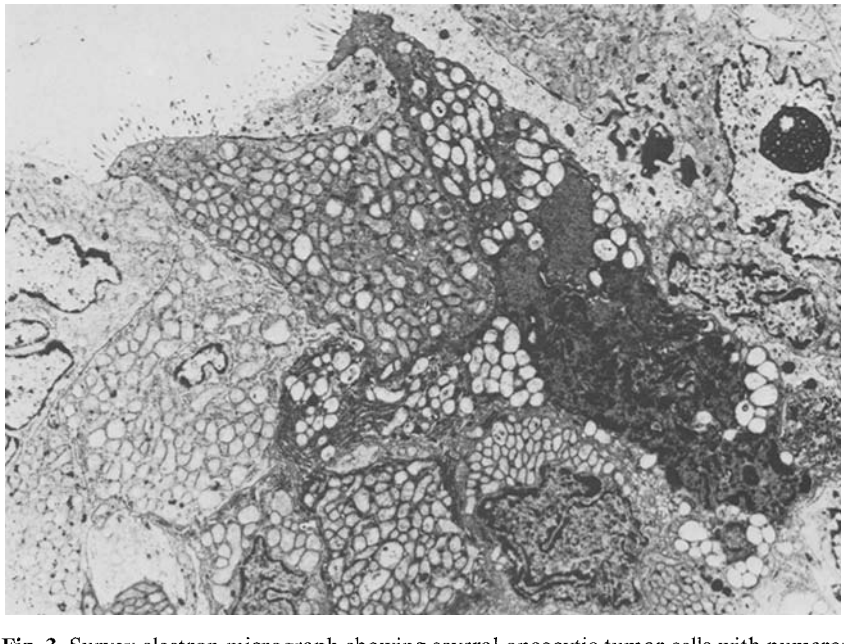

**Fig. 3.** Survey electron micrograph showing several oncocytic tumor cells with numerous mitochondria in their cytoplasm. ×3,375

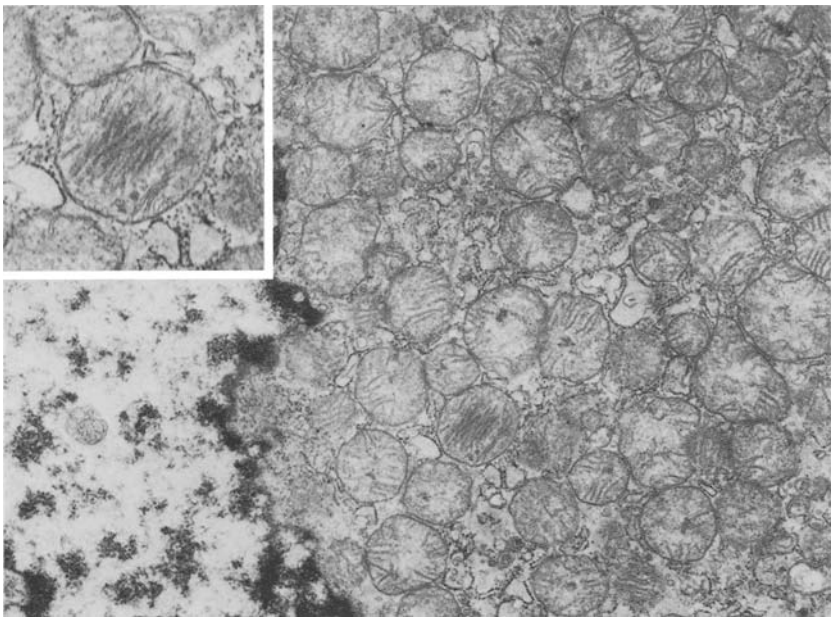

**Fig. 4.** Electron micrograph of a typical oncocyte with cytoplasm occupied by numerous round-shaped mitochondria. ×10,800. *Inset.* Mitochondria with centrally-stacked cristae. ×21,000

in color. No extra-capsular invasion or metastases was found. The uterus and right ovary showed no remarkable findings.

*Light microscopic findings*

Light microscopically, the tumor was diagnosed as well-differentiated adenocarcinoma (Fig. 2). The neoplastic glands, composed of columnar-shaped cells, generally showed papillo-tubular proliferation, and the stromal invasion was also noted in some areas. Most of the tumor cells examined showed a oncocytic character with a faintly granular and eosinophilic cytoplasm. These oncocytes were found in all fifteen parts of the tumor tissues examined and distributed diffusely throughout the tumor tissues. The nuclei with prominent nucleolei were located in the central region of the cytoplasm. Stromal infiltration by plasma cells and eosinophils was prominent in some areas. Grimelius-positive tumor cells were not found. No teratomatous elements were found in either ovary.

*Electron microscopic findings*

Electron microscopically, most of the tumor cells were characterized by numerous mitochondria which occupied most of the cytoplasm (Fig. 3). As in cases of oncocytoma of the salivary gland (Tandler et al. 1970; Sun et al. 1975) the tumor cells with mitochondrial hyperplasia could be classified into two types: typical oncocytes and condensed oncocytes. Condensed

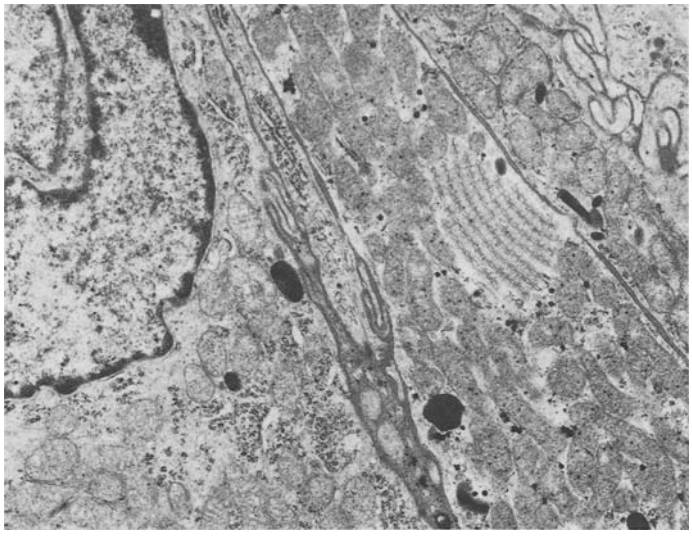

**Fig. 5.** Electron micrograph of annulate lamellae found in the cytoplasm of a typical oncocyte. Numerous mitochondria are also evident. × 11,000

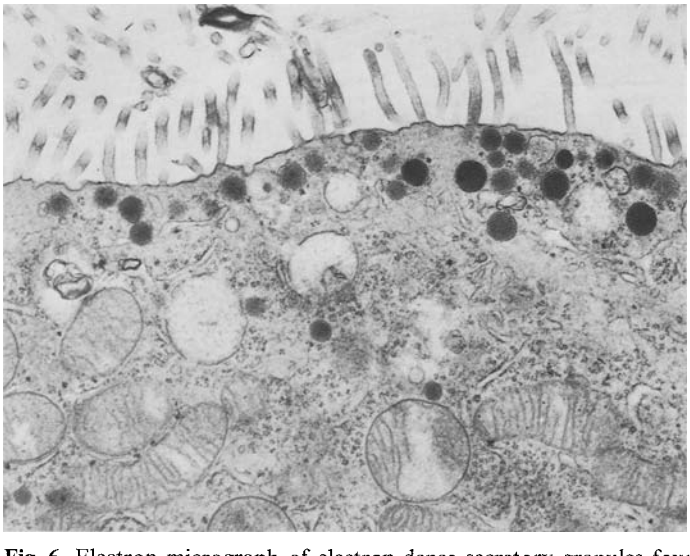

**Fig. 6.** Electron micrograph of electron-dense secretory granules found in the apical portion of a typical oncocyte. Numerous microvilli are also noted. × 13,200

oncocytes seemed to be in the stage of degeneration, whereas typical oncocytes were considered to be active. Typical oncocytes appeared as a group within the glandular structures and possessed numerous mitochondria which occupied most of the cytoplasm (Fig. 4). These mitochondria were round or oval in shape and measured 1.2 μ in diameter. Mitochondrial cristae were sometimes stacked in their center (Fig. 4, inset). Intramitochondrial

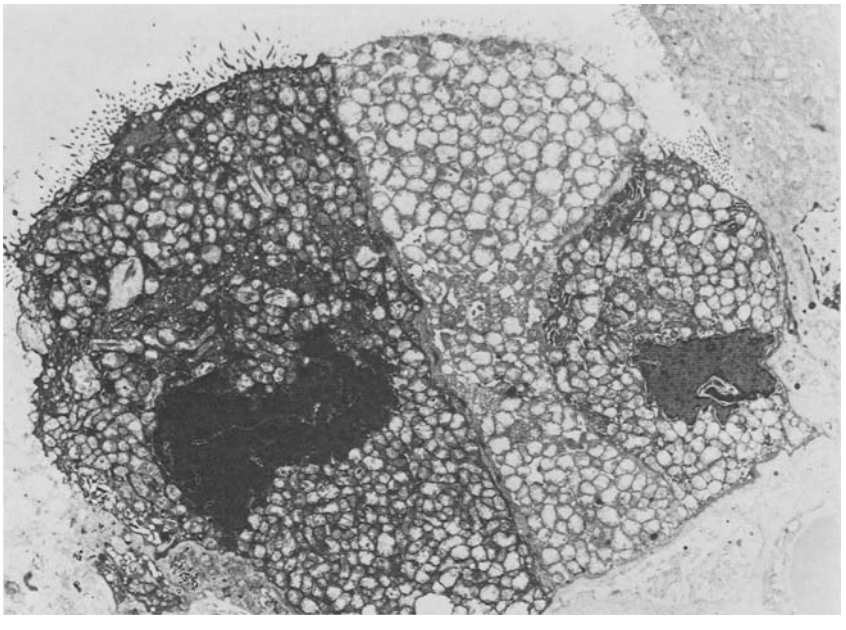

**Fig. 7.** Electron micrograph of some condensed oncocytes with cytoplasm virtually packed by mitochondria. × 2,700

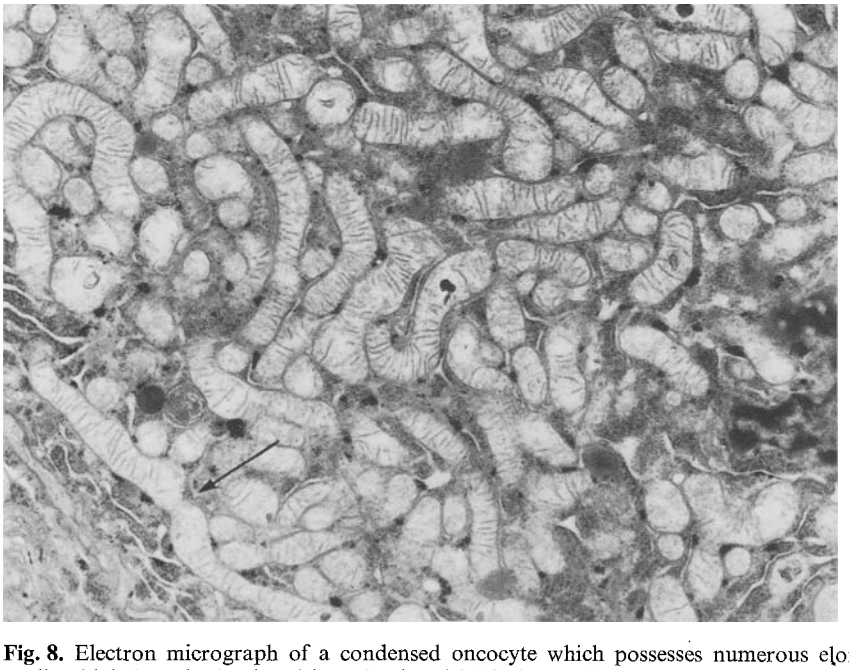

**Fig. 8.** Electron micrograph of a condensed oncocyte which possesses numerous elongated- or discoidal-shaped mitochondria. Mitochondrial fusion is also noted (*arrow*). × 10,800

glycogen granules were sometimes noted, but no dividing mitochondria were found. In the small areas of the cytoplasm where mitochondria were scanty, lipid droplets, glycogen granules, lysosomal granules and well developed rER were noted. Annulate lamellae were also found in the cytoplasm of some typical oncocytes (Fig. 5). Typical oncocytes possessed microvilli on their surface, and cellular attachment was "done" by desmosomes and interdigitation of the plasma membranes. Electron-dense secretory granules, measuring from 200 to 300 nm in diameter, were sometimes found on the apical portion of typical oncocytes (Fig. 6). A basal lamina was also noted. Nuclei with indentation possessed prominent nucleolei, suggesting the malignant nature of the cells. Condensed oncocytes were isolated or appeared as a small group in the nest of the typical oncocytes (Fig. 7). They had dark nuclei with a pyknotic appearance. The cytoplasm of these cells was also filled with numerous mitochondria, which were elongated or discoidal in shape and measured from 0.9 μ to 5.2 μ in length and 0.5 μ in width (Fig. 8). Sometimes, fairly long mitochondria, supposedly resulting from mitochondrial fusion, were also noted (Fig. 8, arrow). Most of the mitochondria in condensed oncocytes were thought to reveal a degenerative process. Intramitochondrial dense bodies were frequently noted. Some lysosomal granules were found but the development of rER was not prominent.

## Discussion

A case of ovarian adenocarcinoma mainly composed of oncocytes was presented and its ultrastructural features were discussed. Although oncocytes and oncocytic tumors have been known to occur in several organs (Hamperl 1962), recent electron microscopic investigations showed a variety of organelles other than mitochondria can cause an eosinophilic cytoplasm. Such organelles were neurosecretory granules (Grimley and Glenner 1967), large secretory granules (Black 1969), smooth and rough endoplasmic reticulum (Jenson and Fechner 1969; Erlandson 1981) and lysosomal-like bodies (Christ and Ozello 1972). Thus, the ultrastructural criteria of mitochondrial hyperplasia for diagnosis of oncocytes and oncocytic tumors were stressed (Tandler et al. 1970; Askew et al. 1971; Fechner and Bentinck 1973). Based on their opinions, most of the tumor cells in the present case possessed the characteristics of oncocytes both on light and electron microscopic levels. Although oncocytes were reported to occur in carcinoid tumor (Walter et al. 1978) and we found electron-dense secretory granules in some oncocytes of the present case, Grimelius-positive tumor cells could not be found even by careful examinations. Thus, we resulted that these granules are not neurosecretory granules but exocrine-type granules.

Although oncocytes have been observed in several mature organs (Tremblay 1969), their existence in female genital tract has not been generally recognized. Oxyphilic (eosinophilic) metaplasia of endometrium (Abell 1975; Hendrickson and Kempson 1980; Demopoulos 1982) and oncocytes in the fallopian tubes (Tremblay 1969) have been reported, however. As

these findings by light microscopy have not been confirmed by the demonstration of mitochondrial hyperplasia by electron microscopy (Hendrickson and Kempson 1980), the existence of oncocytes associated with mitochondrial hyperplasia in the female genital tract is not certain. Thus, one can not reach definite conclusions about the histogenetic origin and histological classification of this tumor. Further studies should be undertaken to ascertain the presence of oncocytes and oncocytic tumors in the female genital tract.

Oncocytic tumors can be either benign or malignant, and the diagnosis of malignancy depends on the lack of encapsulation, local invasion, invasion of blood or lymph vessels, size of the tumor and regional or distant metastases (Meijer and Hoitsma 1982). In the present case, stromal invasion of the tumor cells was characteristic of the malignant nature of this tumor. Meijer and Hoitsma (1982) reported that the malignant oncocytoma shows a relatively benign course after surgical excision, including their case of malignant intrathoracic oncocytoma. In the present case, the patient also showed a good course after the operation, but further clinico-pathologic studies should be done to define the prognosis.

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## References

Abell MR (1975) Endometrial biopsy: normal and abnormal diagnostic characteristics. In: Gold JJ (ed) Gynecologic endocrinology. Harper & Row, New York, pp 156–190

Askew JB jr, Fechner RE, Bentinck DC, Jenson AB (1971) Epithelial and myoepithelial oncocytes. Ultrastructural study of a salivary gland oncocytoma. Arch Otolaryngol 93:46–54

Black WC III (1969) Pulmonary oncocytoma. Cancer 23:1347–1357

Christ ML, Ozello L (1972) Myogenous origin of a granular cell tumor of the urinary bladder. Am J Clin Pathol 56:736–749

Demopoulos RI (1982) Eosinophilic metaplasia. In: Blaustein A (ed) Pathology of the female genital tract. 2th edition. Springer, Berlin Heidelberg New York, pp 264

Erlandson RA (1981) Oncocytes. In: Diagnostic transmission electron microscopy of human tumors. Masson Publishing USA Inc., New York, pp 23–27

Fechner RE, Bentinck BR (1973) Ultrastructure of bronchial oncocytoma. Cancer 31:1451–1457

Grimley P, Glenner G (1967) Histology and ultrastructure of carotid body paragangliomas: comparison with the normal gland. Cancer 20:1473–1488

Hamperl H (1962) Benign and malignant oncocytoma. Cancer 15:1019–1027

Hendrickson MR, Kempson RL (1980) Eosinophilic metaplasia. In: Bennington JL (ed) Surgical pathology of the uterine corpus. WB Saunders, Philadelphia, pp 206–207

Jenson AB, Fechner RE (1969) Ultrastructure of an intermediate Sertoli-Leydig cell tumor: A histologic misnomer. Lab Invest 21:527–535

Meijer S, Hoitsma HFW (1982) Malignant intrathoracic oncocytoma. Cancer 49:97–100

Sidhu GS, Waldo ED (1975) Oncocytic change in mucoepidermoid carcinoma of the parotid gland. Arch Pathol 99:663–666

Sun CN, White HJ, Thompson BW (1975) Oncocytoma (Mitochondrioma) of the parotid gland. An electron microscopic study. Arch Pathol 99:208–214

Tandler B, Hutter RVP, Erlandson RA (1970) Ultrastructure of oncocytoma of the parotid gland. Lab Invest 23:567–580

Tremblay G (1969) The oncocytes. In: Bajusz E, Jasmin G (eds) Meth Achievm Exp Pathol, vol 4. Karger, Basel New York, pp 121–140

Walter P, Warter A, Morand G (1978) Carcinoïde oncocytaire bronchique. Etude histologique, histochimique et ultrastructurale. Virchows Arch [Pathol Anat] 379:85–97

Warter A, Walter P, Sabountchi M, Jory A (1981) Oncocytic bronchial adenoma. Histological, histochemical and ultrastructural study. Virchows Arch [Pathol Anat] 392:231–239

Yu GSM, Rendler S, Herskowitz A, Molnar JJ (1980) Renal oncocytoma. Report of five cases and review of the literature. Cancer 45:1010–1018

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