case report

Low-grade malignant myoepithelioma arising in a pleomorphic adenoma: a rare case

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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. The patient was a 60-year-old man who presented with a multinodular mass lesion over left side of the face and neck. He had undergone removal of a pleomorphic adenoma of the left parotid gland twice (8 and 22 years ago). Histological examination showed locally concentrated highly invasive myoepithelial cells with bland-looking morphology and no evidence of mitosis or necrosis. Immunohistochemistry confirmed the myoepithelial differentiation (S-100+, SMA+) and a low Ki-67 labeling index (<5%).

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 account for less than 1% of all salivary gland tumors, most of which are benign.[2,3] The malignant counterpart (malignant myoepithelioma or myoepithelial carcinoma) is even more rare, with less than 50 cases on record. It was considered a distinct entity in the revised edition of the WHO classification of salivary gland tumors in 1992.[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 observed was the frank tumor invasion without cytological atypia, mitosis, or necrosis, and that had most probably arisen in a pre-existing pleomorphic adenoma.

CASE

A 60-year-old man presented with painless firm, irregular, and nodular swellings on the left side of the face. They had been 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 was resected again in Sudan after 14 years from the primary resection. The glass slides were reviewed by one of the authors (ER) and the diagnosis of pleomorphic adenoma was confirmed (**Figure 1**).

On local examination we observed multiple, firm-to-hard masses located in the region of the left parotid gland, on the ear pinna, and in the temporal region. The skin was ulcerated focally. The facial nerve was completely paralyzed since his second surgery and no cervical lymphadenopathy was reported. The hematological and biochemical profiles were normal. The chest x-ray was normal. A CT scan of the head and neck revealed a large multilobulated left parotid mass with extensive calcifications invading the skin and the auricle. The temporal and zygomatic bones showed significant sclerosis. The tumor also extended to the parapharyngeal 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 auriculectomy, excision of the zygoma and

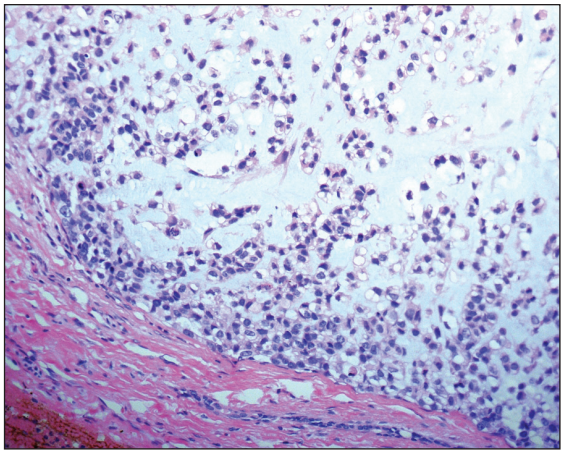

Figure 1. Pelomorphic adenoma of the parotid gland. A well-defined tumor has a thin fibrous capsule and shows chondroid stroma resembling the hyaline cartilage (hematoxylin and eosin stain, 100×).

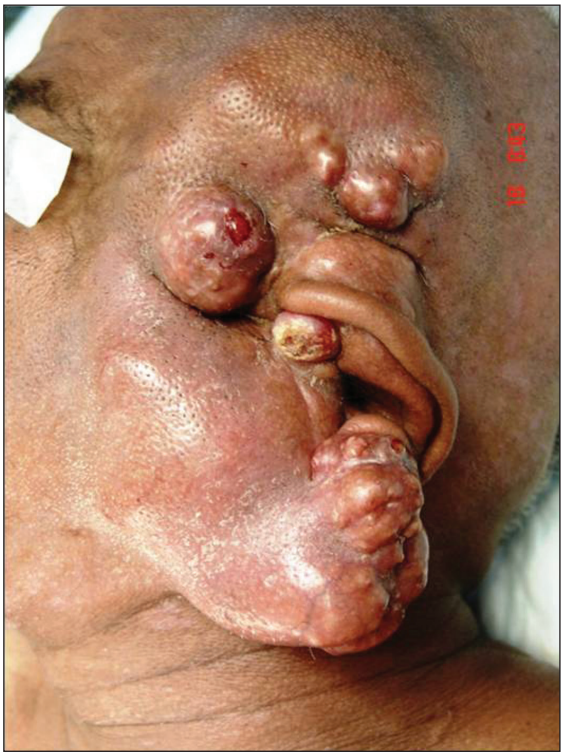

Figure 2. Left parotid area swelling, showing the multinodular mass with focally ulcerated skin.

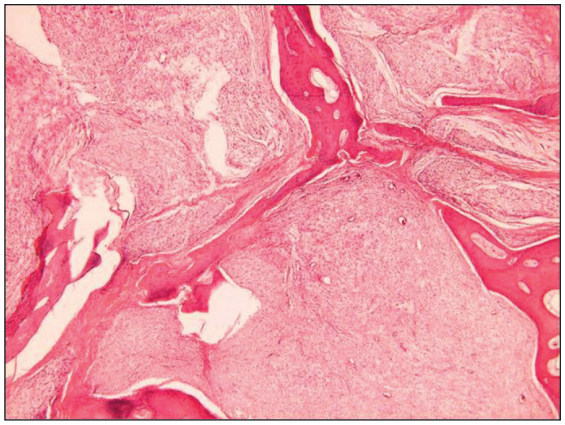

Figure 3a. Sheets and thick cords of ovoid to spindle cell component with moderate amount of pale to eosinophilic cytoplasm (hematoxylin and eosin stain, 100×).

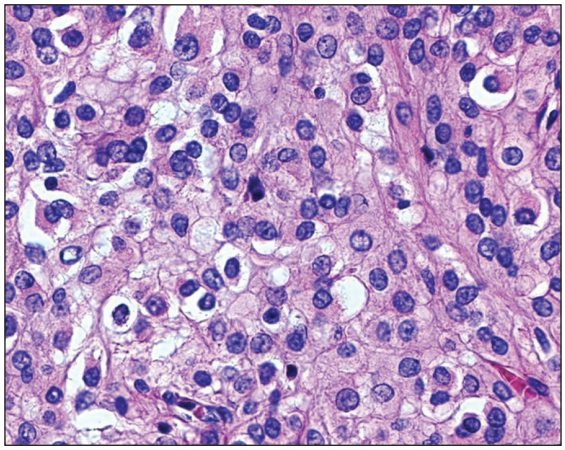

Figure 3b. Uniform, mildly hyperchromatic nuclei and inconspicuous nucleolei (hematoxylin and eosin stain, 400×).

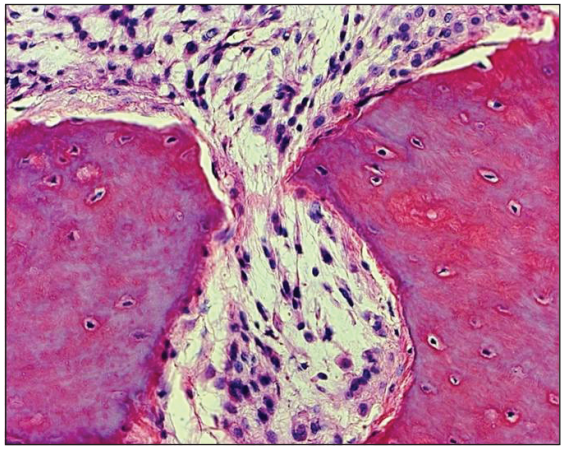

Figure 4. Maxillary bone permeation by the tumor (hematoxylin and eosin stain, 400×).

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.

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 (**Figure 2**). The nodules ranged in size from 1 to 8 cm. The cut surface showed solid multinodular grayish-white to mucoid nodules. The tumor extended into the skin with focal ulceration and invading deeply into the underlying bone. The histological sections showed an invasive multinodular tumor composed of cells with variable morphology: clear cells, epithelioid cells, and spindle cells. The clear and epithelioid cells predominated (**Figures 3a and 3b**). The tumor cells showed bland nuclear morphology with round-to-oval nuclei, fine chromatin, small or inconspicuous nucleoli, and a moderate amount of clear-to-eosinophilic cytoplasm embedded in a myxoid background, resulting in a "lace-like" pattern. Some areas showed a hyalinized background.

The tumor cells invaded the skin, the surrounding soft tissue, and the underlying bone (**Figure 4**). The focal area showed a rim of normal parotid tissue. Rare epithelial elements consisting of benign ducts and tubules with squamous metaplasia were focally present. No evidence of cellular atypia, mitosis coagulative necrosis, or vascular invasion was reported. The tumor was very close to the deep and lateral soft tissue margins. The tumor cells showed diffuse strong positivity for S-100 protein, focal positivity for α-SMA and AE1/AE3, and negativity for glial fibrillary acidic protein. Ki-67 was positive in less than 5% of the tumor cells.

DISCUSSION

Myoepitheliomas are very rare tumors, accounting for less than 1% of all salivary gland tumors. The majority of the myoepitheliomas described in published reports have been benign, and the malignant counterpart is considered very rare. Malignant myoepitheliomas may appear de novo or develop from a pre-existing pleomorphic adenoma. Grossly, malignant myoepitheliomas range in size from 2 to 20 cm in the largest dimension. They are unencapsulated with multinodular growth pattern and grayish-white cut surface. Necrosis and cystic degeneration can be seen. Microscopically, they are composed of a single cell type or several cell types: spindle, plasmacytoid, epithelioid, and clear cells.

Table 1. Brief summary of clinico-pathological features of published cases of malignant myoepithelioma arising in pleomorphic adenoma.

Source /Year	Number of cases	Age (years)/Sex	Anatomical location	Histological subtype of myoepithelial carcinoma
Singh and Cawson,[7] 1988	1	66/F	Parotid	Low-grade myoepithelial carcinoma
Di PalmaandGuzzo,[8] 1993	10	14-63/ 6 females and 4 males	8-parotid and 2-intraoral	Histomorphologic spectrum ranging from round cells to spindle-shaped and stellate cells
Suzuki et al.,[10] 1998	1	62/F	Parotid	Plasmacytoid predominant myoepithelial carcinoma
Daneshbod et al.,[11] 2007	1	29/F	Parotid	Epithelial- myoepithelial carcinoma
Parwani et al.,[12] 2006	1	76/F	Parotid	Low-grade myoepithelial carcinoma
Karatzanis et al.,[13] 2005	1	70/F	Soft palate	Low-grade myoepithelial carcinoma
McCluggage et al.,[14] 1998	1	55/M	Parotid	Low-grade myoepithelial carcinoma
Rammeh-Rommani et al.,[15] 2007	1	57/M	Parotid	Low-grade myoepithelial carcinoma
Wong and Lee,[9] 2010	1	69/M	Parotid	Oncocytic variant of myoepithelial carcinoma
Raddaoui et al (present)	1	60/M	Parotid	Low grade myoepithelial carcinoma

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, wherein 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 have tumor infiltration into adjacent tissues. 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 the diagnosis of malignant myoepithelioma.[3,5,6] In our case, the tumor showed only one feature (tumor infiltration without atypia, mitosis, or necrosis). Our case 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. In such cases, the diagnosis of malignancy based on fine-needle aspiration cytology is difficult or even impossible.[7]

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

Di Palma and Guzzo et al described 5 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 that had been present for 15 years.[7] Pleomorphic adenoma is the most common neoplasm of the salivary gland and is well known for its tendency to recur locally following surgical resection. Malignant transformation is uncommon (**Table 1**). The most common malignant tumor arising in a pleomorphic adenoma is carcinoma, which is usually an undifferentiated carcinoma or adenocarcinoma not otherwise specified. These carcinomas are highly aggressive, while malignant myoepitheliomas are of low-grade malignancy unless they arise de novo.[4,5]

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