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Undifferentiated carcinoma of the parotid gland

Case report with electron microscopic findings

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Summary. Two cases of undifferentiated carcinoma of the parotid gland were studied by light and electron microscopy. Light microscopy showed nests of ovoid cells with scanty cytoplasm and pyknotic nuclei in two cases. One case was the small-cell type, and another one was the large-cell type histopathologically. Electron microscopy showed two distinct cell types in each tumor: Case 1 (small-cell type). – An epithelial-like cell, and an irregular-shaped cell containing bundles of filaments suggesting myoepithelial differentiation. Case 2 (large-cell type). – An epithelial-like cell, and a large cell containing secretory-like granules. These findings support a salivary duct epithelial origin for these tumors.

Key words: Undifferentiated carcinoma – Parotid gland – Myoepithelial cell – Epithelial cell – Ultrastructure

Undifferentiated carcinomas of the parotid gland are rare and highly malignant. They make up from 1 to 4.5% of all malignant epithelial neoplasms of the parotid gland (Eneroth 1971; Blanck et al. 1974). This type of carcinoma has been reported in the literature (Blanck et al. 1974; Wirman and Battifora 1976; Dubois et al. 1977; Donath et al. 1982; Nagao et al. 1982) but because of its rarity, ultrastructural findings in undifferentiated carcinomas of the parotid gland have been mentioned in only a few reports (Wirman and Battifora 1976; Donath et al. 1982). Recently, Donath et al. (1982) subclassified the cell types of undifferentiated carcinoma of the parotid gland on the basis of ultrastructural analysis. Nagao et al. (1982) divided their cases of this carcinoma into the small-cell type and the large-cell type histopathologically.

In the present study, we report the light and electron microscopic appearances of two cases of undifferentiated carcinoma of the parotid gland origin.

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One is the small-cell type, and the other is the large-cell type light microscopically.

Materials and methods

Case 1 was a 52-year-old man with a tumor in his right parotid gland. Case 2 was a 42-year-old woman with the tumor also in the right parotid gland. Both were operated on at the Chiba University Hospital.

Tissues obtained by surgery were embedded in a routine way in paraffin blocks. Sections were stained with hematoxylin-eosin.

Materials for electron microscopy were cut into small pieces, fixed in 3% glutaraldehyde in 0.1 M phosphate buffer, pH 7.4, post-fixed in 1% osmium tetroxide in the same buffer, dehydrated in graded ethyl alcohol and embedded into Epon 812. Ultrathin sections were stained by uranyl acetate and lead citrate, and examined with a Hitachi HU-12 electron microscope.

Results

Light microscopy

Case 1. The tumor revealed a solid pattern. The tumor nest was composed of small and ovoid cells, and was not circumscribed. The tumor cells had scanty cytoplasm and the nuclei coarsely clumped chromatin. No discernible glandular or organoid structure was found. Eosinophilic fibrillar stromal proliferation was severe (Fig. 1 a).

Case 2. The tumor was composed of well defined nests of round to ovoid cells and had grown in a solid pattern. The tumor cells were bigger than those of case 1. Although an indistinct adenoid cystic structure was found in some parts of the tumor cell cluster, it appeared as one undifferentiated type collectively (Fig. 1 b).

Electron Microscopy

Case 1. The tumor cell nests were composed of a bimodal cell population. In some areas the two cell types were randomly intermixed, in others they formed separate small groups. The first cell type was small and round or oval shaped with a large nucleus and scanty cytoplasm. The nucleus frequently contained a prominent nucleolus and there were occasional invaginations of the nuclear membrane. The cytoplasmic organelles consisted of several mitochondria and lysosomes, free ribosomes and very few lamellae of endoplasmic reticulum. Desmosomes were seldom observed between these tumor cells. Extensions of cytoplasm suggesting microvillous processes extended into occasional widening of the intercellular space (Fig. 2). These first type cells predominated and were mainly located in the central portion of the tumor cell nest.

The second cell type was a little larger and was irregularly shaped. These cells were mainly located peripherally. They also contained large nuclei

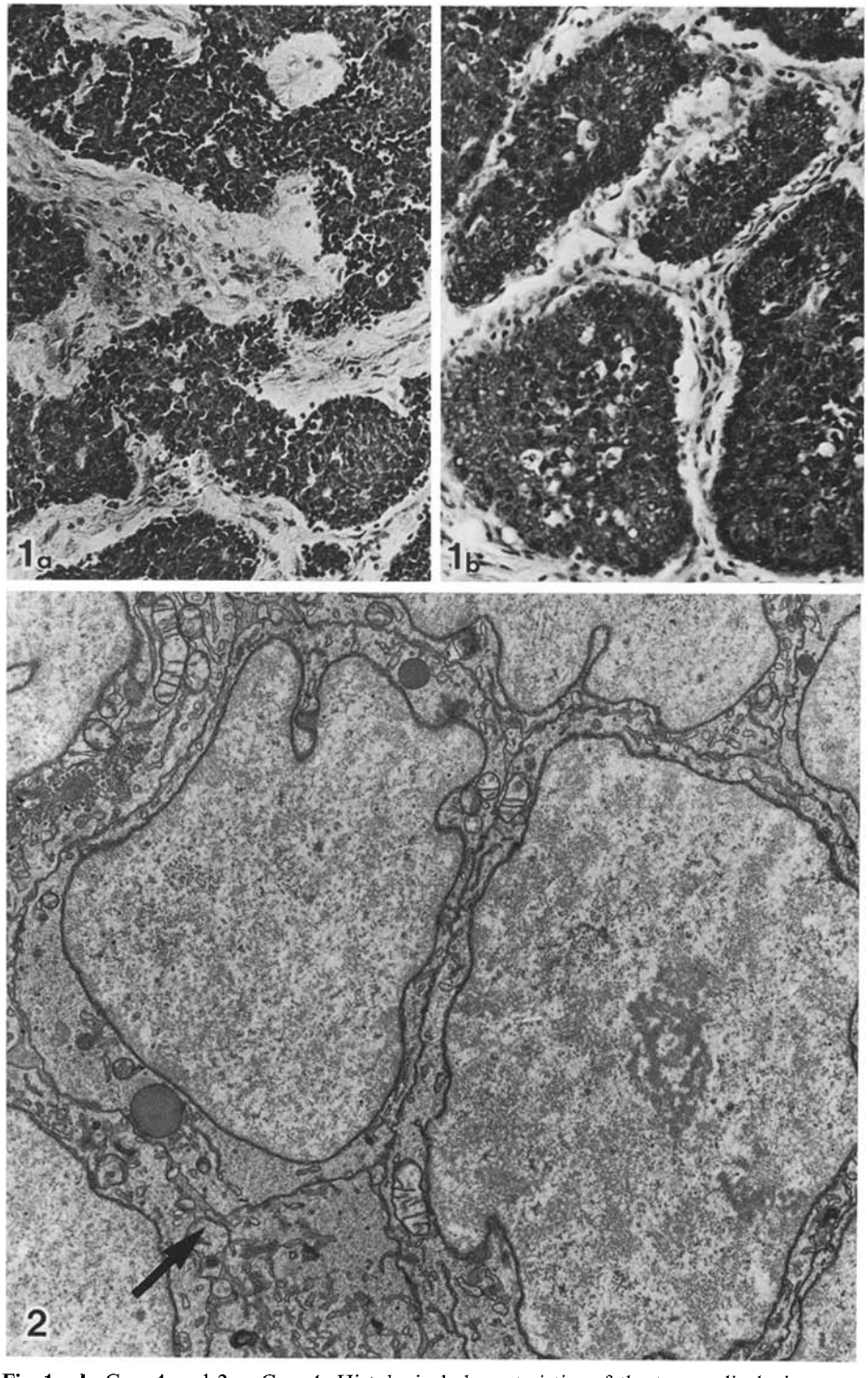


Fig. 1a, b. Case 1 and 2. **a** Case 1. Histological characteristics of the tumor displaying nests of small tumor cells with oval, hyperchromatic nuclei and scanty cytoplasm (× 300). **b** Case 2. Well defined tumor nests showing indistinct adenoid cystic structure, but solid (× 300)

Fig. 2. Case 1. Undifferentiated cells showing large centrally located nuclei with frequent invaginations and scanty cytoplasmic organelles. Note the blunt microvillous-like cytoplasmic extensions (*arrow*) (× 9,300)

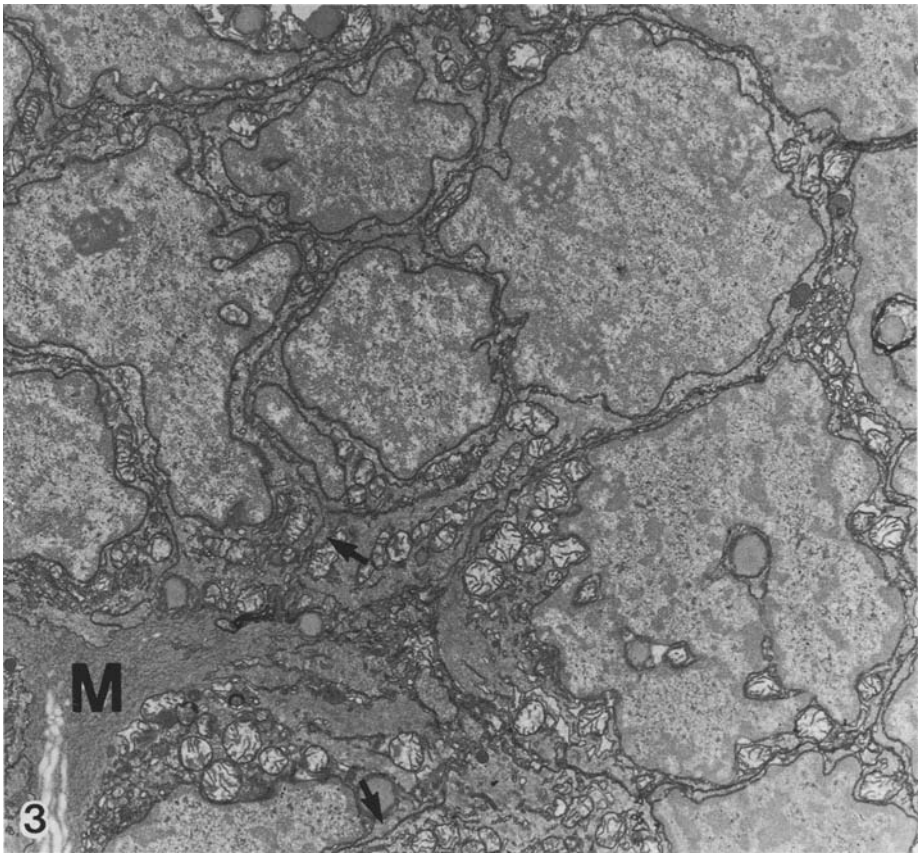


Fig. 3. Case 1. Group of myoepithelial-like cells showing difference in shape. Cells are conjoined by a few desmosomes (*arrow*). Myofilaments are discernible within the cytoplasm. Note filamentous material (*M*) in the intercellular space (× 7,000)

with invaginations of the nuclear membrane and prominent nucleoli. Moderate numbers of mitochondria, a few lysosomes, lipid droplets, lamellae of rough endoplasmic reticulum, and free ribosomes were distributed throughout the cytoplasm. The cells were conjoined by a small number of desmosomes (Fig. 3). Bundles or irregular arrays of myofilaments were seen in their cytoplasm (Fig. 4a, b). Pinocytotic vesicles were found along the plasma membrane of some cells. An accumulation of filamentous or amorphous matrial was present between the cells (Fig. 3).

No structure resembling neurosecretory or secretory granules was seen in either of these cell types.

Case 2. The neoplastic mass mostly consisted of one cellular type. This tumor cell was polygonal and contained a nucleus with one or two prominent nucleoli. Moderate numbers of mitochondria and lipid droplets were

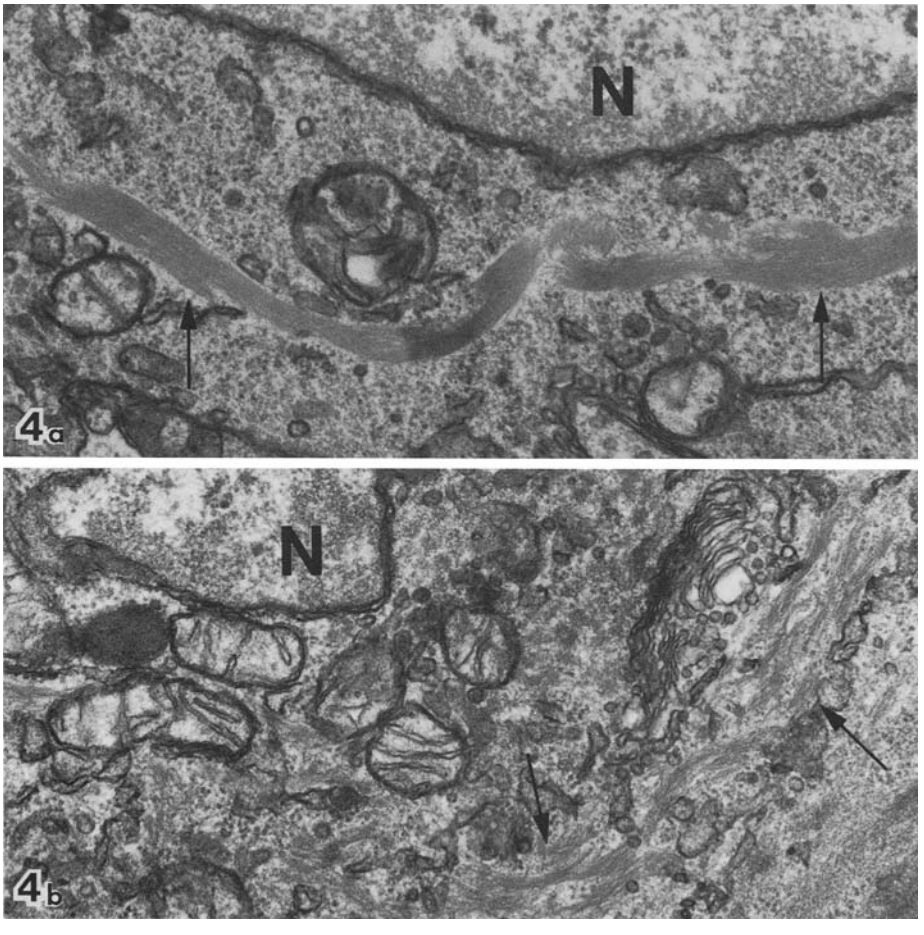
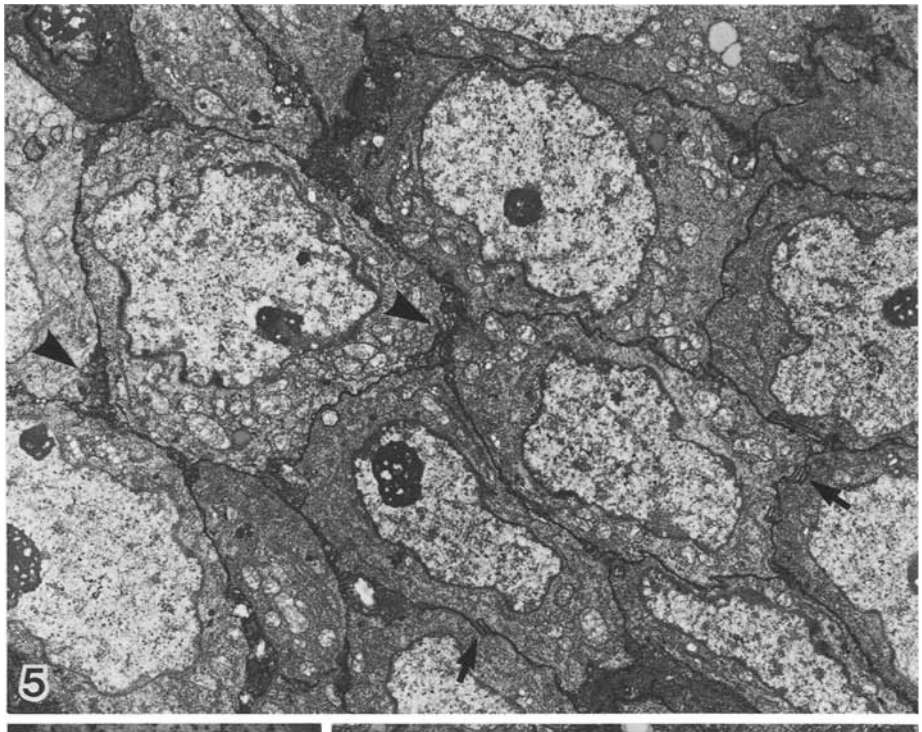


Fig. 4a, b. Case 1. Myofilament bundle (*arrow*) and interlacing myofilaments (*arrow*) in the cytoplasm of the myoepithelial-like cell (× 32,000, × 32,000)

distributed throughout the cytoplasm. Microvillous protrusions of the cytoplasm into the intercellular space and the infoldings of plasma membrane between tumor cells were observed. No desmosomes or cytoplasmic filaments were found (Fig. 5).

Among the tumor cells, some infrequently found large cells were seen containing many vesicles presumed to be secretory granules and many electron dense cytoplasmic inclusions. The secretory-like granules of these tumor cells were membrane-bound and had moderately electron dense homogeneous content with an electron lucent core. Glycogen particles were observed throughout the cytoplasm of these cells (Fig. 6).

The fibrotic stroma and degenerate tumor cells were observed in the area which presented the adenoid cystic structure by light microscopy.



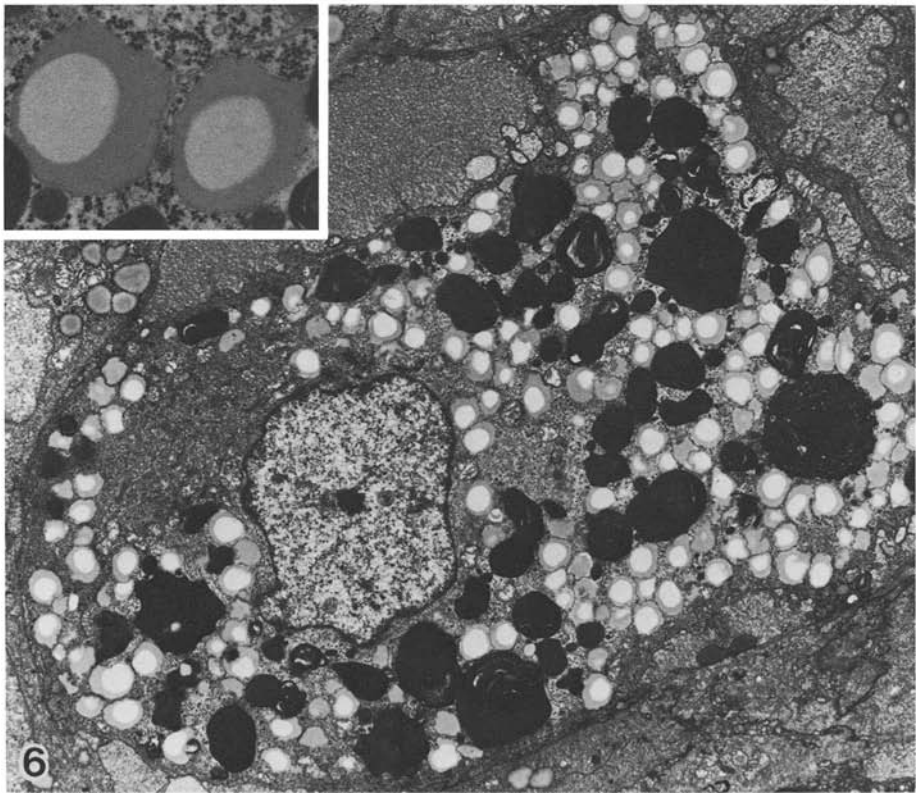


Fig. 5. Case 2. Tumor cells showing microvillous protrusions of the cytoplasm in the intercellular space (*arrow head*) and lateral foldings of the plasma membrane (*arrow*). Note prominent nucleoli and organelle-poor cytoplasm (× 4,800)

Fig. 6. Case 2. Tumor cell containing secretory-like granules. Note many electron dense inclusions and glycogen particles throughout cytoplasm (× 4,800). *Inset:* Higher magnification of secretory-like granules (× 17,000)

Discussion

The undifferentiated and poorly differentiated carcinomas of the parotid gland usually grow in solid or trabecular patterns and have been divided into spheroidal, spindle, round and small cell types in light microscopy (Batsakis 1979). This simplistic cell typing, however, is of little clinicopathological significance. For further cytological and morphological analysis of undifferentiated carcinomas, ultrastructural studies should be carried out.

Koss et al. (1972) reported 14 cases of anaplastic carcinomas of minor salivary gland origin. Because of their striking morphological resemblance to bronchogenic oat cell carcinoma of the lung, they speculated that these tumors were of neuroectodermal origin.

Blanck et al. (1974) described the histological and clinical features of poorly differentiated solid parotid carcinomas in a series of cases with a long control period.

Wirman and Battifora (1976) distinguished epithelial-like cells and myoepithelial-like cells in a small cell undifferentiated carcinoma of the parotid gland ultrastructurally, and considered that this tumor derived from the salivary duct epithelium. No neurosecretory granules were demonstrated in their case electron microscopically.

Donath et al. (1982) subclassified five cell types in their 11 cases of undifferentiated carcinomas of the parotid gland by ultrastructural findings – undifferentiated epithelial cells, undifferentiated ductal cells, secretory active cells, immature epidermoid cells and myoepithelial cells. They concluded that the salivary duct system can be considered to be a tumor matrix of undifferentiated carcinoma, because homogeneous cell types – except the epidermoid cell – existed in the embryonal development of the human parotid gland.

Nagao et al. (1982) divided their 18 cases of undifferentiatd carcinoma of the parotid gland into the small-cell type (12/18) and the large-cell type (6/18) on the basis of the cell size. They examined one case (small-cell type) electron microscopically, and reconfirmed the results of Wirman and Battifora (1976). As for the large-cell type, they suggested this variety is a variant of poorly differentiated epidermoid carcinoma or adenocarcinoma.

In our cases, the tumor of case 1 corresponded to the small-cell type, and that of case 2 to the large-cell type histopathologically (Nagao et al. 1982).

Ultrastructurally, the tumor cells of case 1 consisted of a bimodal cell population – myoepithelial-like cell and undifferentiated cells. Myoepithelial-like cells were not predominant in the tumor in case 1. Their myofilaments were poorly developed, and pinocytotic vesicles and desmosomes were not marked, as reported in the typical myoepithelial cell (Tandler 1965) and the myoepithelioma of the salivary gland (Calvin et al. 1974). Therefore, the tumor in case 1 did not fit into the category of myoepithelioma.

Though the undifferentiated cells of case 1 presented no characteristic features, they had poorly developed cytoplasmic extensions, suggesting mi-

crovillous processes. This finding supports the suggestion that these cells are of epithelial origin. The finding that tumor cells in case 1 were epithelial-like or myoepithelial-like cells, is similar to the findings in the case reported by Wirman (1976). The tumor cells of case 2 were also undifferentiated morphologically. However, microvillous protrusions and infoldings of the plasma membrane indicated their epithelial features, in spite of the lack of desmosomes. These ultrastructural findings in case 1 and 2 support the suggestion that they originate from the salivary duct epithelium and particularly from the intercalated ducts.

It was not clear whether the large tumor cells containing many secretory-like granules in case 2 were derived from undifferentiated tumor cells. These granules were different from the secretory granules reported in acinic cell carcinomas of the parotid gland (Erlandson 1972; Bloom 1979) and in the acinar cell of the normal parotid gland (Riva and Riva-Testa 1973). These large tumor cells were considered to be of little significance in the second tumor, because of their scarcity and the existence of many electron dense cytoplasmic inclusions suggesting low cellular activity.

According to the ultrastructural cellular subclassification of Donath et al. (1982), it can be considered that the undifferentiated cells in case 1 correspond to undifferentiated epithelial cells, the myoepithelial-like cells in case 1 to myoepithelial cells and the undifferentiated tumor cells in case 2 to undifferentiated ductal cells. The large tumor cells in case 2 containing many secretory-like granules, have not yet been reported in the previous literature on undifferentiated parotid carcinoma. This cell type might be newly subclassified as an acinar-like cell.

The patient in case 1 subsequently developed multiple metastases to the brain and died 27 months after surgery. Case 2 survived, is well, and is free of neoplasm about 2 years after the operation.

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