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Article Type: Editorial

Keywords: Low Grade Malignant Myoepithelioma

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Abstract:
LOW GRADE MALIGNANT MYOEPITHELIOMA
ARISING IN A PLEOMORPHIC ADENOMA

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**Abstract**

Malignant myoepithelioma is a very rare salivary gland tumor that can arise de novo or within a pre-existing pleomorphic adenoma. We report a case of malignant myoepithelioma most probably arising in a pre-existing pleomorphic adenoma of the left parotid gland. A 60 year-old man presented with multinodular mass lesion over left side of the face and neck. He had a history of twice removal of a pleomorphic adenoma of the left parotid gland in 8 years and 22 years ago. Histological examination showed a highly, locally invasive myoepithelial cells with bland-looking morphology and with no evidence of mitosis or necrosis. The immunohistochemistry confirmed the myoepithelial differentiation (S-100 +, SMA+) and Ki-67 labeling index was low (<5%).

**Introduction:**

Myoepithelial cells form a significant component of several types of benign and malignant salivary gland tumors [1]. Tumors
composed exclusively or predominantly of myoepithelial cells
“myoepitheliomas” are uncommon and accounting for less than
1% of all salivary gland tumors [2, 3]. Most behave in a benign
fashion. The malignant counterpart (malignant myoepithelioma
or myoepithelial carcinoma) is even more rare with less than 50
cases on records. It was considered a distinct entity in the revised
edition of WHO classification of salivary gland tumors in 1991[2,
3]. Malignant myoepithelioma can arise de novo or from a pre-
existing pleomorphic adenoma [4, 5]. It most commonly affects
the parotid gland but other major or minor salivary glands can
also be affected. The histological features that signify malignancy
include tumor infiltration, nuclear atypia, frequent mitosis and
coagulative necrosis [5].

We report a case of malignant myoepithelioma of the left
parotid gland, the only feature we have is the frank tumor
invasion without cytological atypia, mitosis or necrosis and that
was most probably arising in a pre-existing pleomorphic
adenoma.
CASE REPORT

60 year-old man presented with painless firm, irregular and nodular swellings on the left side of the face. They were slowly growing over a period of 6 years. He gave a history of a benign parotid tumor on the same side which was resected 22 years ago. The tumor recurred and resected again after 14 years from the primary resection. The Histologic diagnosis in both was pleomorphic adenoma.

On examination, there was a multiple, firm to hard masses located in the region of the left parotid gland, on the ear pinna and the temporal region. The skin was ulcerated focally. The facial nerve was completely paralyzed since his second surgery and no cervical lymphadenopathy. The hematological and biochemical profile were normal. The CXR is normal. The head & neck CT-scan revealed a large multilobulated left parotid mass with extensive calcifications invading the skin and the auricle. The temporal and zygomatic bone show significant sclerosis. The tumor also extends to the Para pharyngeal space and the infratemporal fossa.
Fine needle aspiration cytology was performed and the diagnosis was consistent with pleomorphic adenoma. The patient underwent a left radical parotidectomy along with resection of the involved left facial skin, total auricloectomy, excision of the zygoma and the infratemporal fossa with canal wall down mastoidectomy, facial nerve grafting and pectoralis major myocutaneous flap.

The patient apparently was doing well and the anticoagulants were discontinued. On postoperative day 14, he died after developing deep vein thrombosis and pulmonary embolism.

**Pathological Findings**

**Gross features:**

The specimen consisted of a wide excision of a multinodular tumor along with the facial skin and left ear lobe measuring 15×9×5 cm. (Fig.1).

The nodules range in size from 1 cm to 8 cm. The cut surface showed solid multinodular white–grayish to mucoid nodules. The tumor was extending into the skin with focal ulceration and invading deeply into the underlying bone.
**Microscopic features:**

The histological sections showed invasive multinodular tumor composed of cells with variable morphology: 1- clear cells 2- epithelioid cells 3- spindle cells .The clear and epithelioid cells predominates (Fig.2,Fig.3).

The tumor cells showed bland nuclear morphology with round to oval nuclei, fine chromatin, small or inconspicuous nucleoli and moderate amount of clear to eosinophilic cytoplasm embedded in a myxoid background resulting in a "lace-like" pattern. Some areas showed hyalinized background.

The tumor cells invaded the skin, the surrounding soft tissue and the underlying bone( Fig.4). Focal area showed a rim of normal parotid tissue. Rare epithelial elements consisting of benign ducts and tubules with squamous metaplasia were focally present. There was no cellular atypia, mitosis coagulative necrosis or evidence of vascular invasion. The tumor was very close to the deep and lateral soft tissue margins.
**Immunohistochemical findings**

The tumor cells showed diffuse strong positivity for S-100 protein, focal positivity for SMA and AE1/AE3 and they were negative for GFAP. Ki-67 was positive in less than 5% of the tumor cells.

**Discussion:**

Myoepitheliomas is a very rare tumor accounting for less than 1% of salivary gland tumor. The majority of the myoepitheliomas described in the literature has been benign and the malignant counterpart is considered very rare. Malignant myoepitheliomas may appear de nova or develop from a pre-existing pleomorphic adenoma. Grossly, malignant myoepitheliomas range in size from 2 to 20 cm in largest dimension. They are unencapsulated with multinodular growth pattern and gray-white cut surface. Necrosis and cystic degeneration can be seen. Microscopically, they are composed of one or several cell types: spindle, plasmacytoid, epithelioid and clear cells. Frequently, one of the cell types predominates [3]. These cells can grow in a nodular, trabecular or solid fashion.
The stroma is usually myxoid or hyalinized. The diagnosis of malignant myoepithelioma is based on two main histological criteria: exclusively myoepithelial and unequivocally malignant [3]. The neoplastic cells must show myoepithelial differentiation and lack ductal or acinar differentiation although the presence of a minor epithelial component (e.g. less than 5-10%) is still accepted [6].

In our case, the myoepithelial differentiation was established by immunohistochemistry where the tumor cells were positive for S-100 and α-SMA.

The malignancy is usually supported by the following histological features: tumor infiltration, cytological atypia, easily identifiable mitosis and coagulative necrosis.

Most malignant myoepitheliomas show more than one feature [5]. Nearly all malignant myoepitheliomas had tumor infiltration into adjacent tissue. The cytological atypia, mitosis and necrosis may or may not all be present in each case [3, 5].

Therefore, tumor infiltration into adjacent tissues is the most important histological feature of malignancy and should be considered the minimum requirement for malignant
myoepitheliomas [3, 5, 6, 7]. Interestingly; in our case; the tumor showed one feature only which is the tumor infiltration without atypia, mitosis or necrosis.

Our case report showed a highly invasive myoepithelial cells with bland-looking morphology and with no mitosis or necrosis. The diagnosis of malignancy was based solely on the highly infiltrative growth pattern. On such cases, the diagnosis of malignancy on fine needle aspiration cytology is difficult or even impossible [7].

In one study, Nagao et al. suggested that assessment of cell proliferation activity may be helpful in the differential diagnosis between benign and malignant myoepitheliomas and that more then 7 mitosis per 10HPFs or Ki-67 labeling index of more than 10% is diagnostic of malignant myoepitheliomas[4,5,7]. In our case, there was no mitosis and Ki-67 labeling index was less than 5%.

Di Palma and Guzzo et al described five cases of malignant myoepithelioma arising in a pleomorphic adenoma [8]. Malignancy developed after variable time intervals ranging from 6 to 43 years. In the case described by Singh and Cawson, the
malignancy developed in a parotid gland mass which had been present for 15 years [8, 9].

Pleomorphic adenoma is the most common neoplasm of salivary glands and is well-known for tendency to recur locally following surgical resection. Malignant transformation is uncommon. The most common malignant tumor arising in a pleomorphic adenoma is carcinoma which is usually undifferentiated carcinoma or adenocarcinoma, not otherwise specified. These carcinomas are highly aggressive while malignant myoepitheliomas are low grade malignancy unless they arise de novo [4, 5, 9].
REFERENCES


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Figure 1  Left parotid area swelling, showing the multinodular
Mass with focally ulcerated skin.
Figure 2b

Figure 2a and Figure 2b  Sheets and thick cords of ovoid to spindle component with moderate amount of pale to eosinophilic cytoplasm.

Uniform, mildly hyperchromatic nuclei and inconspicuous nucleoli.
Figure 4

Maxillary bone permeation by tumor.