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Case report

Sebaceous carcinoma of the parotid gland

An immunohistochemical and ultrastructural study

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Summary. Sebaceous carcinoma of salivary gland origin is extremely rare and, because of its rarity, the clinicopathological characteristics and the histogenesis are not fully understood. We present a case of sebaceous carcinoma of the parotid gland which brings the total number of reported cases to 22.

The tumor showed epithelial cell nests which were mainly composed of sebaceous cells with marked cellular atypia. In most of the nests, glandular spaces lined by ductal epithelium were present. Scattered mucous cells and flattened eosinophilic cells at the periphery of the nests were also seen. Ultrastructural and immunohistochemical observations of the tumour revealed coexistence of sebaceous and glandular differentiations in some tumour cells. Tumour cells with lipid granules often participated in the formation of glandular structures or exhibited intracytoplasmic lumina, and immunohistochemical localization of lactoferrin and secretory component, the functional markers of ductal epithelium of salivary gland, was demonstrated not only in duct-forming tumour cells but also in many sebaceous tumour cells.

It seems likely that sebaceous carcinoma originates from pluripotential duct cells which can differentiate into sebaceous, ductal and mucous cells.

Key words: Sebaceous carcinoma – Parotid gland – Salivary gland – Ultrastructure – Immunohistochemistry

Introduction

Sebaceous neoplasms of salivary gland origin are extremely rare (Seifert et al. 1984), while sebaceous differentiation in parotid and submandibular glands is known as a relatively common feature (Meza-Chávez 1949). Sebaceous tumours of the salivary glands have been classified into adenomas and carcinomas; the adenomas are further subclassified into a sebaceous adenoma and sebaceous lymphadenoma. The carcinomas are similarly classified into a sebaceous carcinoma and sebaceous lymphadenocarcinoma (Gnepp 1983).

Sebaceous carcinoma is a malignant tumour composed predominantly of sebaceous cells with various degrees of cellular atypia. Gnepp (1983) collected 125 cases of sebaceous neoplasms of salivary gland origin from the literature, among which 19 cases were regarded as a sebaceous carcinoma and analyzed clinicopathologically. However, owing to the rarity of the tumour its clinicopathological behavior and histogenesis are not fully understood. This paper describes a case of sebaceous carcinoma arising in the parotid gland along with a brief review of the literature. The possible histogenesis of this unique malignancy is discussed on the basis of ultrastructural and immunohistochemical features of the present case.

Case report

A 50-year-old Japanese man with about a 1-year history of right facial paralysis presented with a firm tumour mass, 1 cm in diameter, at the lower portion of the right parotid gland. The tumour was adhered to surrounding soft tissues but the overlying skin was normal in appearance. The mass was totally excised for biopsy and the tentative diagnosis of oncocytoid adenocarcinoma was made. The patient received a total 2000 mg of Timadin and 12 g of Minofultol. Three months later, difficulty in hearing on the affected side and recurrent growth at the primary site were recognized. The new tumour, measuring $22 \times 15 \times 10$ mm, was excised together with several swollen juxtaparotid lymph nodes. Histological diagnosis of sebaceous carcinoma was made on the surgical specimen. No invasion into the adjacent parotid gland tissue nor metastasis

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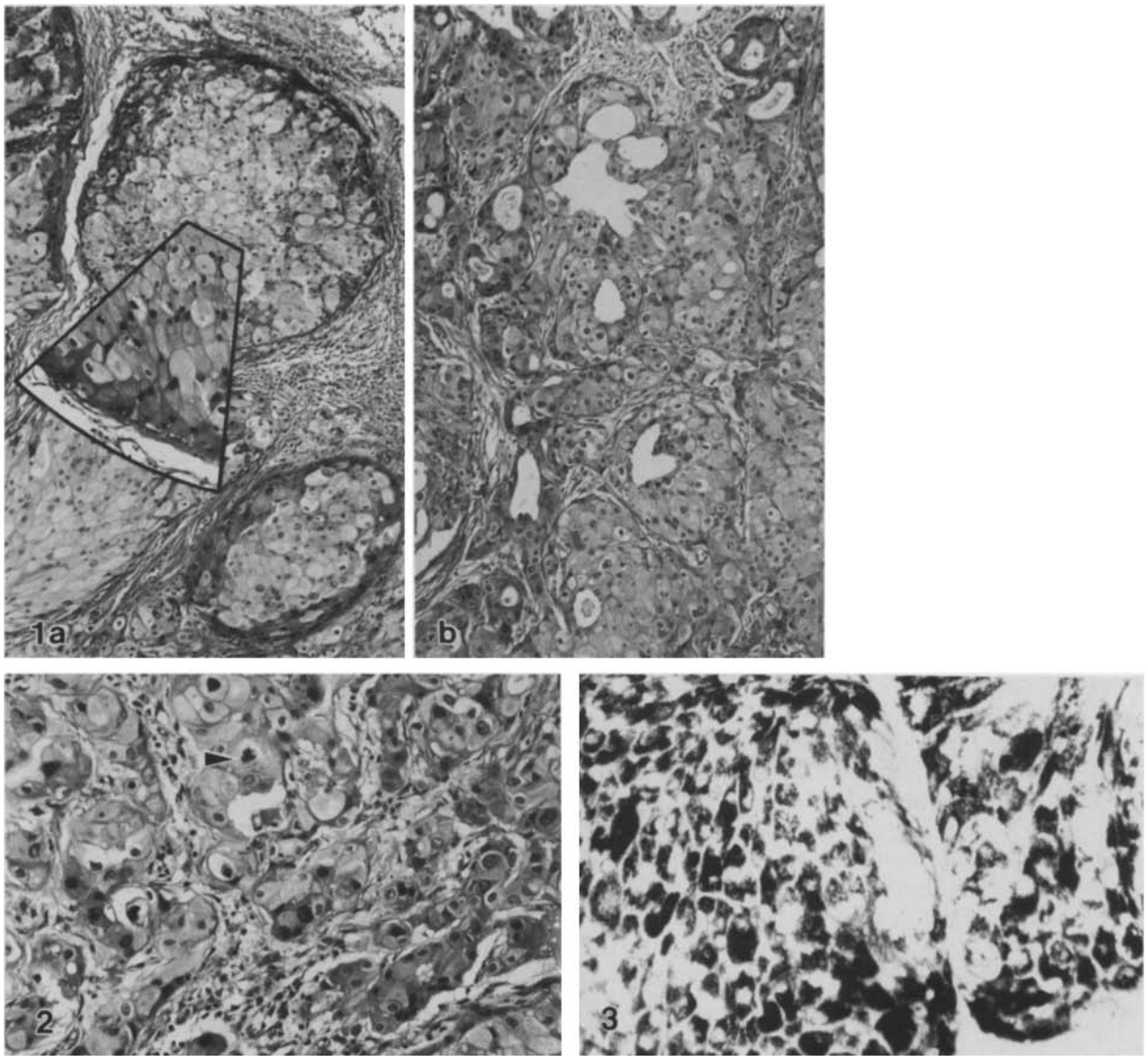


Fig. 1. The recurrent tumour. (**a**) Tumour nests are mainly composed of sebaceous-like cells with a voluminous, finely granular or vacuolated cytoplasm. The outermost basaloid cells of the nests are often flattened and show an eosinophilic cytoplasm and dark nucleus (HE, ×75, insert; ×150). (**b**) Glandular spaces lined by duct-like epithelium with apocrine-like secretion are seen in many nests (HE, ×100)

Fig. 2. Tumour cells of the sebaceous carcinoma show marked cellular and nuclear pleomorphism and high mitotic activity (*arrowhead*) (HE, ×200)

Fig. 3. Abundant lipid material is revealed in the majority of tumour cells (Sudan black B staining, ×250)

to the lymph nodes examined was found. After three years, a metastatic lesion was found at the cerebello-pontine angle and a palliative operation was done. The patient died of this intracranial tumor at nineteen months after the operation.

Results

The biopsied specimen, diagnosed as oncocytoid adenocarcinoma, showed solid tumour cell nests infiltrating into normal salivary gland tissues. These nests were composed of large, eosinophilic epithelial cells with abundant granular cytoplasm and a vesicular and/or pyknotic nucleus. In places, the tumour cells were arranged in a glandular or tubular fashion. The lining epithelial cells often showed apocrine-like secretion.

The recurrent lesion was composed of numerous large epithelial sheets separated by a fibrosed connective tissue stroma with a mild to moderate chronic inflammatory infiltrate (Fig. 1). The tumour nests were mainly composed of sebaceous-like cells which had a voluminous, finely granular

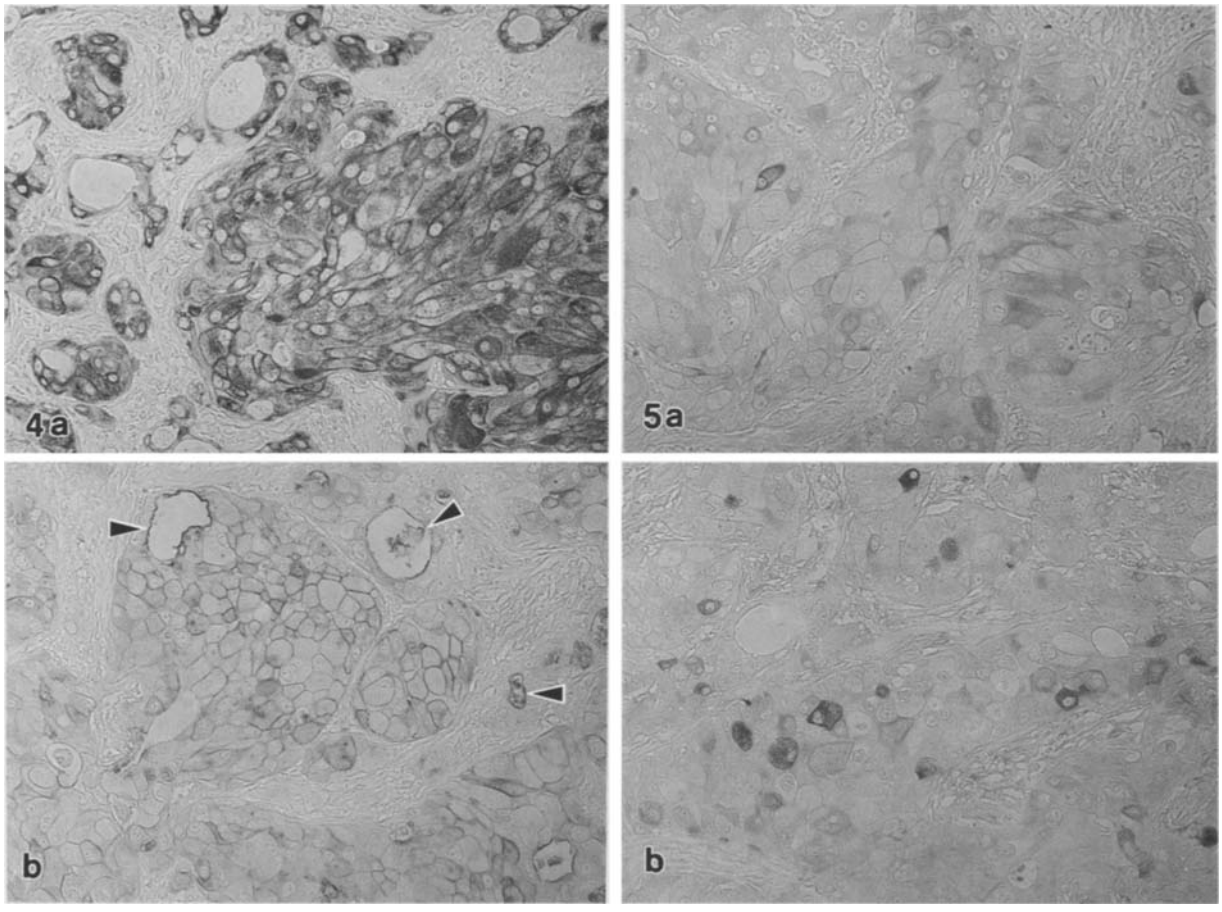
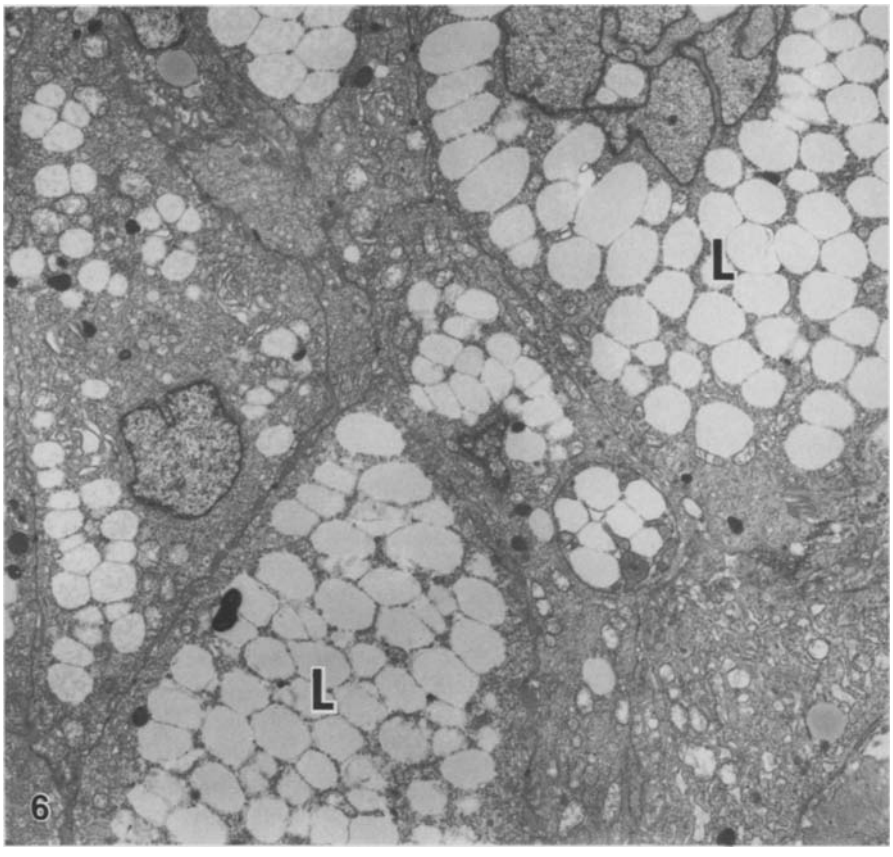


Fig. 4. Immunohistochemical demonstration of keratin (**a**) and epithelial membrane antigen; EMA (**b**). Keratin is stained over the cytoplasm of tumour cells, whereas EMA is localized mainly on the cytoplasmic membrane, especially at the luminal surface (*arrowheads*) (× 150)

Fig. 5. Immunohistochemical demonstration of secretory component (**a**) and lactoferrin (**b**). Both markers are expressed not only in the tumour cells showing ductal differentiation but also in those with sebaceous differentiation (× 150)

or vacuolated cytoplasm and a large vesicular nucleus. The outermost cells of these nests were often flattened and had an eosinophilic dense cytoplasm and dark nucleus (Fig. 1a). Central areas of large nests frequently showed a liquefaction. Glandular spaces lined by the duct-like epithelium with apocrine-like secretion were present in most of these sebaceous-like nests (Fig. 1b). Tumour cells showed marked cellular and nuclear pleomorphism, prominent nucleoli and numerous, sometimes atypical, mitotic figures (Fig. 2). Presence of abundant lipid material was demonstrated in the majority of tumor cells by Sudan black B staining (Fig. 3). Scattered mucous cells were revealed among these sebaceous cells by special stains such as PAS, mucicarmine and alcian blue. The presence of epithelial markers (keratin and epithelial membrane antigen; EMA), secretory functional markers (amylase, lactoferrin, secretory component and lysozyme), and other markers often usable for the identification of salivary gland tumor cells (S-100 protein, actin, neuron specific enolase, and vimentin) was investigated on paraffin sections from both the primary and recurrent tumours by the peroxidase-antiperoxidase method or biotin streptavidin system.

The majority of the tumour cells in both tumours showed immunoreactivity for keratin of 56 and 64 KD molecular weight and EMA. Keratin was stained over the cytoplasm of tumour cells, whereas EMA was localized mainly on the cytoplasmic membrane, especially at the luminal surface (Fig. 4). Scattered positive reaction of secretory component and lactoferrin was also revealed not only in the tumour cells showing ductal differentiation but also in those with sebaceous differentiation (Fig. 5). All other markers were negative in the tumour cells.



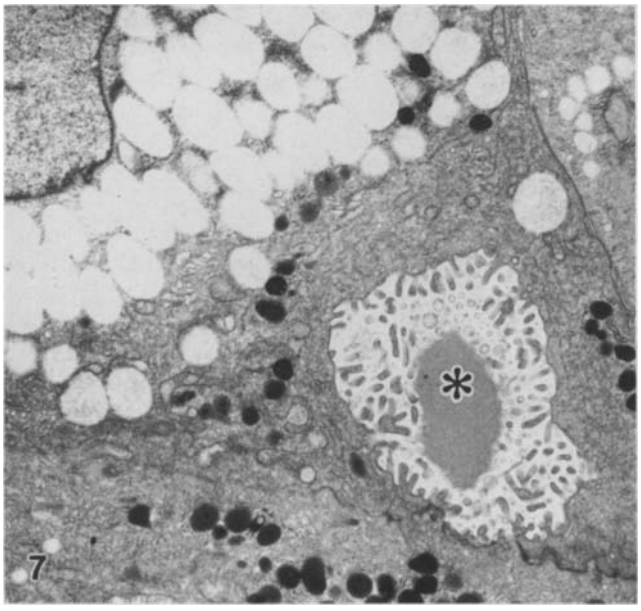


Fig. 6. Ultrastructure of the sebaceous carcinoma. Sebaceous tumour cells show a numbers of intracytoplasmic lipid droplets (L) (×4300)

Fig. 7. A sebaceous tumour cell showing an intracytoplasmic lumen (*). (×7200)

Parts of the two specimens were fixed with 2.5% glutaraldehyde and 1% osmium tetroxide and processed for transmission electron microscopy. In the electron microscope the tumour cells, which were oncocytoid under light microscopy, showed no mitochondrial aggregation but showed dilatation of membranous structures, such as endoplasmic reticulum and Golgi complex. In some nests, there were neoplastic ducts lined by the cells exhibiting numerous microvilli. Tumour nests in the recurrent lesion were ensheathed by a basal lamina of various thickness and consisted of polygonal cells which were joined together by scattered tiny desmosomes. Sebaceous and glandular differ-

entiation was evident in the tumour cells. Most cells contained a number of lipid droplets throughout the entire cytoplasm (Fig. 6). There were many ductal spaces lined by tumour cells and intracytoplasmic lumina with protruding microvilli. The duct-forming cells did not usually contain many lipid granules but showed well developed cell organellae. Interestingly, some tumour cells containing numerous lipid droplets in the cytoplasm participated in the formation of a glandular structure on their apical end or exhibited intracytoplasmic lumina (Fig. 7).

Many lysosomal dense bodies were seen both in the duct-forming cells and sebaceous cells (Figs. 6 and 7). No obvious myoepithelial differentiation was revealed in the basaloid cells at the periphery of the nests.

Table 1. Clinicopathological summary of 22 sebaceous carcinomas of salivary glands

Site	22: parotid gland
Age at diagnosis* (yr)	17–92 [mean: 60] 16: 50–90 4: 20–30
Sex	F. 12: M. 10
Size** (cm)	0.6 to 8.5
Follow-up	16: alive without recurrence 6: with recurrence/metastasis (3: died of the tumours)

* The age distribution for the tumour showed a bimodal pattern with peak incidences in the 3rd and the 6th to 9th decades
** in maximum diameter

Discussion

Only 21 cases of sebaceous carcinoma of salivary glands have been reported in the literature (Akhtar et al. 1973; Cheek and Pitcock 1966; Constant and Leahy 1968; Evans and Cruickshank 1970; Gnepp and Brannon 1984; Granström et al. 1987; Hayashi et al. 1985; Kleinsasser et al. 1970; MacFarlane et al. 1975; Mathis 1968; Schmid und Albrich 1973; Shulman et al. 1973; Silver and Goldstein 1966; Tsukada et al. 1964; Zechner und Albegger 1973) and the present case brings the total number of recorded cases to 22. The clinicopathological findings of 22 tumours are summarized in Table 1.

The histogenesis of sebaceous carcinoma of salivary glands is most controversial. An aetiological relation between sebaceous carcinoma and other well documented tumour types such as a mucoepidermoid tumor or a pleomorphic adenoma has been speculated. In discussing this problem, the histogenesis of the sebaceous differentiation in normal salivary glands should be considered, because the knowledge of it may be a key to understanding of the pathogenesis of sebaceous neoplasms. The internal displacement of epidermal material into the parotid bud during embryogenesis may explain some ectopias in salivary glands. Development of accessory ectodermal structure may reasonably be expected within an ectodermal organ such as the parotid gland, but this aberrant theory does not account for the occurrence of sebaceous elements in submandibular gland that is of endodermal origin. However, Meza-Chávez (1949) described that sebaceous glands occurring in the salivary gland originated from intercalated and striated ducts owing the presence of latent potentiality of differentiation in such a ductal epithelium. He also showed a higher incidence of sebaceous differentiation in parotid glands harboring neoplasms than in normal parotid glands. It may be that pluripotential salivary duct epithelium has a latent ability to develop sebaceous structures with the proper stimulus.

Some authors have considered that sebaceous carcinoma represents an aggressive variant or a derivative of mucoepidermoid tumour or pleomorphic adenoma (Cheek and Pitcock 1966; Evans and Cruickshank 1970; Shulman 1973; Tsukada et al. 1964). Akhtar et al. (1973) and MacFarlane et al. (1975), however, have considered that sebaceous tumours in salivary glands arise from duct cells which presumably possess inherent potentiality to differentiate into a variety of cell types including sebaceous, squamous, oncocytic and mucous cells. They concluded that the occasional presence of mucous cells in a sebaceous carcinoma should not be considered as evidence for the presence of a preexisting mucoepidermoid tumour or a mixed tumour.

In the present case, the tumour was composed of sebaceous, ductal and mucous cells. However, there were no histological features suggesting the close relationship to other well documented types such as a mucoepidermoid tumour or a pleomorphic adenoma. Interestingly, the ultrastructural and immunohistochemical observations of the tumour cells demonstrated coexistence of sebaceous and glandular differentiations. Tumour cells with lipid granules often participated in the formation of glandular structures or exhibited intracytoplasmic lumina, and immunohistochemical localization of lactoferrin and secretory component, the functional markers of ductal epithelium of salivary gland (Seifert and Caselitz 1985), was demon-

strated not only in duct-forming tumour cells but also in some sebaceous cells. These findings seem to suggest that sebaceous carcinoma originates from pluripotential duct cells which can differentiate into sebaceous, ductal and mucous cells.

Sebaceous carcinoma of salivary gland origin should be differentiated from that of skin origin (Batsakis et al. 1972). Akhtar et al. (1973) showed that the ultrastructure of salivary sebaceous carcinoma was almost similar to that of the normal cutaneous sebaceous glands. However, they pointed out the presence of the intracytoplasmic lumina, not noted in normal sebaceous glands, in the tumour cells of salivary sebaceous carcinoma. In addition to such electron microscopic features, the immunohistochemical demonstration of salivary functional markers such as lactoferrin and secretory component may also offer useful information for differential diagnosis from neoplasms of cutaneous origin.

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