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Hybrid Tumours of Salivary Glands. Definition and Classification of Five Rare Cases

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Hybrid tumours are very rare tumour entities which are composed of two different tumour entities, each of which conforms with an exactly defined tumour category. The tumour entities of a hybrid tumour are not separated but have an identical origin within the same topographical area. In contrast, biphasically differentiated tumours are a mixture of two cellular patterns with a corresponding term in the tumour classification. Examples of a biphasic differentiation are: basaloid-squamous carcinoma, adeno-squamous carcinoma or sarcomatoid carcinoma, and epithelial-myoepithelial carcinoma, mucoepidermoid carcinoma or adenoid cystic carcinoma. Hybrid tumours must also be distinguished from the multiple occurrence of salivary gland tumours which can develop syn- or metachronously. In the tissue samples of more than 6600 salivary gland tumours covered by the Salivary Gland Register (Institute of Pathology, University of Hamburg, Germany) only 5 cases of hybrid tumours were recorded between 1965 and 1994. This means less than 0.1% of all registered tumours. Case 1 was a very rare example of a hybrid adenoma with differentiation as a basal cell adenoma and a canalicular adenoma of the parotid gland. The similar cellular origin of both types of adenoma may be an explanation for its development into a hybrid adenoma. Case 2 is a hybrid tumour with a composition of basal cell adenoma and a glandular type of adenoid cystic carcinoma. In both types of tumours the two cell types (duct-lining cells and modified myoepithelial cells) have a similar histogenetic origin. Therefore, the development of both cell types in a hybrid tumour with two trends of differentiation is possible. Case 3 represents a hybrid adenoma as a mixture of a Warthin tumour and a sebaceous adenoma. Although inclusions of sebaceous cells are observed in Warthin tumours, this hybrid tumour shows a composition of two different epithelial structures in a varied mixture. Case 4 is a very rare and unique hybrid carcinoma with two absolutely different components: acinic cell carcinoma and salivary duct carcinoma. The poor prognosis of this hybrid carcinoma is determined by the salivary duct carcinoma. Case 5 represents a hybrid carcinoma whose two components have a similar histogenetical basis: epithelial-myoepithelial carcinoma and a glandular type of adenoid cystic carcinoma. Both carcinomas are composed of variable proportions of duct-lining cells and myoepithelial cells. **Copyright © 1996 Elsevier Science Ltd**

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INTRODUCTION

In the great number of salivary gland tumours rare isolated cases are composed of two different tumour entities, each of which conforms with an exactly defined tumour category. Such tumours, composed of two tumour entities, are designated hybrid tumours. Both tumour entities are not separated but have an identical origin in the same topographical area.

The older term "collision tumour" must be distinguished from the term "hybrid tumour" by definition. In Meyer's original definition [1] a collision tumour is a meeting of two malignant neoplasms arising at independent topographical sites. During further growth the two tumours invade each other, especially in the border zone. Such very rare collisions have been described in various locations including the oral cavity [2], gastric cardia [3, 4], lung, cervix, anorectal junction, liver and urinary bladder. Most reported cases are collisions between adenocarcinomas and sarcomas or lymphomas whereas collisions between two types of carcinoma are very rare.

In contrast to hybrid tumours, biphasically differentiated tumours are characterized by a regular, repetitive mixture of two cellular patterns with a corresponding term in the tumour classification. Examples of biphasically differentiated tumours

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of the salivary glands are: epithelial–myoepithelial carcinoma; mucoepidermoid carcinoma; basaloid-squamous carcinoma; adeno-squamous carcinoma; sarcomatoid carcinoma (older term: carcinosarcoma); and carcinoma in pleomorphic adenoma with differentiation as squamous cell carcinoma as well as adenocarcinoma.

Basaloid-squamous carcinoma of the oral cavity is very rare and mostly localised at the base of the tongue or in the floor of the mouth [5, 6], but in isolated cases it is also found at the palate [7, 8] or at the cheek [9]. The tumour is characterised by a biphasic differentiation as a squamous cell carcinoma and solid type of adenoid cystic carcinoma.

The development of a primary *adeno-squamous carcinoma* of the salivary glands is controversial [10, 11]. The tumour shows manifestation of an epidermoid component with intercellular bridges or keratin demonstrable in the squamous formation and glandular features with true lumina in separate and definitive areas. From the sparse reports in the literature [12–15] it is not clear whether the carcinomas of the mouth floor, palate or tongue come from the oral mucosa or the adjacent minor salivary glands.

The debate about the histogenesis of *carcinosarcoma* has continued for more than 100 years [16]. Current ultrastructural, cell-culture and immunohistological data support a monoclonal nature for carcinosarcoma and suggest that biphasic *sarcomatoid carcinoma* is a more apt designation for this tumour entity. The totipotential cell hypothesis suggests that reserve cells exist in any tissue with the ability to pursue epithelial, mesenchymal or mixed lineages of differentiation. Sarcomatoid carcinomas of the salivary glands which were called carcinosarcomas in the earlier publications are very rare [17–19]. Carcinomas of the salivary glands with focal sarcomatoid stromal reaction contain mostly osteoclastic multinuclear giant cells or, very rarely, show an association with a giant cell tumour [19–22].

PATIENTS AND METHODS

More than 6600 salivary gland tumours were pathohistologically diagnosed in the Salivary Gland Register at the Institute of Pathology, University of Hamburg, Germany, between 1965 and 1994. The tumours were classified using the revised edition of the *WHO Histological Typing of Salivary Gland Tumours* [11]. The types of tumours are listed in Table 1.

The paraffin-embedded slides were stained with haematoxylin–eosin, PAS-reaction, Astrablue and, when necessary, other special stainings or immunocytochemical reactions were also used.

Table 1. Pathohistological typing of salivary gland tumours (Salivary Gland Register Hamburg 1965–1994)

Pathohistological type	No. of cases	% of all tumours
Adenomas	3797	57
Carcinomas	1863	28
Non-epithelial tumours	291	4
Malignant lymphomas	255	4
Secondary tumours (metastases)	316	5
Non-classified tumours	36	1
Periglandular tumours	88	1
Total	6646	100

Table 2. Clinical data and classification of five hybrid tumours (Salivary Gland Register Hamburg 1965–1994)

Case location	Age	Sex (M/F)	Classification
1 Parotid gland	70	M	Basal cell adenoma (trabecular type) and canalicular adenoma
2 Parotid gland	62	M	Basal cell adenoma (trabecular type) and adenoid cystic carcinoma (glandular type)
3 Parotid gland	60	M	Warthin tumour and sebaceous gland lymphadenoma
4 Parotid gland	53	M	Acinic cell carcinoma (solid type) and salivary gland carcinoma
5 Palate	66	F	Epithelial–myoepithelial carcinoma and adenoid cystic carcinoma (glandular type)

In the total material only 5 cases of hybrid tumours were included. This result corresponds to a value of less than 0.1% of all registered tumours. The 5 cases are listed in Table 2.

RESULTS

Case 1

A 70-year-old man with a slow-growing swelling of the left parotid region for 15–20 years. A well-demarcated tumour with dimensions of $7 \times 6 \times 4$ cm was removed by subtotal parotidectomy.

Pathohistologically, the composition of the tumour showed two different adenomatous components. Predominantly the adenoma consisted of isomorphic basaloid cells with a prominent basal cell layer arranged in trabecular bands (Fig. 1). In isolated areas, tubular differentiation could be observed

Fig. 1. Hybrid adenoma (Case 1). Basal cell adenoma with trabecular isomorphic basaloid cells. Haematoxylin–eosin. ×160.

with ductal structures. Between these epithelial cells, a small fibrous stroma had developed without a mucoid stromal component. The other smaller part of the adenoma consisted of columnar epithelial cells which were arranged in bilayered anastomosing strands which had formed a beading pattern (Fig. 2). In contrast to the other part of the adenoma, the stroma was loose, highly vascular and not fibrous. In conclusion, this type of adenoma had a hybrid differentiation as a trabecular type of basal cell adenoma as well as a canalicular adenoma.

Case 2

A 62-year-old man with a tumorous swelling of the right parotid region for some months. Clinical symptoms of pain or facial nerve paralysis could not be observed. The tumour was removed by total parotidectomy.

The pathohistological structure was characterised by two different kinds of tissue. The predominant part showed an arrangement of trabecular formations of isomorphic basaloid cells with a prominent basal cell layer (Fig. 3). The outer layer of the trabecular pattern is often palisaded (Fig. 4). The fibrous stromal component contained no mucoid material. The other smaller part of the tumour consisted of epithelial cell nests permeated by numerous cylindrical spaces with a sieve-like configuration (Fig. 5). Most of the cystic spaces were pseudocysts (Fig. 6) which were surrounded by modified flat myoepithelial cells. Other spaces were true cysts which were surrounded by duct-like cuboidal cells. This tumour part was more localised in the peripheral areas of the hybrid tumour, but showed neither perineural spread nor cellular stromal reaction. In conclusion, this hybrid tumour consisted of a trabecular type of basal cell adenoma and of a glandular type of adenoid cystic carcinoma.

Case 3

A 60-year-old man with a slowly increasing mass in recent months in the lower parotid region. The surgical specimen

Fig. 2. Hybrid adenoma (Case 1). Canalicular adenoma with anastomosing bilayered strands and highly vascular stroma. Haematoxylin–eosin. × 100.

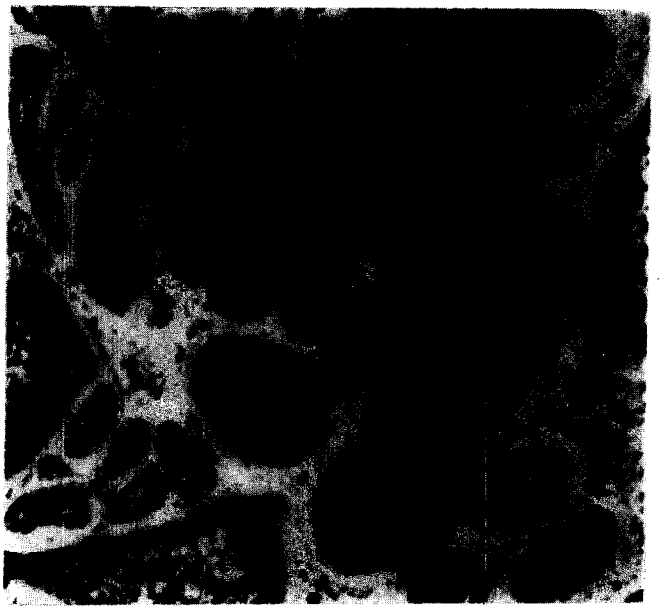

Fig. 3. Hybrid tumour (Case 2). Basal cell adenoma with predominantly solid pattern. Haematoxylin–eosin. × 100.

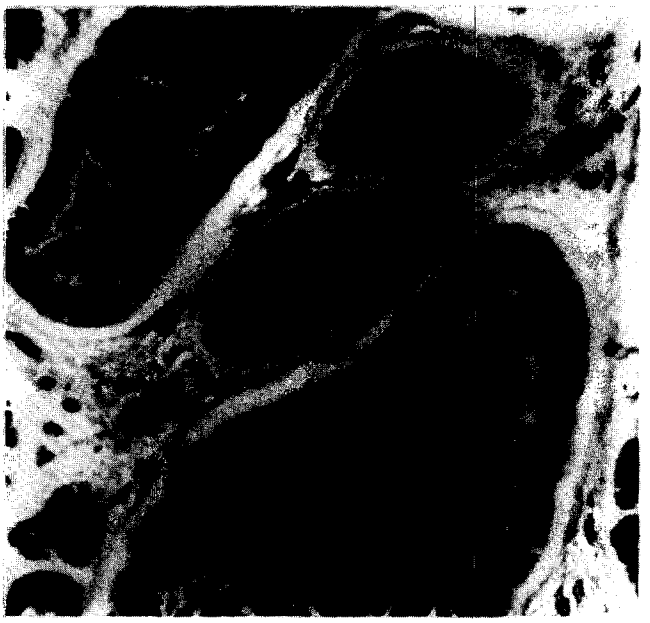

Fig. 4. Hybrid tumour (Case 2). Basal cell adenoma with palisaded cells on the outside of the cell formations. Haematoxylin–eosin. × 250.

contained a 5 × 2.5 × 3 cm great encapsulated tumour with the inclusion of yellow–brown necrotic material in small cystic spaces.

The tumour was composed of two different epithelial structures in a varied mixture. One part showed glandular and cystic structures, sometimes with a papillary cystic arrangement and lined by eosinophilic oncocytic cells (Fig. 7). The stroma contained a variable amount of lymphoid tissue with lymph follicles. The epithelium was double-layered. The other part of the tumour consisted of irregular nests of sebaceous cells without cellular atypia (Fig. 8). In conclusion,

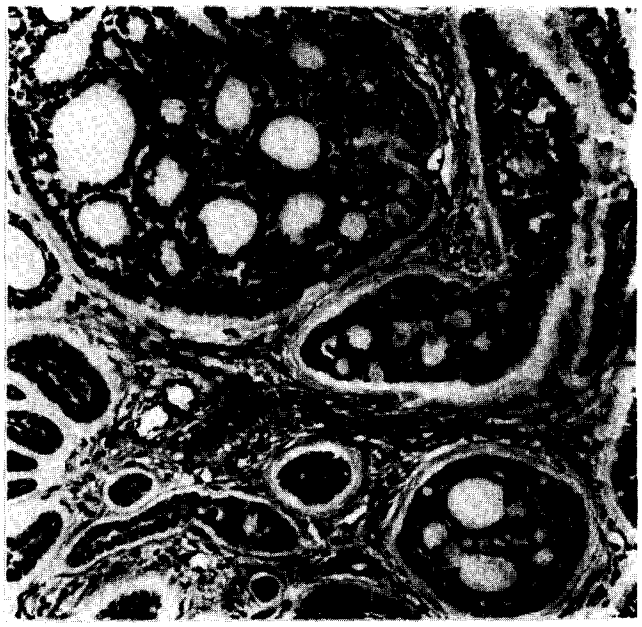

Fig. 5. Hybrid tumour (Case 2). Adenoid cystic carcinoma with cylindrical spaces. Haematoxylin–eosin. × 100.

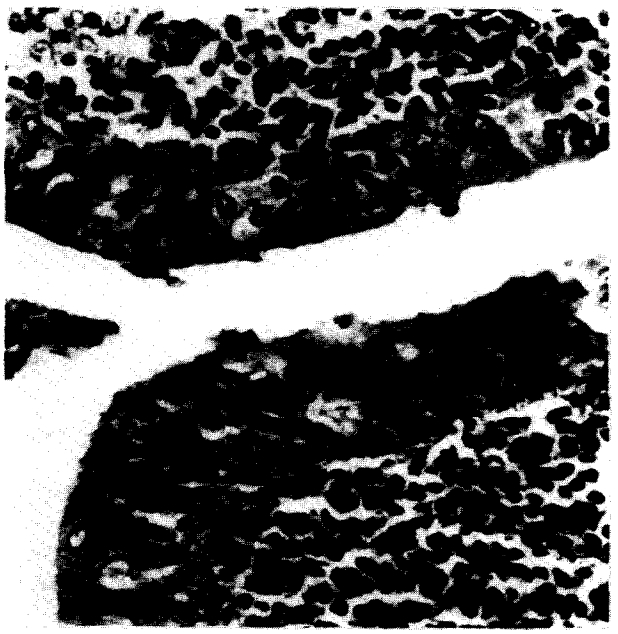

Fig. 7. Hybrid adenoma (Case 3). Warthin tumour with cysts lined by eosinophilic oncocytic cells and lymphoid stromal component. Haematoxylin–eosin. × 250.

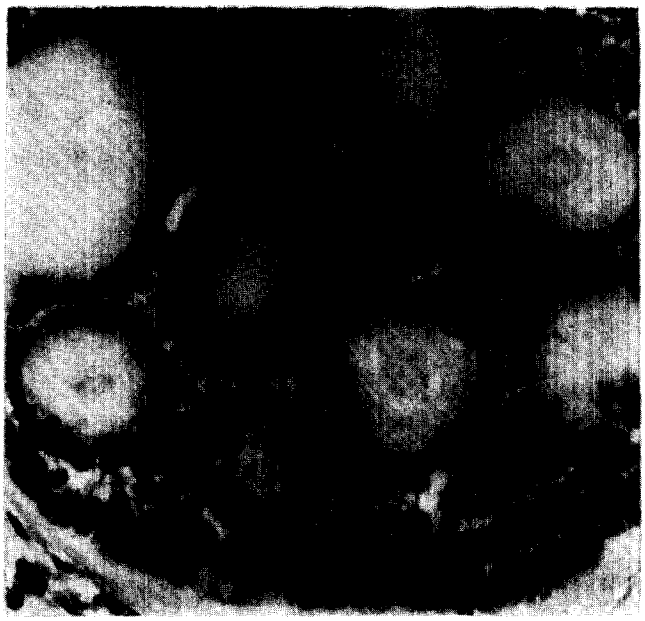

Fig. 6. Hybrid tumour (Case 2). Adenoid cystic carcinoma with inclusion of multiple pseudocysts. Haematoxylin–eosin. × 250.

Fig. 8. Hybrid adenoma (Case 3). Sebaceous adenoma with vacuolisation of the cytoplasm. Haematoxylin–eosin. × 250.

this hybrid adenoma was a mixture of a typical Warthin tumour and a sebaceous adenoma.

Case 4

A 53-year-old man with a rapid swelling of the right parotid region in recent weeks. A facial nerve paralysis was not observed. A total parotidectomy was performed with a $6 \times 3 \times 2$ cm operation specimen which was infiltrated by a tumorous mass.

The tumour was composed of two different nodular components which showed a mixture within the tumour. One component consisted of a multinodular pattern of solid nests of polygonal acinar cells with cytoplasmic PAS-positive granules (Fig. 9). Some other acinar cells showed a little more clear cytoplasm with the inclusion of small cytoplasmic vacuoles. Another feature is the frequent association with a lymphoid infiltrate in the supporting stroma (Fig. 10). The other nodular tumorous component was characterised by the formation of large cell aggregates distending salivary ducts. The neoplastic cells present a combination of cribriform (Fig. 11), looping

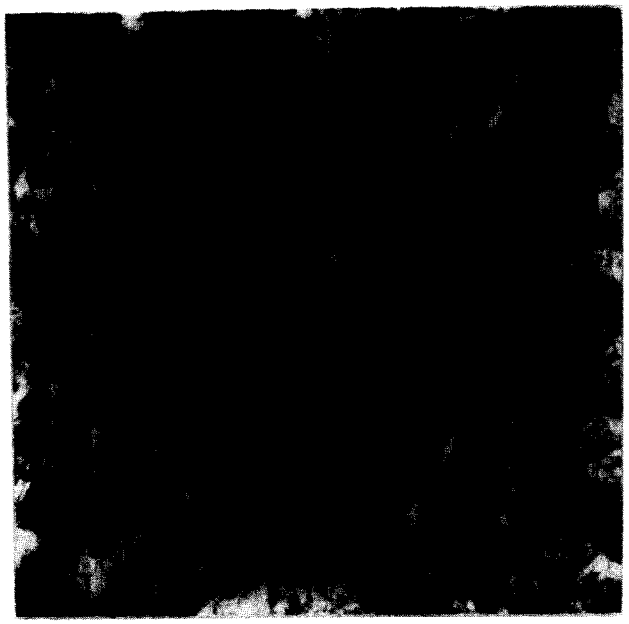

Fig. 9. Hybrid carcinoma (Case 4). Acinic cell carcinoma with solid nests of acinar cells. Distinct PAS-positive enzyme granules in the cytoplasm. PAS reaction. × 250.

Fig. 11. Hybrid carcinoma (Case 4). Salivary duct carcinoma with cribriform growth pattern and small comedo necrosis. Haematoxylin–eosin. × 100.

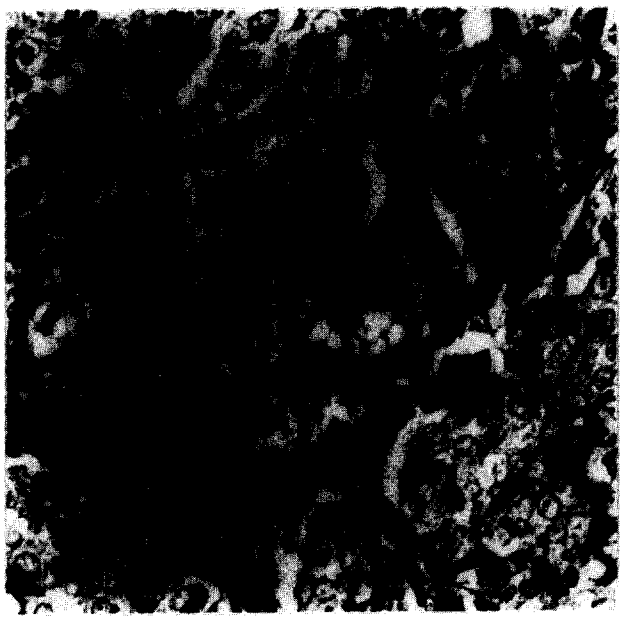

Fig. 10. Hybrid carcinoma (Case 4). Acinic cell carcinoma with solid and duct-like pattern surrounded by a lymphoid infiltrate. PAS reaction. × 250.

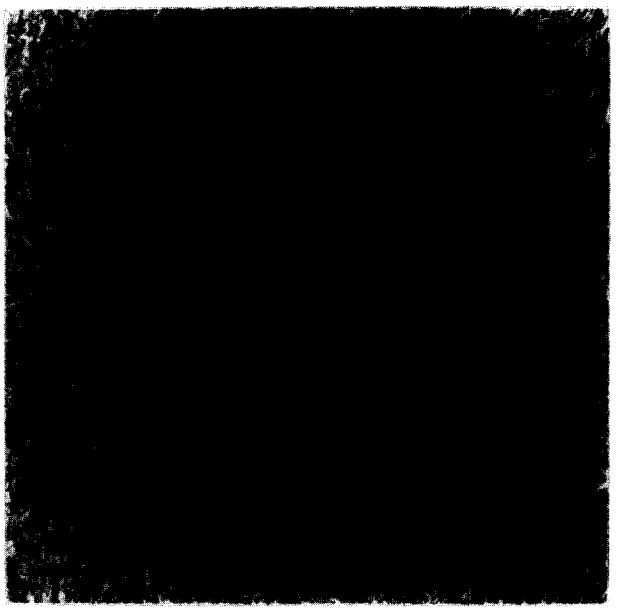

Fig. 12. Hybrid carcinoma (Case 4). Salivary duct carcinoma with solid growth pattern and inclusion of distinct comedo necrosis. Haematoxylin–eosin. × 100.

("Roman bridges") and solid growth pattern with inclusion of central necroses of comedo type (Fig. 12). The tumour cells showed nuclear pleomorphism and frequent mitoses. The tumour infiltrates adjacent tissues and involves the cervical lymph nodes. In conclusion, this hybrid carcinoma was composed of foci of acinic cell carcinoma (solid type) and salivary duct carcinoma with comedo necroses.

Case 5

A 66-year-old woman with a circumscribed tumour node of the left paramedian palate. The tumour was intramurally localised, clearly limited and movable to the surrounding tissue.

The tumour showed a distinct mixture of two components. One component was composed of two cell types which typically form duct-like structures (Fig. 13). There was an inner layer of small duct-lining cells with a dark cytoplasm and an outer layer of clear cells. These tumour areas were

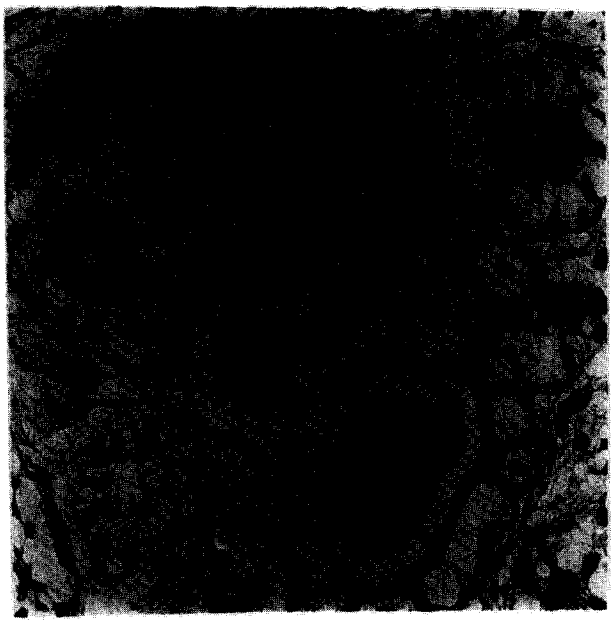

Fig. 13. Hybrid carcinoma (Case 5). Epithelial–myoepithelial carcinoma with inner layer of duct-lining cells and outer layer of clear myoepithelial cells. PAS reaction. × 250.

Fig. 14. Hybrid carcinoma (Case 5). Adenoid cystic carcinoma of glandular type with inclusion of cylindrical spaces. PAS reaction. × 100.

multinodular. The other component showed a typical structure of the glandular type of adenoid cystic carcinoma with inclusion of multiple cylindrical spaces (Fig. 14). The pseudocysts contained basal membrane-like material and mucopolysaccharides. Infiltrating growth could not be observed. In conclusion, this hybrid carcinoma contained parts of an epithelial–myoepithelial carcinoma as well as parts of the glandular type of adenoid cystic carcinoma.

DISCUSSION

Hybrid tumours or biphasically differentiated tumours of the salivary glands must be distinguished from the multiple occurrence of salivary gland tumours. *Multiple salivary gland tumours* were observed in different variations which are listed in Table 3. In temporal terms the development can take place synchronously or metachronously [23–27]. Another aspect is the occurrence of salivary gland tumours with other oral tumours or the association of primary salivary gland tumours with extraoral secondary carcinomas, such as thyroid gland carcinoma, breast carcinoma, lung carcinoma and larynx or colon carcinoma.

Case 1 of our collection was a very rare example of a hybrid adenoma with differentiation as a basal cell adenoma as well as a canalicular adenoma. We could find only one similar case report in the literature [28]. In sporadic reports basal cell adenomas were mentioned with inclusion of focal stromal microcystic areas which were characterised by a distinctive vascularity and an arrangement of small bilayered strands of cells similar to those in canalicular adenomas [29]. But this focal lesion was at first misdiagnosed as an adenoid cystic carcinoma and was not classified as canalicular adenoma. In the new WHO histological typing of salivary gland adenomas [30] basal cell adenoma and canalicular adenoma are classified as two different types of adenoma. In contrast to basal cell adenoma the canalicular adenoma has a loose, highly vascularised stroma and an arrangement of anastomosing bilayered strands of epithelial cells forming a beading pattern [31, 32]. Basal cell adenoma occurs in solid, trabecular, tubular and membranous variants and is composed of basaloid cells with a prominent basal cell layer [33–36]. Other characteristics are

Table 3. Multiple occurrence of salivary gland tumours

1.	**Multiple, histologically identical salivary gland tumours**
	Bilateral parotid gland tumours
	—more frequent: Warthin tumour, pleomorphic adenoma, acinic cell carcinoma, oncocytoma, basal cell adenoma
	—isolated instances: epithelial–myoepithelial carcinoma, adenoid cystic carcinoma, mucoepidermoid carcinoma
	Unilateral parotid gland tumours
	—Warthin tumour, pleomorphic adenoma, oncocytoma
2.	**Multiple, histologically different salivary gland tumours**
	—Pleomorphic adenoma with Warthin tumour, oncocytoma, basal cell adenoma, sebaceous adenoma, mucoepidermoid carcinoma, adenoid cystic carcinoma, epithelial–myoepithelial carcinoma, oncocytic carcinoma
	—Warthin tumour with pleomorphic adenoma, oncocytoma, basal cell adenoma, sebaceous adenoma, mucoepidermoid carcinoma, acinic cell carcinoma, adenoid cystic carcinoma
3.	**Salivary gland tumours with other oral tumour**
	—Warthin tumour with ameloblastoma, squamous cell carcinoma, malignant lymphoma
	—Pleomorphic adenoma with haemangiopericytoma
	—Oncocytic carcinoma with malignant lymphoma
4.	**Salivary gland tumours with extra oral tumours**
	—Thyroid carcinoma
	—Breast carcinoma
	—Larynx carcinoma
	—Colon carcinoma

the development of distinct basement membrane-like structures, the absence of a mucoid stroma and the association of the membranous variant (dermal anlage type) with dermal cylindroma or other tumours of the scalp. Another aspect is the possible transformation of basal cell adenoma into basal cell adenocarcinoma. The results of immunocytochemistry and electron microscopy show that both types of adenomas are composed mostly of duct epithelia and a small compartment of myoepithelial cells. The duct-like cells express cytokeratin, CEA and secretory markers whereas the more outer localised cells also express vimentin. The similar cellular origin of both adenomas may be an explanation for the development of a hybrid adenoma.

Case 2 is a hybrid tumour with a composition of basal cell adenoma and adenoid cystic carcinoma. Adenoid cystic carcinoma shows various histological features with glandular (cribriform), tubular or solid patterns [37, 38]. Isolated casuistic reports describe the common occurrence of adenoid cystic carcinoma and basal cell adenoma [39–43]. One of these 5 case reports deals with a "congenital hybrid basal cell adenoma–adenoid cystic carcinoma" [40]. The other case report concerned a child with "the so-called hybrid basal cell adenoma–adenoid cystic carcinoma", but the author classified this tumour as a "low-grade basaloid adenocarcinoma" [41]. Other studies describe cystic formations in basal cell adenomas with mucinous, faintly Alcian blue-positive material in the cystic lumen and oedematous swelling of the stroma with dilatation of lymphatic vessels [43]. In 10% of the examined cases of basal cell adenoma adenoid cystic patterns became apparent with mucoid stroma degeneration. Another report mentions a solid-cribriform type of basal cell adenoma as an unusual variant [35]. In our case the adenoid cystic carcinoma shows the typical structure of the glandular subtype and no mucoid stromal degeneration with dilated lymphatic vessels. The predominant part is the trabecular type of basal cell adenoma without cystic spaces and the smaller component the glandular type of an adenoid cystic carcinoma. Both types of differentiation reflect the similar histogenetic origin of the two cell types: duct-lining cells and cells of more myoepithelial type on the outside of the cell nests. Therefore, the development of both cell types in a hybrid tumour with two trends of differentiation is possible.

Case 3 represents a hybrid adenoma as a mixture of Warthin tumour and sebaceous adenoma. In Warthin tumours inclusions of goblet cells, sebaceous cells or focal squamous metaplasia can be observed [44–46]. But in our case we have a composition of two different epithelial structures in a varied mixture. A comparable observation can be made in the occurrence of a Warthin tumour with a sebaceous lymphadenoma [47]. However, in the case reported in the literature there was a greater separation of both tumour differentiations, whereas in our case there was a distinct mixture. In the group of sebaceous neoplasms of salivary gland origin, sebaceous lymphadenoma is a rare but distinct variant of sebaceous adenoma [48–50].

Case 4 is a very uncommon and unique hybrid carcinoma with two absolutely different components. The component of acinic cell carcinoma is regarded as a low-grade malignancy with a relatively good prognosis [51–54], whereas the component of salivary duct carcinoma is characterised by high malignancy with a poor prognosis because this tumour is usually found to infiltrate adjacent tissue and involve cervical lymph nodes. The majority of patients die within 3 years [55–60]. The tumorous nodules of acinic cell carcinoma show a solid growth pattern with acinar cells which contain cytoplasmic PAS-positive enzyme granules. A lymphoid infiltrate has developed between the acinar cells. These tumorous parts have not metastasised to the cervical lymph nodes. On the other side, the nodules of salivary duct carcinoma infiltrate the surrounding tissue and involve the cervical lymph nodes. In this hybrid carcinoma the poorer prognosis is determined by the salivary duct carcinoma.

Case 5 represents a hybrid carcinoma whose two components have a similar histogenetical basis. Epithelial–myoepithelial carcinoma is composed of variable proportions of two cell types which typically form duct-like structures: an inner layer of duct-lining cells and an outer layer of clear myoepithelial cells [61–67]. On the other hand, the glandular type of adenoid cystic carcinoma consists of flat, modified myoepithelial cells and duct-like cuboidal cells. In our case both types of carcinoma are arranged in a distinct pattern. We could not find a casuistic report of the same kind in the literature. Only two rare case reports mention hybrid tumours with a little different composition. One tumour was a sebaceous lymphadenocarcinoma which also includes three further tumorous differentiations, namely epithelial–myoepithelial carcinoma, a solid type of adenoid cystic carcinoma and a poorly differentiated carcinoma [10]. The other case demonstrated a spectrum of histological features that were compatible with three different types of salivary gland carcinoma: epithelial–myoepithelial carcinoma, adenoid cystic carcinoma and basal cell adenocarcinoma [68]. However, whether this case represents one neoplasm or multiple neoplasms remains speculative although the gross pathology description and the microscopic anatomy suggested separate neoplasms.

1. Meyer R. Beitrag zur Verständigung über die Namengebung in der Geschwulstlehre. *Zbl Allg Path Path Anat* 1919, **30**, 292–296.
2. Sirsat MV, Shrikhande SE. Collision tumor in the oral cavity. A report of 2 cases. *Indian J Pathol Bact* 1966, **9**, 340–343.
3. Wanke M. Collision-tumour of the cardia. Case report. *Virchows Arch A Pathol Anat* 1972, **357**, 81–86.
4. Spagnolo DV, Heenan PJ. Collision carcinoma at the esophagogastric junction: Report of two cases. *Cancer* 1980, **46**, 2702–2708.
5. Coppola D, Catalano E, Tang Ch-K, Elfenbein IB, Harwick R, Mohr R. Basaloid squamous carcinoma of floor of mouth. *Cancer* 1993, **72**, 2299–2305.
6. Campman StC, Gandour-Edwards RF, Sykes JM. Basaloid squamous carcinoma of the head and neck. Report of a case occurring in the anterior floor of the mouth. *Arch Pathol Lab Med* 1994, **118**, 1229–1232.
7. Lovejoi HM, Matthews BL. Basaloid-squamous carcinoma of the palate. *Otolaryngol Head Neck Surg* 1992, **106**, 159–162.
8. Hellquist HB, Dahl F, Karlsson MG, Nilsson C. Basaloid squamous cell carcinoma of the palate. Case report. *Histopathology* 1994, **25**, 178–180.
9. Cadier MA, Kelly SA, Parkhouse N, Brough MD. Basaloid squamous carcinoma of the buccal cavity. *Head Neck* 1992, **14**, 387–391.
10. Ellis GL, Auclair PL, Gnepp DR, Goode RK. Other malignant epithelial neoplasms. In Ellis GL, Auclair PL, Gnepp DR, eds. *Surgical Pathology of the Salivary Glands*. Philadelphia, Saunders, 1991, 455–488.
11. Seifert G. *WHO Histological Typing of Salivary Gland Tumours*, 2nd ed. Berlin, Springer, 1991.
12. Gerughty RM, Hennigar GR, Brown RM. Adenosquamous carcinoma of the nasal, oral and laryngeal cavities: A clinicopathologic survey of ten cases. *Cancer* 1968, **22**, 1140–1155.

13. Sanner JR. Combined adenosquamous carcinoma and ductal adenoma of the hard and soft palate: Report of a case. *J Oral Surg* 1979, **37**, 331–334.
14. Siar CH, Ng KH. Adenosquamous carcinoma of the floor of the mouth and lower alveolus: A radiation-induced lesion? *Oral Surg Oral Med Oral Pathol* 1987, **63**, 216–220.
15. Napier SS, Gormely JS, Newlands C, Ramsay-Baggs P. Adenosquamous carcinoma. A rare neoplasm with an aggressive course. *Oral Surg Oral Med Oral Pathol* 1995, **79**, 607–611.
16. Wick MR, Swanson PE. Carcinosarcoma. Current perspectives and an historical review of nosological concepts. *Sem Diagn Pathol* 1993, **10**, 118–127.
17. Bleiweiss IJ, Huvos AG, Lara J, Strong EW. Carcinosarcoma of the submandibular gland. Immunohistochemical findings. *Cancer* 1992, **69**, 2031–2035.
18. Grenko RT, Tytor M, Boeryd B. Giant-cell tumour of the salivary gland with associated carcinosarcoma. *Histopathology* 1993, **23**, 594–595.
19. Hayashi Y, Aoki N. Undifferentiated carcinoma of the parotid gland with bizarre giant cells: Clinicopathologic report with ultrastructural study. *Acta Pathol Jpn* 1983, **33**, 169–176.
20. Eusebi V, Martin SA, Govoni E, Rosai J. Giant cell tumor of major salivary glands: Report of three cases, one occuring in association with a malignant mixed tumor. *Am J Clin Pathol* 1984, **81**, 666–675.
21. Batsakis JG, Ordónez NG, Sevidal PA, Baker JR. Osteoclast-type giant cell neoplasms of the parotid gland. *J Laryng Otol* 1988, **102**, 901–904.
22. McDaniel RK, Benign mesenchymal neoplasms. In Ellis GL, Auclair PL, Gnepp DR, eds. *Surgical Pathology of the Salivary Glands*. Philadelphia, Saunders, 1991, 489–513.
23. Krogdahl AS, Bretlau P, Hastrup N. Multiple tumours of the parotid gland. *J Laryng Otol* 1983, **97**, 1035–1037.
24. Seifert G, Miehlke A, Haubrich J, Chilla R. *Diseases of the Salivary Glands. Pathology–Diagnosis–Treatment–Facial Nerve Surgery*. Stuttgart, Thieme, 1986.
25. Gnepp DR, Schroeder W, Heffner D. Synchronous tumors arising in a single major salivary gland. *Cancer* 1989, **63**, 1219–1224.
26. Toida M, Mukai K, Shimosato Y, Ebihara S. Simultaneous occurrence of bilateral Warthin's tumors and pleomorphic adenoma in the parotid glands. *J Oral Maxillofac Surg* 1990, **48**, 1109–1113.
27. Ellis GL, Auclair PL, Gnepp DR. *Surgical Pathology of the Salivary Glands*. London, Saunders, 1991.
28. Kratochvil FJ. Canalicular adenoma and basal cell adenoma. In Ellis GL, Auclair PL, Gnepp DR, eds. *Surgical Pathology of the Salivary Glands*. Philadelphia, Saunders, 1991, 202–224.
29. Bernacki EG, Batsakis JG, Johns ME. Basal cell adenoma: Distinctive tumor of salivary glands. *Arch Otolaryngol* 1974, **99**, 84–87.
30. Seifert G. Die neue pathohistologische WHO-Klassifikation der Speicheldrüsenadenome. *Pathologe* 1992, **13**, 322–335.
31. Daley DT. The canalicular adenoma: Considerations on differential diagnosis and treatment. *J Oral Maxillofac Surg* 1984, **42**, 728–730.
32. McMillan MD, Smith CJ, Smillie AC. Canalicular adenoma: report of five cases with ultrastructural observations. *J Oral Pathol Med* 1993, **22**, 368–373.
33. Kratochvil FJ, Auclair PL, Ellis GL. Clinical features of 160 cases of basal cell adenoma and 121 cases of canalicular adenoma. *Oral Surg Oral Med Oral Pathol* 1990, **70**, 605.
34. Batsakis JG, Luna MA, El-Naggar AK. Basaloid monomorphic adenomas. *Ann Otol Rhinol Laryngol* 1991, **100**, 687–690.
35. Dardick I, Lytwyn A, Bourne AJ, Byard RW. Trabecular and solid-cribriform types of basal cell adenoma. A morphologic study of two cases of an unusual variant of monomorphic adenoma. *Oral Surg Oral Med Oral Pathol* 1992, **73**, 75–83.
36. Ferreiro JA. Immunohistochemistry of basal cell adenoma of the major salivary glands. *Histopathology* 1994, **24**, 539–542.
37. Nascimento AG, Amaral ALP, Prado LAF, Kligerman J, Silveira TRP. Adenoid cystic carcinoma of salivary glands. A study of 61 cases with clinicopathologic correlation. *Cancer* 1986, **57**, 312–319.
38. Tomich ChE. Adenoid cystic carcinoma. In Ellis GL, Auclair PL, Gnepp DR, eds. *Surgical Pathology of the Salivary Glands*. Philadelphia, Saunders, 1991, 333–348.
39. Daley TD, Dardick I. An unusual parotid tumor with histogenetic implications for salivary gland neoplasms. *Oral Surg Oral Med Oral Pathol* 1983, **55**, 374–381.
40. Simpson PR, Rutledge JC, Schaefer SD, Anderson RC. Congenital hybrid basal cell adenoma–adenoid cystic carcinoma of the salivary gland. *Pediatr Pathol* 1986, **6**, 199–208.
41. Adkins GF. Low-grade basaloid adenocarcinoma of salivary gland in childhood: the so-called hybrid basal cell adenoma–adenoid cystic carcinoma. *Pathology* 1990, **22**, 187–190.
42. Ellis GL, Auclair PL. Basal cell adenocarcinoma. In Ellis GL, Auclair PL, Gnepp DR, eds. *Surgical Pathology of the Salivary Glands*. Philadelphia, Saunders, 1991, 441–454.
43. Nagao K, Matsuzaki O, Saiga H, *et al.* Histopathologic studies of basal cell adenoma of the parotid gland. *Cancer* 1982, **50**, 736–745.
44. Seifert G, Bull HG, Donath K. Histologic subclassification of the cystadenolymphoma of the parotid gland. Analysis of 275 cases. *Virchows Arch A Pathol Anat* 1980, **388**, 13–38.
45. Lamelas J, Terry JH, Jr, Alfonso AE. Warthin's tumor: multicentricity and increasing incidence in women. *Am J Surg* 1987, **154**, 347–351.
46. Lefor AT, Ord RA. Multiple synchronous bilateral Warthin's tumors of the parotid glands with pleomorphic adenoma. Case report and review of the literature. *Oral Surg Oral Med Oral Pathol* 1993, **76**, 19–24.
47. Dreyer Th, Battmann A, Silberzahn J, Glanz H, Schulz A. Unusual differentiation of a combination tumor of the parotid gland. A case report. *Path Res Pract* 1993, **189**, 577–581.
48. Gnepp DR. Sebaceous neoplasms of salivary gland origin. A review. *Pathol Annu* 1983, **18**, 71–102.
49. Gnepp DR, Brannon R. Sebaceous neoplasms of salivary gland origin. Report of 21 cases. *Cancer* 1984, **53**, 2155–2170.
50. Batsakis JG, El-Naggar AK. Sebaceous lesions of salivary glands and oral cavity. *Ann Otol Rhinol Laryngol* 1990, **99**, 416–418.
51. Ellis GL, Corio RL. Acinic cell adenocarcinoma. A clinicopathologic analysis of 294 cases. *Cancer* 1983, **52**, 542–549.
52. Hamper K, Mausch HE, Caselitz J, *et al.* Acinic cell carcinoma of the salivary glands: The prognostic relevance of DNA cytophotometry in a retrospective study of long duration (1965–1987). *Oral Surg Oral Med Oral Pathol* 1990, **69**, 68–75.
53. Lewis JE, Olsen KD, Weiland LH. Acinic cell carcinoma: clinicopathologic review. *Cancer* 1991, **67**, 172–179.
54. Oliveira P, Fonseca I, Soares J. Acinic cell carcinoma of the salivary glands. A long term follow-up study of 15 patients. *Eur J Surg Oncol* 1992, **18**, 7–15.
55. Brandwein MS, Jagirdar J, Patil J, Biller H, Kaneko M. Salivary duct carcinoma (cribriform salivary carcinoma of excretory ducts). A clinicopathologic and immunohistochemical study of 12 cases. *Cancer* 1990, **65**, 2307–2314.
56. Butterworth DM, Jones AW, Kotecha B. Salivary duct carcinoma: report of a case and review of the literature. *Virchows Arch A Pathol Anat* 1992, **429**, 371–374.
57. Delgado R, Vuitch F, Albores-Saavedra J. Salivary duct carcinoma. *Cancer* 1993, **72**, 1503–1512.
58. Hellquist HB, Karlsson MG, Nilsson Ch. Salivary duct carcinoma—a highly aggressive salivary gland tumour with overexpression of c-erbB-2. *J Pathol* 1994, **172**, 35–44.
59. Barnes L, Rao U, Krause J, Contis L, Schwartz A, Scalamogna Ph. Salivary duct carcinoma. Part I. A clinicopathologic evaluation and DNA image analysis of 13 cases with review of the literature. *Oral Surg Oral Med Oral Pathol* 1994, **78**, 64–73.
60. Grenko RT, Gemryd P, Tytor M, Lundquist P-G, Boeryd B. Salivary duct carcinoma. *Histopathology* 1995, **26**, 261–266.
61. Donath K, Seifert G, Schmitz R. Zur Diagnose und Ultrastruktur des tubulären Speichelgangcarcinoms. Epithelial-myoepitheliales Schaltstückcarcinom. *Virchows Arch A Pathol Anat* 1972, **356**, 16–31.
62. Corio RL, Sciubba JJ, Brannon RB, Batsakis JG. Epithelial–myoepithelial carcinoma of intercalated duct origin. A clinicopathologic and ultrastructural assessment of sixteen cases. *Oral Surg Oral Med Oral Pathol* 1982, **53**, 280–287.
63. Hamper K, Brügmann M, Koppermann R, *et al.* Epithelial–myoepithelial duct carcinoma of salivary glands: a follow-up and cytophotometric study of 21 cases. *J Oral Pathol Med* 1989, **18**, 299–304.
64. Simpson RHW, Clarke TJ, Sarsfield PTL, Gluckman PGC.

Epithelial–myoepithelial carcinoma of salivary glands. *J Clin Pathol* 1991, **44**, 419–423.
65. Batsakis JG, El-Naggar A, Luna MA. Epithelial–myoepithelial carcinoma of salivary glands. *Ann Otol Rhinol Laryngol* 1992, **101**, 540–542.
66. Fonseca I, Soares J. Epithelial–myoepithelial carcinoma of the salivary glands. A study of 22 cases. *Virchows Arch A Pathol Anat* 1993, **422**, 389–396.
67. Palma S Di. Epithelial–myoepithelial carcinoma with co-existing multifocal intercalated duct hyperplasia of the parotid gland. Case report. *Histopathology* 1994, **25**, 494–496.
68. Corio RL. Epithelial–myoepithelial carcinoma. In Ellis GL, Auclair PL, Gnepp DR, eds. *Surgical Pathology of the Salivary Glands*. Philadelphia, Saunders, 1991, 412–421.

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