

# Hybrid Carcinoma Of Minor Salivary Gland: Report Of A Case Of Adenoid Cystic And Mucoepidermoid Carcinoma, An Unusual Combination

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## Abstract

A 73 years-old Saudi male presented with an upper lip swelling. Incisional biopsy diagnosis was adenoid cystic carcinoma and total excision was recommended. On histopathological analysis of the excised lesion, a single mass comprising two well defined tumors, namely, adenoid cystic (20 %) and mucoepidermoid (80%) carcinomas was identified. These were lying adjacent to each other with a transitional zone in between. The final diagnosis was hybrid carcinoma of minor salivary gland origin. Hybrid salivary gland tumors are very rare and, to the best of our knowledge only two cases of hybrid adenoid cystic-mucoepidermoid carcinoma have been previously reported. Synchronous or metachronous recognition of two components in a salivary gland tumor is practically important to both the pathologist and the clinician becoming particularly significant when the constituent entities have different biological behaviors. The more aggressive component modulates the line of treatment conferred upon the patient. Pathologists are, therefore, urged to rule out the presence of additional tumoral components in any given salivary gland tumor.

## INTRODUCTION

The presence of two entirely distinct tumors in salivary glands is an extreme rarity. Since its original description by Seifert and Donath in 1996 [1], less than thirty cases of "hybrid" tumors of salivary glands have been described, most of which have been detected in parotid and palatine glands [2,3]. Diverse combinations of tumors as regards histological classification, localization, and origin are documented [4]. Hybrid tumors of the salivary glands are defined as lesions comprising two different neoplasms, each of which conforms with an exactly defined tumor entity, arising in a single anatomical location, and producing a single mass both clinically and microscopically [1]. The purpose of this article is to report a case of hybrid carcinoma of upper lip minor salivary glands, composed of adenoid cystic carcinoma (ACC) and mucoepidermoid carcinoma (MEC), as well as to discuss its probable histogenesis and describe its salient clinico-pathological features, prognosis and therapeutic approach. To the best of our knowledge, the combination of adenoid cystic carcinoma and mucoepidermoid carcinoma in a hybrid salivary gland tumor has been previously reported in only two instances [3].

## CASE REPORT

A 73 year-old Saudi male presented to the dental clinics at the College of Dentistry, University of Dammam with an upper lip swelling of one year duration. Physical examination revealed a painless, firm swelling in the upper lip, measuring 3.5 x 3 x 2cm and extending from the upper central to the left canine region. The swelling was covered by intact mucosa (Fig. 1). It was not fixed to the surrounding tissue. There was no tenderness over the swelling nor parasthesia of the surrounding areas. The past medical history was unremarkable. The lesion was clinically diagnosed as a minor salivary gland tumor and, to confirm its nature, an incisional biopsy was performed. A diagnosis of adenoid cystic carcinoma was made and wide excision with safety margin was advised. A multisequential, multiplanar MRI of the head and neck revealed a well defined soft tissue mass measuring about 1.5 x 1cm. in the left paramedian aspect of the upper lip, showing high signal intensity with a central area of low signal and evidence of post contrast enhancement; there was no bony erosion (Fig. 2). Excision biopsy with safety margin was carried out under local anesthesia. Grossly the specimen consisted of a firm grayish white tissue fragment measuring 2.5 x 1.7 x 1.5cm.

Upon sectioning a well circumscribed yellowish nodule measuring 1.5 cm in longest diameter was identified. On microscopic examination, two separate, well defined tumors in variable proportion were identified, lying side by side in a single slide with an intervening transitional zone in between the two (Fig. 3). The smaller tumor, comprising 20% of the total lesion, recapitulated the pattern of the originally diagnosed tumor i.e. adenoid cystic carcinoma, with small, basaloid appearing cells exhibiting hyperchromatic, angulated nuclei, scant cytoplasm and ill defined cell borders, arranged in solid sheets and cystic and cribriform spaces containing Alcian blue positive material (Figs. 4A & 4B). Diffuse immunoreactivity for p63 (Fig. 4C), calponin and S100 protein and focal reactivity for CD117 (C-kit, Fig. 4D) were demonstrated in this tumor. Immediately adjacent to it and comprising the major proportion of the lesion (80%) was a low to intermediate grade mucoepidermoid carcinoma comprising predominantly intermediate cells showing ample, pale eosinophilic cytoplasm and mild nuclear pleomorphism. These were arranged as solid nests as well as glands containing PAS positive material (Figs. 5A & 5B). Focal squamoid differentiation and intracytoplasmic mucin could also be demonstrated (Fig. 5C). Immunostaining for p63, calponin and S100 protein showed reactivity limited to myoepithelial cells scattered focally around the neoplastic glands (Fig. 5D). There was no immunoreactivity for C-kit. The margins of resection were clear. The patient is well with no tumor recurrence 9 months after the excision.

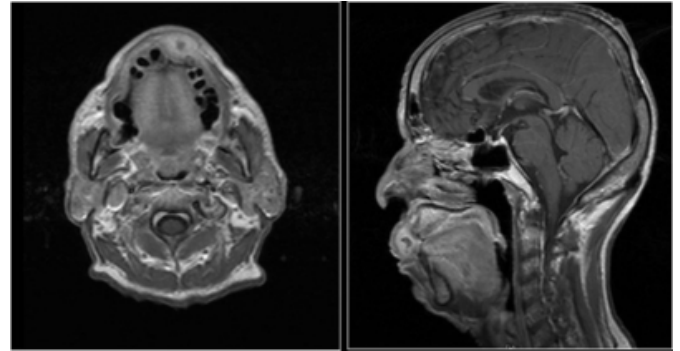
#### Figure 1

Fig. 1. Hybrid salivary gland carcinoma. Left upper lip swelling after incisional biopsy



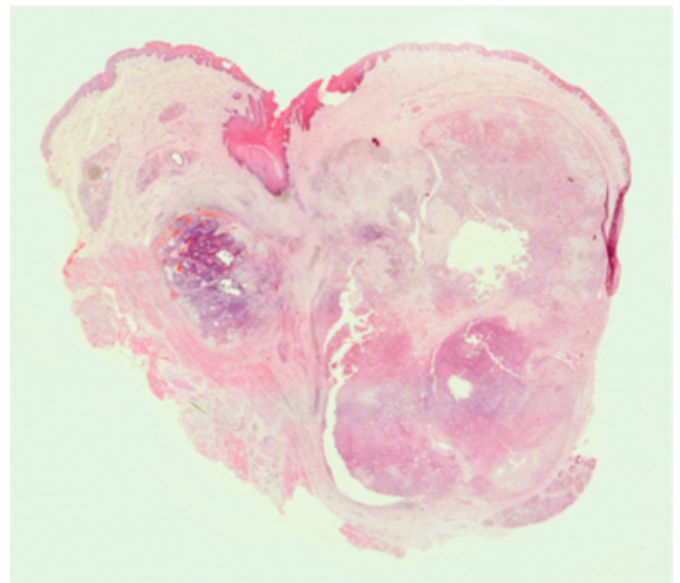
#### Figure 2

Fig. 2. Hybrid salivary gland carcinoma. MRI showing high signal intensity upper lip mass with central area of low signal. T2 axial (left) and T1 (post contrast) sagittal (right) views.



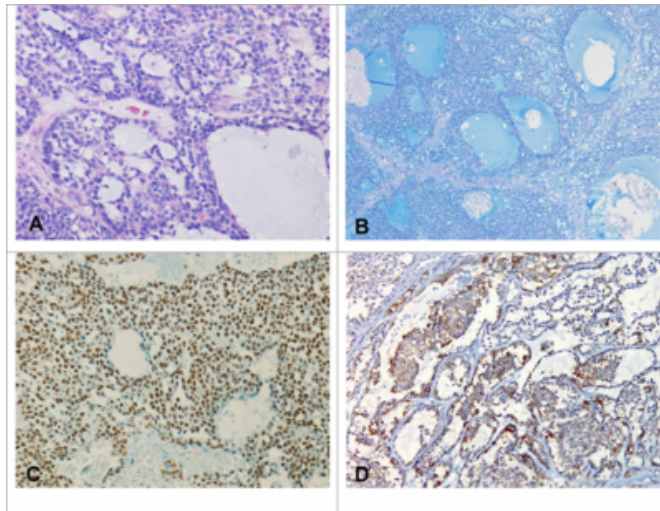
#### Figure 3

Fig. 3. Hybrid salivary gland carcinoma. Whole mount section of lesion showing two separate, well defined tumor masses lying side by side



**Figure 4**

Fig. 4. Hybrid salivary gland carcinoma, adenoid cystic carcinoma component



A) Note small cells with scant cytoplasm in solid and microcystic growth patterns. H & E x 200.

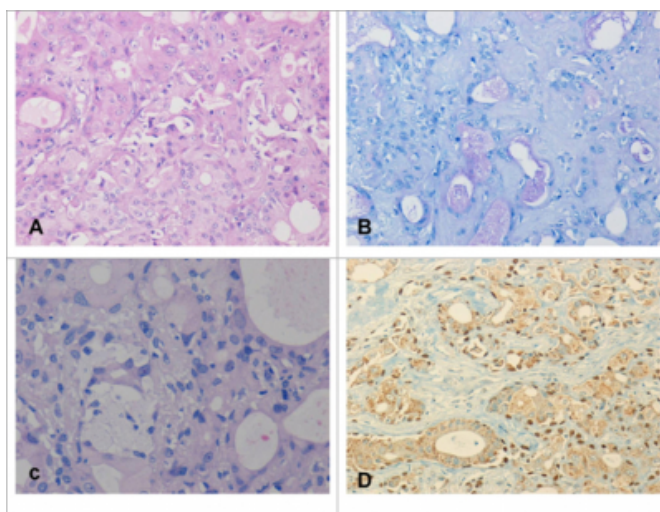
B) Note alcian blue positive material within cystic spaces. Alcian blue x 100

C) Note diffuse nuclear staining of neoplastic cells for p63. IHC x 100

D) Note focal reactivity of neoplastic cells for CD117. IHC x 100

**Figure 5**

Fig. 5. Hybrid salivary gland carcinoma, mucoepidermoid carcinoma component



A) Note intermediate cells with ample pale eosinophilic cytoplasm. H & E x 200

B) Note PAS positive material within glandular lumena. PAS x 200

C) Note mucous cells with finely vacuolated cytoplasm. H & E x 400

D) Note reactivity for p63, limited to myoepithelial cells scattered focally around neoplastic glands. IHC x 200

## DISCUSSION

The term “hybrid tumors of salivary glands” was initially coined by Seifert and Donath in 1996 to designate a very rare tumor entity, consisting of a combination two entirely distinct, well defined, separable carcinomas in the same topographical area producing a single mass clinically [1].

The two neoplasms in a hybrid tumor often reveal an identical, common origin as evidenced by presence of a transitional zone between the two components [1].

Various carcinoma combinations have been described, salivary duct carcinoma, epithelial-myoepithelial carcinoma (EMC) and adenoid cystic carcinoma being frequently involved [5 -13].

Investigators have suggested that the aggressiveness of the lesion depends on the histologically higher grade neoplasm [1, 8, 10, 11, 13].

Since the original description, less than 30 cases of hybrid tumors of salivary gland origin have been reported to date [1- 4, 11]. Most cases have developed within parotid and palatine glands [3], but the entity has also been found in submandibular glands [2, 11], maxillary sinus [4] and lacrimal glands [2]. Although there are hybrid tumors with benign components, most of the reported cases are malignant neoplasms (hybrid carcinomas) in which the most frequently identified neoplasm has been ACC (14 out of 25 reported cases). The combination of ACC with EMC has been found in seven instances.

Defining the precise criteria for hybrid carcinomas has been a matter of controversy. According to Gnepp et al [14] each component of hybrid carcinoma should show differentiation towards a distinct salivary glandular element i.e. excretory duct versus acinar or intercalated duct. Grenko et al. [15] have documented three adenoid cystic carcinomas and two epithelial-myoepithelial carcinomas that focally shared both

histological features. They consider that, as these two entities shared a common differentiation pathway, so presence of adenoid cystic carcinoma-like areas in EMC may be regarded as an anomalous differentiation in a single tumor and not as a hybrid neoplasm. Intercalated duct hyperplasia being the basis of multidirectional differentiation and responsible for simultaneous occurrence of more than one tumor was suggested by Di Palma [16]. Seifert and Donath [1,17], Croitoru et al. [10], Nagao et al. [2], and Chetty [13] opined that complete divergent differentiation may produce two distinct, well defined tumor entities e.g. adenoid cystic and mucoepidermoid carcinoma (hybrid tumor), whereas incomplete divergence may produce tumors with overlapping histological features e.g. adenoid cystic carcinoma and EMC. Based on this concept, our case may be considered a “true” hybrid carcinoma and, to the best of our knowledge, it is the third hybrid adenoid cystic - mucoepidermoid carcinoma to be reported in the literature [3].

Hybrid tumors need to be distinguished from certain entities in the salivary gland in which a neoplastic lesion may exhibit two or more different morphologies. Leading the list are: Collision tumors comprising neoplasms that originate in separate, independent topographical regions but coalesce in a particular area [1-4, 17] and show no transitional zone at the meeting point

[1, 17] - tumors with biphasic differentiation (single entities containing two different cellular types, such as pleomorphic adenomas) – synchronous and multiple tumors [2-4,16] - carcinomas with metaplastic change [2-4, 18,19] - dedifferentiated carcinomas [20-22] - sarcomatoid salivary duct carcinoma [23] - adenosquamous carcinoma [24, 25] and malignant mixed tumors [25]. While the possibility of developing multiple tumors that coalesce and invade each other with the production of collision tumors that simulate a single entity does exist in major salivary glands, the probability of this phenomenon to occur in “minor” salivary glands is remote, and, therefore, the diagnosis of a hybrid tumor and tumors with biphasic differentiation should be strongly considered when the tumor contains two different tumor entities which are not separated and are located in the same topographical area [1, 4].

An important issue is that the prognosis of a hybrid carcinoma is not dependent on the proportion of each constituent neoplasm. The minor one, if more aggressive, can produce a metastatic lesion and studies do exist,

documenting a metastasis originating from the tumor that comprised hardly 20% of the total lesion [10]. Treatment strategy, therefore, needs to be directed towards the more aggressive component, which is in fact the therapeutic recommendation in all such cases [1 -4, 10,26]. In addition a hybrid neoplasm also mandates a prolonged and close follow up in order to ascertain its overall biological behavior, i.e. to what extent it bears homology to the behavior of its individual constituent neoplasms. Pathologists are, therefore, urged to rule out the presence of additional tumoral components in any given salivary gland tumor.

## CONCLUSIONS

Hybrid salivary gland tumors are generally very rare. The particular combination of adenoid cystic carcinoma and mucoepidermoid carcinoma is even more rare and also unusual as it probably results from a divergent rather than a common differentiation pathway of the salivary epithelium. Recognition of two components in a salivary gland tumor is practically important, becoming particularly significant when the constituent entities have different biological behaviors. The more aggressive component modulates the treatment which the patient will receive. Pathologists are, therefore, urged to rule out the presence of additional tumoral components in any given salivary gland tumor.

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