Virchows Arch [Pathol Anat] (1985) 407:151–158

Virchows Archiv A

Ultrastructural study of glycogen-rich oxyphilic adenoma of the nasopharyngeal minor salivary gland

Yuji Yaku[1], Yutaka Mori[1], Takashi Kanda[2], Toshio Kaneko[2], and Takeshi Kitamura[2]

[1] Department of Otolaryngology, Yokosuka-Kyosai Hospital, Yokosuka, Kanagawa 238
[2] Department of Otolaryngology, School of Medicine, Chiba University, Chiba 280, Japan

Summary. A glycogen-rich adenoma occurring in the minor salivary gland of the nasopharynx in a 41-year-old woman was studied ultrastructurally. The cytoplasm of the tumour cells was abundantly filled with glycogen particles. The tumour cells possessed many mitochondria, a great number of microvillous processes and microvilli and were joined to each other by desmosomes. These findings suggest that this adenoma is of salivary duct epithelial origin most probably from storing striated ductal cells, and is a variant of monomorphic oxyphilic adenoma.

Key words: Glycogen-rich adenoma – Salivary gland – Epithelial cell – Ultrastructure

An extremely rare tumour of the salivary gland, containing a large amount of glycogen particles in the cytoplasm, has been described as glycogen-rich adenoma. This lesion has been included with the nonmucinous "clear cell tumour" because of its light microscopical appearance, and has not yet been given a definite place in the classification of salivary gland tumours. However, recently this tumour has been differentiated from other clear cell tumours by the results of histochemical and ultrastructural analyses demonstrating the intracytoplasmic glycogen (Corridan 1956; Echevarria 1967; Hamperl 1970; Goldman and Klein 1972; Seifert and Donath 1978).

Since Corridan (1956) first reported a glycogen-rich adenoma of parotid gland origin, a few similar cases have been reported in the literature (Feyrter 1963; Goldman and Klein 1972). However, because of its rarity, ultrastructural findings have not been available, but have been reported for the glycogen-rich adenocarcinoma (Mohamed and Cherrik 1975; Mohamed 1976; Kessoku et al. 1980).

The origin of this tumour remains to be identified. The myoepithelial cell (Feyrter 1963; Goldman and Klein 1972) or the epithelial cell of the

Offprint requests to: Y. Yaku at the above address

salivary duct (Mohamed and Cherrick 1975) have been considered to be possible origins of this tumour.

In the present study, we report the light and electron microscopic appearances of a glycogen-rich adenoma of nasopharyngeal minor salivary gland, and discuss the cell of origin of this tumour.

Materials and methods

The patient was a 41-year-old Japanese woman who had been complaining of nasal obstruction for a few weeks. Indirect nasopharyngoscopic examination disclosed a tumour mass, apparently projecting with a broad pedicle from the posterior wall of the nasopharynx. There was no cervical lymphadenopathy, and results of the remainder of the physical examination were within normal limits. Chest X-ray revealed no abnormal findings. The tumour was removed by the transpalatal approach. The tumour was a $3.0 \times 2.5 \times 2.0$ cm mass and was encapsulated. There is no evidence of recurrence 2 years after the operation.

Tissues obtained by surgery were fixed in formalin and embedded in a routine way in a paraffin block. Sections were stained with haematoxylin-eosin, PAS before and after diastase digestion, and alcian blue.

Materials for electron microscopy were cut into small pieces, immediately fixed in 5% glutaraldehyde in 0.1 M phosphate buffer, pH 7.4, postfixed in 1% osmium tetroxide in the same buffer, dehydrated through graded ethyl alcohol and embedded into Epon 812. Ultrathin sections were stained by uranyl acetate and lead citrate, and examined with a JEM 100 cx electron microscope.

Results

Light microscopy

The tumour was encapsulated and the nasopharyngeal surface was covered by a stratified squamous epithelium. Aggregations of small lymphocytes were present underneath the epithelium. The tumour was composed of nests of both clear cells and cells with a fine pale eosinophilic cytoplasm. These tumour nests had grown in a solid pattern and were separated by the fibrous connective tissue stroma. In some areas the two cell types were randomly intermixed, in others they formed separate small groups. The cytoplasm of clear cell was abundant, with a round and slightly eccentric nucleus. The nucleoli of both cell types were unremarkable. Mitotic figures and the luminal structure were also unremarkable (Fig. 1). Clear cells contained a large amount of glycogen in the cytoplasm, as was revealed by PAS stain before and after diastase digestion. Cells with a fine pale eosinophilic cytoplasm were slightly PAS positive (Fig. 2). Alcian blue stain was negative for the cytoplasm of both cells.

The pathological diagnosis was a glycogen-rich adenoma that arose from a minor salivary gland of the nasopharynx.

Electron microscopy

The tumour cell nests were composed of a single cell population. The cells were irregular in shape and extended cytoplasmic processes. The nucleus

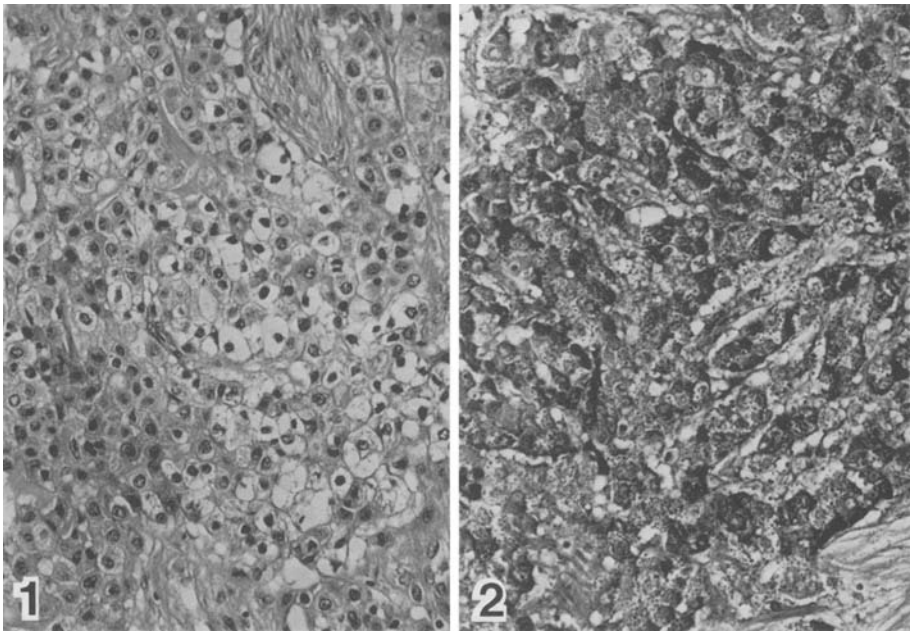

Fig. 1. Histological characteristics of the tumour displaying nests of both clear cells and cells with a pale eosinophilic cytoplasm (H and E, × 500)

Fig. 2. Glycogen granules are present within the tumour cells (P.A.S., × 500)

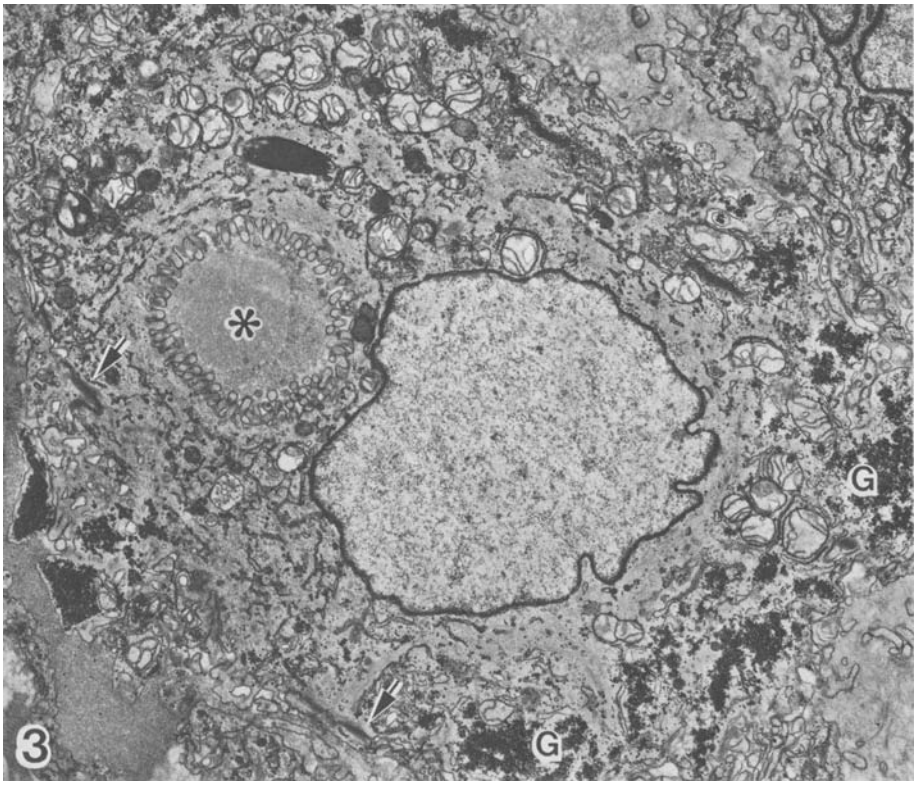

Fig. 3. Tumour cell containing aggregates of glycogen particles (*G*) in the cytoplasm. Note the intracytoplasmic lumina-like structure (*). Arrows indicate desmosomes (× 7,800)

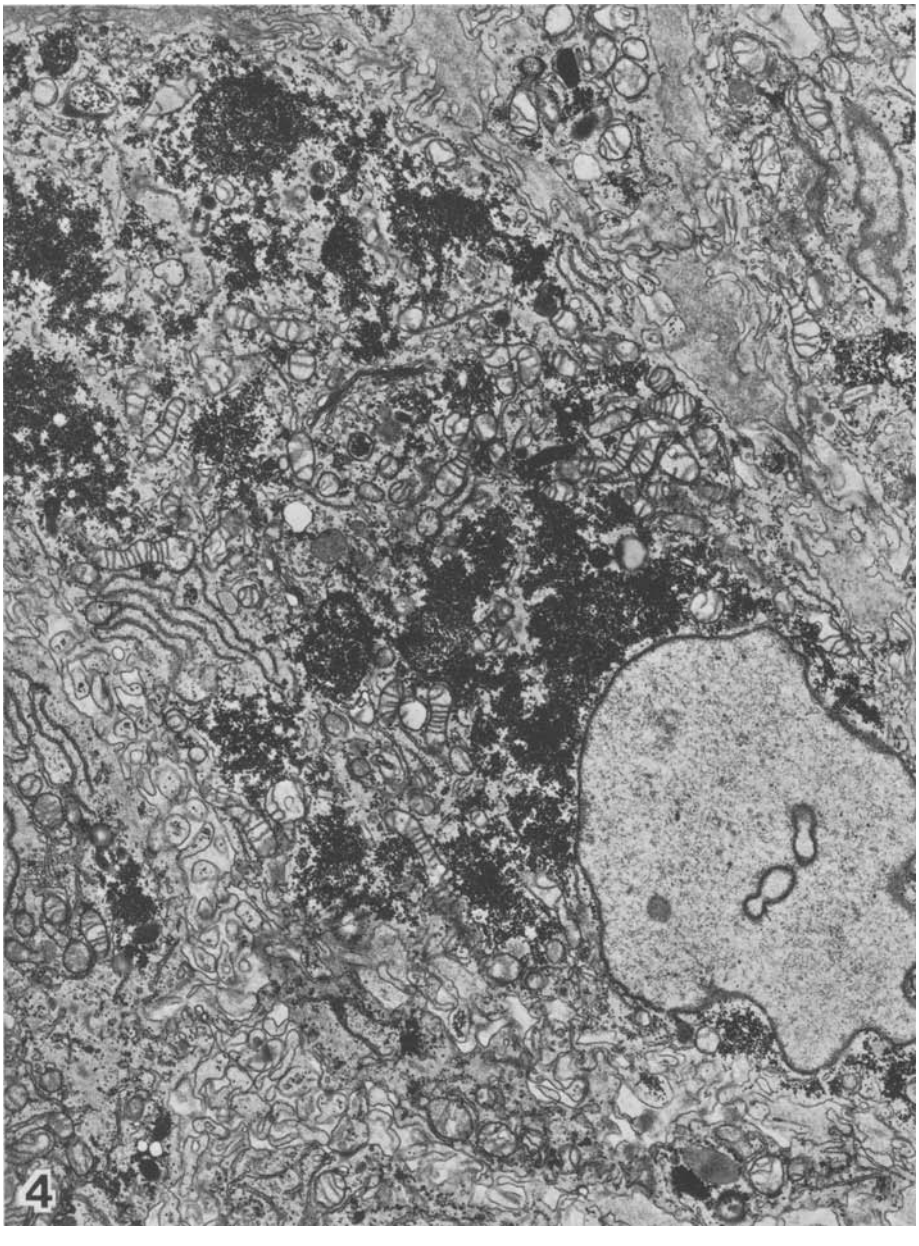

Fig. 4. Tumour cell showing large aggregates of glycogen particles, many mitochondria, a few lamellae of endoplasmic reticulum and Golgi complex in the cytoplasm. A great number of cytoplasmic protrusions interlacing between tumour cells (× 9,000)

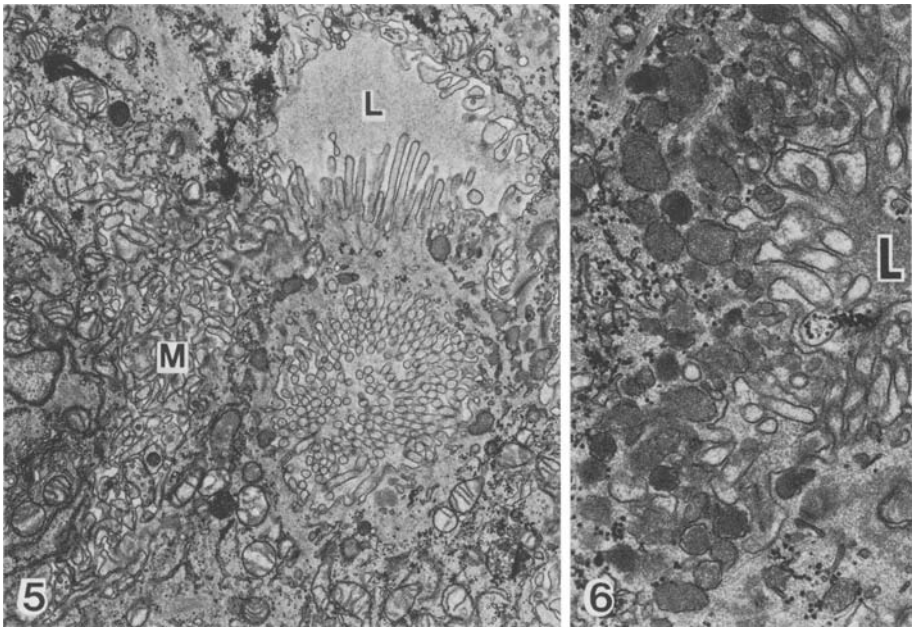

Fig. 5. Prominent microvilli projecting into the lumen (*L*). Microvillous processes (*M*) conspicuously interlacing between adjacent cells (×8,500)

Fig. 6. Tumour cell containing secretory-like granules. Note many microvilli filling in the lumen (*L*) (×21,000)

frequently contained a prominent nucleolus and there were occasional invaginations of the nuclear membrane (Figs. 3, 4). The cells contained a large number of glycogen particles in the cytoplasm, which appeared as large accumulations displacing cytoplasmic organelles (Fig. 4). The quantity of glycogen varied in each tumour cell. The cytoplasmic organelles consisted of many mitochondria, a few lamellae of granular endoplasmic reticulum and Golgi apparatus, several lysosomes and multivesicular bodies, and numerous free ribosomes (Figs. 3, 4). All the tumour cells possessed a great number of cytoplasmic protrusions suggesting microvillous processes, which were conspicuously interlaced between adjacent cells (Figs. 3–5). Desmosomes were commonly noted between the cells (Figs. 3, 4). The cytoplasmic invaginations which represented intracytoplasmic lumina-like structures were occasionally observed. Short microvilli projected into this lumen and were arranged very closely to each other (Fig. 3). Small lumina were sometimes found in the cluster of tumour cells. Microvilli were clearly demonstrable on the luminal surface (Fig. 5). Rare tumour cells possessed secretory-like granules in the luminal site of their cytoplasm, these were membrane-bound with a homogeneous and moderately electron opaque content (Fig. 6). Many cytoplasmic filaments suggesting intermediate filaments were distributed throughout the cytoplasm of the cells. These filaments sometimes formed long bundles or irregular arrangements (Fig. 7). Elongated fibroblasts and collagen fibers were present in the stroma.

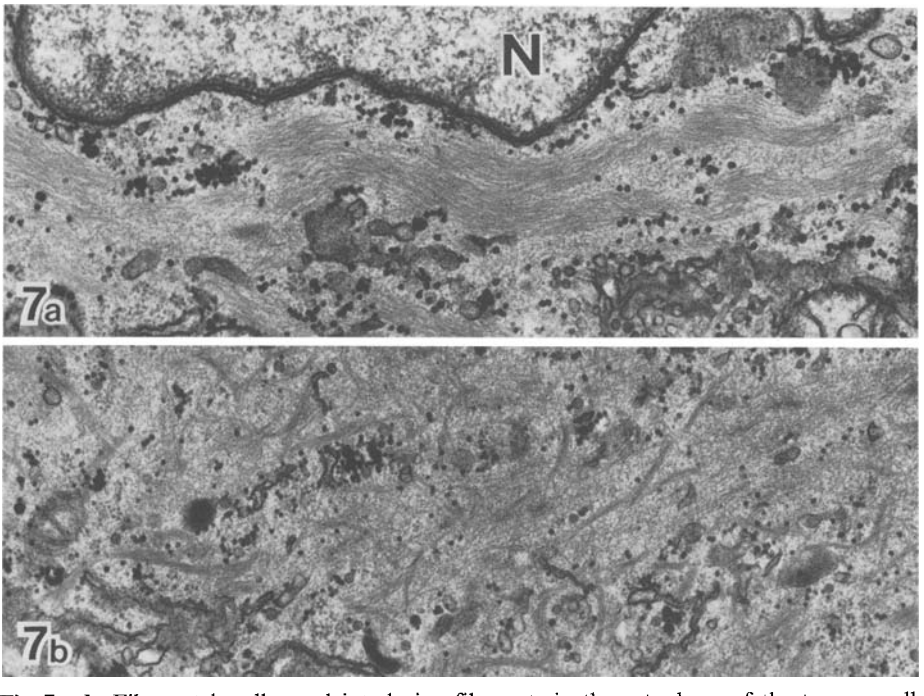

Fig. 7a, b. Filament bundles and interlacing filaments in the cytoplasm of the tumour cell. *N*: nucleus (×23,000, ×23,000)

Discussion

The glycogen-rich tumour of the salivary gland has the appearance of a clear cell tumour by light microscopy. Histologically it is known that the nonmucinous clear cell appearance in the light microscope may be due to a number of factors (1) the clear cell may contain a large amount of glycogen and a normal complement of subcellular organelles in the cytoplasm, (2) the clear cell contains little or no demonstrable glycogen and has a paucity of cytoplasmic organelles, (3) the cell may appear clear because of a fixation artifact (Batsakis 1979).

Seifert and Donath (1978) subclassified seven cell types in clear cell tumours of the salivary gland on the basis of ultrastructural findings – indifferent duct cells, storing striated duct cells, myoepithelial cells, clear epidermoid cells, goblet cells, sebaceous cells and clear acinic cells.

Histochemically, the glycogen revealed a positive reaction to PAS and Best's carmine (Goldstein 1962), which is soluble after diastase digestion. The cell stained negative for mucin by alcian blue and mucicarmine (Spicer et al. 1965). In the electron microscope, it is well known that the glycogen particles stained intensely with lead citrate (Revel 1964), PAM (Thiery 1967), and PA-TSC-SP (Rambourg 1967).

As it is reported that metastatic clear cell tumours such as hyperneph-

roma and parathyroid adenocarcinoma may histochemically simulate the glycogen-rich tumour (Evans and Cruickshank 1970), the exclusion of a primary lesion is necessary for the differentiation of these tumours. In the present case, examination of the kidney was carried out after surgery and revealed normal findings.

As to the origin of the glycogen-rich tumour in the salivary gland, Feyrter (1963) traced the tumour to the myoepithelial cell. Goldman and Klein (1972) thought the glycogen-rich adenoma was a mixed tumour in which the myoepithelial component was not associated with the production of discernible stromal mucopolysaccharides. On the other hand, Mohamed and Cherrick (1975) considered, on the ground of ultrastructural analyses, that a case of glycogen-rich adenocarcinoma of the palatal minor salivary gland was of epithelial origin, most probably of ductal cells. However, Mohamed (1976) reported another case of glycogen-rich clear cell carcinoma of the palate which arose from the palatal epithelium and was very likely a variant of the mucoepidermoid carcinoma.

The accumulations of glycogen have been observed in both the myoepithelial cells (Donath and Seifert 1972) and the ductal cells (Hübner 1969; Yaku et al. 1984) of salivary duct carcinoma. Hamperl (1970) stressed the fact that both normal myoepithelial cells and the myoepithelial cells of mixed tumours sometimes contain large quantities of glycogen. It was also reported that the ductal cells of the fetal salivary glands contained large amounts of glycogen in the cytoplasm (Dietrich 1977; Donath et al. 1978; Yaku 1983). Therefore, it seems likely that the glycogen-rich adenoma (and, from reported data adenocarcinoma) may arise from both ductal cells and myoepithelial cells. However, as the glycogen alone is of little cytological significance for determining the cell of origin, further ultrastructural analysis is called for.

In our case, the glycogen-rich tumour cells had greatly developed microvillous processes and many mitochondria. These cells were joined to each other by both interlacing microvillous processes and a few desmosomes. They sometimes formed small lumina with the projection of many microvilli at the luminal border. Although numerous intermediate filaments were present in the cytoplasm, typical myofilaments and pinocytotic vesicles could not be demonstrated. These ultrastructural findings support the suggestion that the glycogen-rich tumour in our case is not of myoepithelial, but rather of ductal cell origin, most probably from striated ductal cells. The cytological characteristics of the tumour cells in our case, with many mitochondria and microvillous processes, are similar to those of the storing striated ductal cells that were subclassified in clear cell tumours by Seifert and Donath (1978). Generally, it is believed that the oxyphilic adenoma (oncocytoma) which consists of mitochondria-rich cells, arises from striated ductal cells. Further, glycogen has been observed in the cells of oxyphilic adenoma (Tandler et al. 1970; Sun et al. 1975). Therefore, it may be supposed that the glycogen-rich adenoma in our case is a variant of monomorphic oxyphilic adenoma.

References

Batsakis JG (1979) Tumors of the head and neck. 2. edition. Baltimore, Williams and Wilkins Co, p 45

Corridan M (1956) Glycogen-rich clear cell adenoma of the parotid gland. J Pathol Bacteriol 72:623–626

Dietrich H (1977) Histologische und ultrastrukturelle Untersuchungen zur Frage der Zelldifferenzierung von Drüsenepithelien und Myoepithelzellen während der Parotisentwicklung des Menschen. Diss Hamburg

Donath K, Seifert G (1972) Zur Diagnose und Ultrastruktur des tubularen Speichelgangcarcinoms. Virchow Arch [Pathol Anat] 356:16–31

Donath K, Dietrich G, Seifert G (1978) Entwicklung und ultrastrukturelle Cytodifferenzierung der Parotis des Menschen. Virchow Arch [Pathol Anat] 378:297–314

Echevarria RA (1967) Ultrastructure of the acinic cell carcinoma and clear cell carcinoma of the parotid gland. Cancer 20:563–571

Evans RW, Cruickshank AH (1970) Epithelial tumors of the salivary glands, vol. 1. Philadelphia, W.B. Saunders, p 109

Feyrter F (1963) Über das glycogenreiche retikulierte Adenom der Speicheldrüsen. Z Krebsforsch 65:446–454

Goldstein DJ (1962) Ionic and non-ionic bonds in staining, with special reference to the use of urea and NaCl in the staining of elastic fibers and glycogen. Q J Micr Sci 103:477–492

Goldman RL, Klein HZ (1972) Glycogen-rich adenoma of the parotid gland. Cancer 30:649–754

Hamperl H (1970) The myothelia (myoepithelial cells). Normal state; regressive changes; hyperplasia; tumors. Current Topics Pathol 53:162–220

Hübner G, Kleinsasser O, Klein HJ (1969) Zur Feinstruktur der Speichelgangcarcinome. Virchow Arch [Pathol Anat] 346:1–14

Kessoku A, Kitamura T, Kaneko T, Kanda T, Suzuki H (1980) Zur Ultrastruktur des glycogenreichen Adenokarzinoms der Parotis. Laryng Rhinol 59:271–273

Mohamed AH (1976) Ultrastructure of glycogen-rich clear cell carcinoma of the palate. J Oral Pathol 5:103–121

Mohamed AH, Cherrick HM (1975) Glycogen-rich adenocarcinoma of minor salivary glands. A light and electron microscopic study. Cancer 36:1057–1066

Rambourg A (1967) An improved silver methenamine technique for the detection of periodic acid-reactive carbohydrates with the electron microscope. J Histochem Cytochem 15:409–412

Revel JP (1964) Electron microscopy of glycogen. J Histochem Cytochem 12:104–114

Seifert G, Donath K (1978) Über das Vorkommen sog. heller Zellen in Speicheldrüsentumoren. Z Krebsforsch 91:165–182

Speicer SS, Leppi TJ, Stoward PJ (1965) Suggestions for a histochemical terminology of carbohydrate-rich tissue components. J Histochem Cytochem 13:599–603

Sun CN, White HJ, Thompson BW (1975) Oncocytoma (mitochondioma) of the parotid gland. Arch Pathol 99:208–214

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

Thiery JP (1967) Mise en evidence des polysaccharides sur couoes fines en microscopie electronique. J Microbiol 6:987–1018

Yaku Y (1983) Ultrastructural studies on the development of human fetal salivary glands. Arch Histol Jap 46:677–690

Yaku Y, Yoshihara T, Miyazaki M, Kanda T (1984) Ultrastructural study on salivary duct carcinoma of the parotid gland. J Clin Elect Micro 17:109–116

Accepted January 16, 1985