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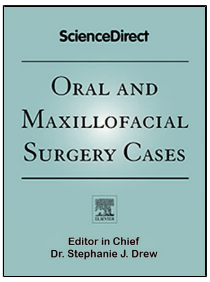

Clear cell myoepithelial carcinoma ex pleomorphic adenoma of parotid gland: case report and review of literature

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Clear cell myoepithelial carcinoma ex pleomorphic adenoma of parotid gland: case report and review of literature

ABSTRACT

Myoepithelial carcinoma (MC), also known as malignant myoepithelioma, shows an infiltrative and destructive growth **[1]**. Myoepithelial neoplasms account for about 1.5% of all salivary tumors, and MC is even more rare, representing about 10% of myoepitheliomas **[1-3]** with a reported incidence of 0.2% of all salivary gland tumors. In this case, the cytological diagnosis (pleomorphic adenoma) and negative lymph nodes, addressed the surgeon for a parotidectomy, following guidelines and literature**[27]**. The best treatment for huge, relapsing tumours, notwithstanding cytological diagnosis, is not only parotidectomy, as lymphadenectomy should be performed too, given myoepithelial carcinoma's high-grade potential and unpredictable biologic behavior. Careful patient follow-up and staging, is therefore essential for better characterization and understanding of this tumor's behavior in the future. We also considered a more conservative treatment following guidelines, as this case was lacking metastases and lymphatic involvement, considering that application of guidelines, surgical and clinical expertise and appropriate technology can contain potential medicolegal implications **[28]**.

Keywords: Myoepithelial carcinoma, neoplasms, parotid gland, salivary gland

INTRODUCTION

Myoepithelial neoplasms are tumors composed of cells with myoepithelial differentiation. Most behave in a benign fashion and are designated myoepithelioma. Myoepithelial carcinoma (MC), also known as malignant myoepithelioma, is the malignant counterpart of benign myoepithelioma, from which is distinguished by its infiltrative, destructive growth **[1]**. Myoepithelial neoplasms account for about 1.5% of all salivary tumors, and MC is even more rare, representing about 10% of myoepitheliomas **[1-3]** with a reported incidence of 0.2% of all salivary gland tumors**[4].** However, some Authors contend that myoepithelial carcinoma (malignant myoepithelioma) may not be as rare as previously suggested **[2,5]**, as a lack of recognition and/or awareness of its diversity and diagnostic criteria may contribute to the relatively small number of reported cases. It was first described by Stromeyer et al. in 1975 **[6]** and Barnes et al. renewed interest in this tumour in 1985, describing 3 cases of myoepithelial carcinoma in their review of head and neck myoepitheliomas. **[7]** Dardick et al. furthered the understanding of myoepithelial tumors**[8,9]** increasing the accuracy of describing reported cases of myoepithelial carcinoma. This kind of tumour was added to the second edition of the World Health Organization (WHO) classifications of malignant salivary gland tumours in 1991**[11]**. Many of these tumours arise as a malignant transformation in the setting of a benign pleomorphic adenoma or a benign myoepithelioma**[12-18]**, and myoepithelial carcinoma is particularly seen in association with recurrence of these benign tumors. Other tumours like this arise de novo. **[12,13,19]**

The differential diagnosis of clear cell salivary neoplasms includes clear cell myoepithelial carcinoma (CCMEC), primary salivary clear cell tumors (CCC), epithelial-myoepithelial carcinoma (EMEC), and clear cell variants of other salivary tumors, including acinic cell carcinoma, oncocytoma and mucoepidermoid carcinoma. Also metastatic tumors, such as renal cell carcinoma

or balloon cell melanoma, are a consideration **[19-21].**

CASE REPORT

A 60-year-old female referred to our Department of Maxillofacial Surgery on February 2017 with a 2 years duration gradual painless mass in the right parotid region. This patient had already a history of pleomorphic adenoma in the same region, treated in 2000 and in 2010 by enucleation, after relapse. On inspection, hyperemic skin coating the mass. On palpation, a painful tender-elastic mass of about 2 x 2,5 cm, adherent to the skin and deep tissues. Facial nerve was not involved.

The patient had already undergone, in December 2016, an ultrasound of the right parotid region and the structural appearance was that of a big nodular, iso-hypoechogenic formation of 1,5 x 1.0 cm. Computed tomography (CT) scan, performed in February 2017, showed a 2.5 × 3 cm oval area in the right parotid gland [Fig. 1]. Moreover, the mass was dishomogeneously enhanced with contrast. No metastatic cervical node was showed. Then, a fine-needle aspiration was performed. Cytology revealed evidence of pleomorphic adenoma. The analysis showed hypercellularity with not atypical, incohesive and cohesive areas.

The patient underwent a radical right parotidectomy with resection of the facial nerve, and preservation of one branch of the temporozygomatic branch was performed [Figg. 2a-2b]. Because of the deep adherence of the tumor to the remaining part of the facial nerve, it could not be preserved. SMAS flap reconstruction was then done. No lymphadenectomy was performed, given the benignity of the pleomorphic adenoma resulting from the cytology.

Histology disclosed, on superficial parotidectomy slices, a multinodular, mixed tumor, with epithelial – myoepithelial pleomorphic adenoma areas and clear cell myoepithelial areas. This last finding is considered as an expression of the clear cell myoepithelial carcinoma, given the proliferation of the salivary glands and the plurinodular growth interesting the surrounding tissues. On deep parotidectomy slices, histology disclosed a predominantly stromal component of pleomorphic adenoma, comparable to the cytological diagnosis.

Tumor cells were negative for HMB45 (monoclonal antibody that reacts against antigen present in melanocytic tumors such as melanomas), CD10 (cluster of differentiation which excluded the possibility of metastasis of renal clear cell adenocarcinoma) DOG-1 (tubular and cribriform predominant adenoid cystic carcinoma are more frequently DOG1 positive) and CD68. Immunohistochemical stains revealed that the tumor cells were positive for S100 protein and CK (cytokeratin) 18 (myoepithelial component), CK 8 (epithelial component).

In the case described here, only postoperative frozen section confirmed the malignant nature of this rare neoplasm. Of course FNAB can confirm the malignant nature of such neoplasm but, when not corresponding to the imaging, it should address the surgeon for further evaluation to best treat the patient, mostly in patients with a relapsing, huge dimension pleomorphic adenoma diagnosis. The best treatment for such malignancy, as a matter of fact, is not only parotidectomy, as lymphadenectomy should be performed, too.

DISCUSSION

In the past, myoepithelial carcinomas (MC) have been underrecognized, primarily by being lumped under a broader category of "malignant mixed tumor." Awareness of their peculiar cytoarchitectural patterns and immunohistochemical profile is fundamental for accurate identification.**[1-3]** MC, also known as malignant myoepithelioma, is a rare, aggressive primary salivary gland neoplasm, accounting for less than 1% of all salivary gland tumours.

About 60% to 70% of MC develop in a benign mixed tumour **[1,2].** This malignant tumor is composed almost exclusively of neoplastic cells with myoepithelial differentiation and characterized by infiltrative growth and potential for distant metastasis **[2,5].**

The mean age of presentation is about 55 years and there is no preference for sex. Thetumor usually appears as an asymptomatic mass that slowly increases in size **[6].** Histologically,myoepithelial carcinomas are variously composed of one or different cell types: plasmacytoid, spindle, epithelioid, and clear cells. Frequently, one type of cells predominates. The neoplastic cells grow either as multiple nodules or as large solid sheets separated by variable amounts of interposing hyaline or myxoid stroma. The cytological patterns in FNABs,**[7-9]** generally reflect the histology. The cytological smear can show epithelioid, spindle, or plasmacytoid cells. Scant fragments of metachromatic stroma intermixed with neoplastic cells might be observed in the cytological specimens, regardless the composition of the cell types.

MC exhibits a propensity for distant metastasis more than for regional lymph node metastasis, **[22]** with an ability for extensive local growth, infiltration, and destruction **[15,22]**. Distant metastasis has been seen to the lungs (most commonly), bone, liver, peritoneum, pleura, kidney, brain, and skin **[7,18,23-25]**. So, MC is an aggressive tumor that is associated with a high rate of distant metastasis and, compared with de novo myoepithelial carcinoma, carcinoma ex-pleomorphic adenoma correlates with worse clinical outcome **[25].** Prognostic reports on MC are generally limited. Surgery is the first line treatment, either for recurrent, or distant metastatic or lymph node metastatic tumours. Postoperative radiotherapy is used in metastatic tumours, with scarce benefits from chemotherapy. **[2,22-28]**

With around 50% to over 65% survival from cases that were followed-up in reported series, myoepithelial carcinoma should probably best considered a tumor with high-grade potential and unpredictable biologic behavior. Careful patient follow-up and staging is therefore essential for better characterization and understanding of this tumor's behavior in the future.

Differential diagnoses of myoepithelial carcinoma include: spindle cell neoplasms (eg, leiomyosarcoma, schwannoma, spindle cell squamous cell carcinoma, metaplastic carcinoma, metastatic malignant melanoma); tumors with clear cell morphology (eg, epithelial-myoepithelial carcinoma, hyalinizing clear cell carcinoma, mucoepidermoid carcinoma, metastatic renal cell carcinoma, clear cell carcinoma of salivary glands); tumors with epithelioid morphology (eg, adenocarcinoma, adenoid cystic carcinoma, metastatic malignant melanoma); tumors with plasmacytoid morphology (eg, plasmacytoma, malignant melanoma, lymphomas, medullary thyroid carcinoma.

CONCLUSION

As first step, this citologically defined pleomorphic adenoma of parotid was treated in our Department, as recommended in literature for pleomorphic adenomas **[27]**, by parotidectomy. In fact, this kind of lesion should be treated conservatively when clinical and imaging findings do not address the surgeon for a malignant diagnosis, lacking metastases and lymphatic involvement. Proper treatment of this kind of lesion is mandatory, as surgical errors and complications in neck surgery are a relevant clinical issue. Only the combination of surgical and clinical expertise, application of guidelines, and appropriate technology can contain potential medicolegal implications. **[28]** Though, in this case, the frozen section diagnosis did not correspond to the cytological diagnosis, as 60% to 70% of MC develops in a benign mixed tumour. **[1,2]**. The myoepithelial clear cell tumor diagnosis, deriving by frozen section analysis, corresponded to the typical aspect, described in literature **[29]**, we observed in CT scans the patient underwent before surgery. Myoepithelial carcinoma has, in fact, characteristic pathologic features and computed tomography imaging findings, including an irregularly lobulated or multinodular lesion with ill-defined margins, moderate and intense inhomogeneous enhancement, intensely enhanced nodules, and small tortuous vessels. Myoepithelial carcinomas arising within a preexisting benign tumour should be suspected if there is long history of benign parotid tumour with history of rapid growth and/or multiple recurrences in a preexisting pleomorphic adenoma with or without lymph node

metastasis.**[30]** In big, relapsing tumours, notwithstanding cytological diagnosis and negative lymph nodes, it is legit to suspect there is some grade of variability in malignant cells, such as those of myoepithelial carcinoma. So, in our experience, we suggest all these factors should address the surgeon for a more appropriate treatment, consisting in a parotidectomy plus omolateral lymphadenectomy.

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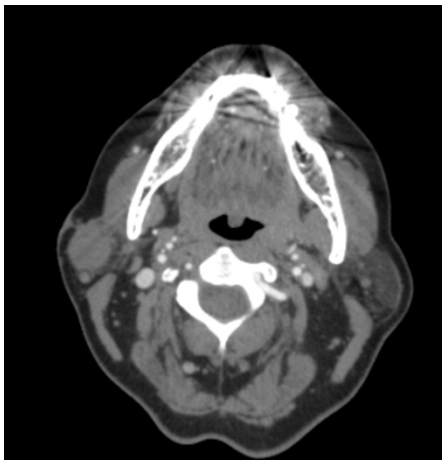
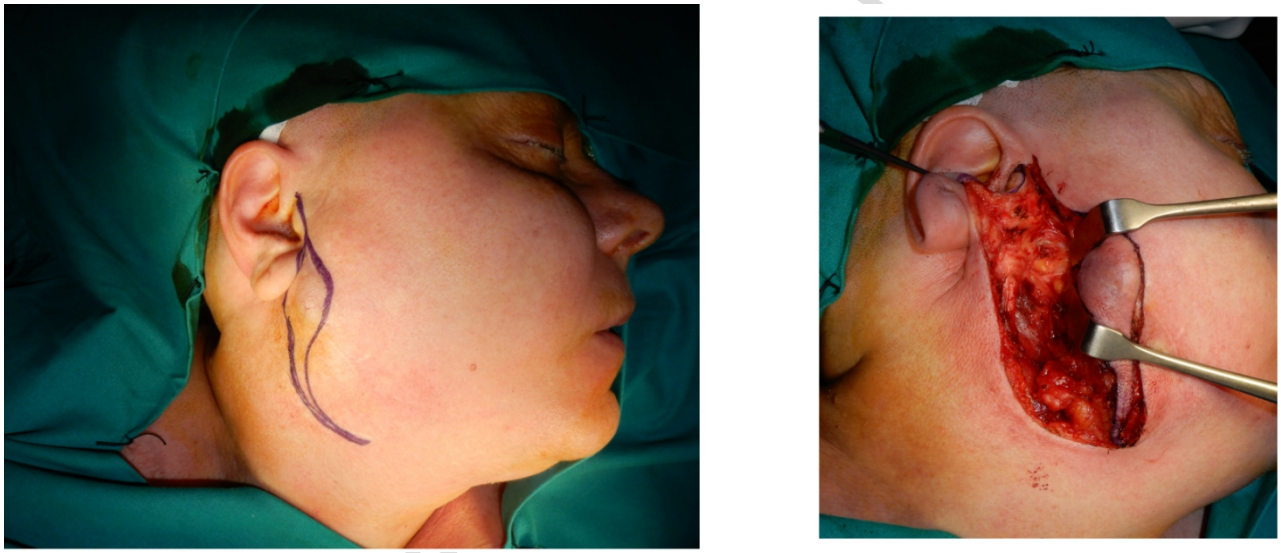


Figure 1:
Cervical CT showing a 2.5 × 3 cm ovalar area in the right parotid gland



a) b)

Figure 2:(a) Preoperative photograph of the tumor, **(b)** Intra-operative photograph showing the area after right parotidectomy

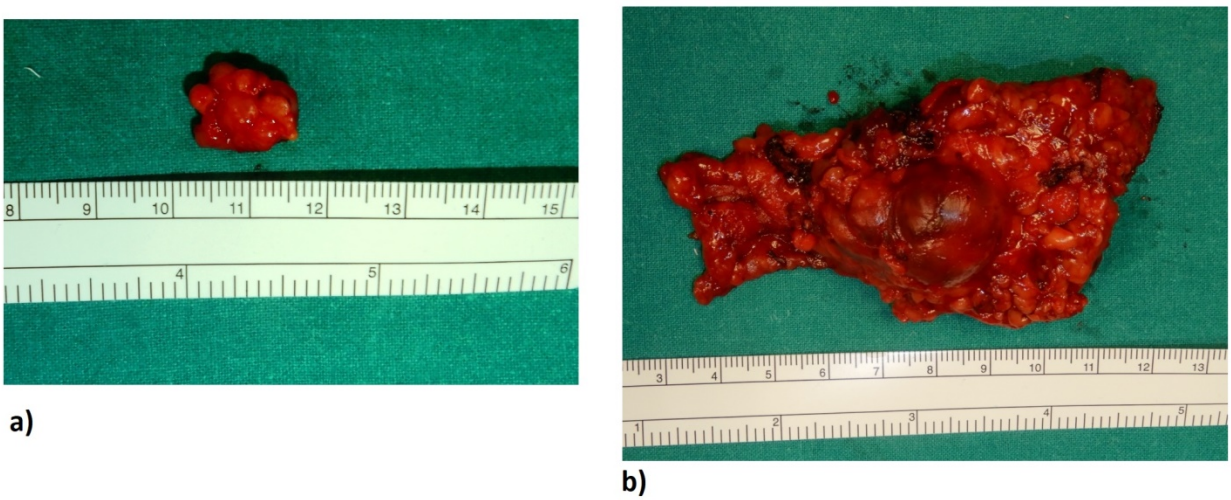


Figure 3: Surgical specimen. **(a)** Gross photopraph showing a multinodular grey-white tumor in the parotid parenchyma. **(b)** Deep parotidectomy.

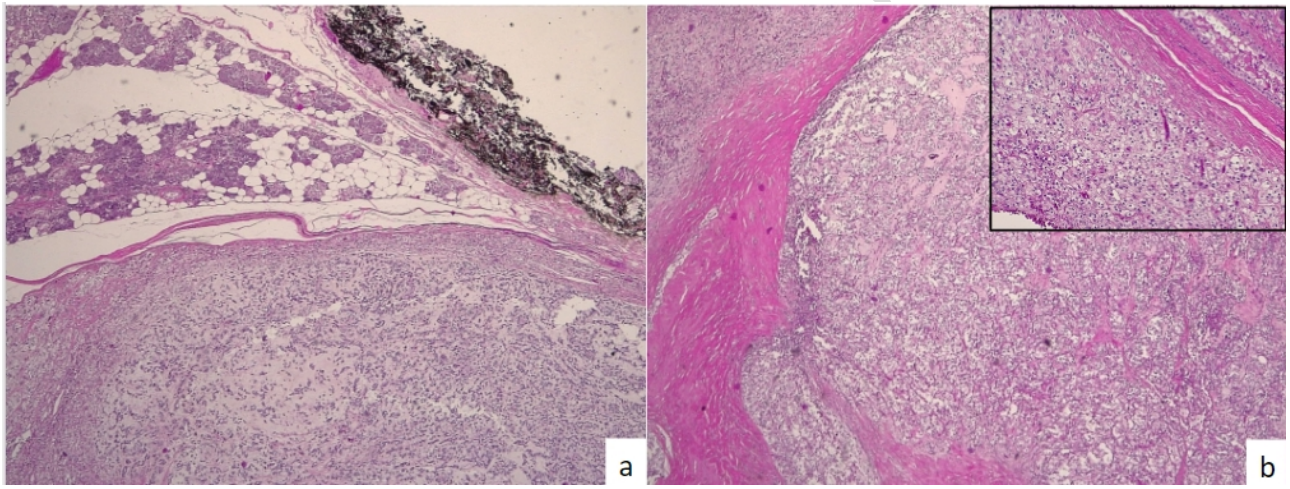


Figure 4: Histological examination: **(a)** a glandular epithelial component and mixoid stroma of the pleomorphic adenoma adjacent to the normal salivary gland; **(b)** a multinodular pattern constituted by a clear cell component. **Inset:** higher magnification shows large vacuolated cells with dislocated nuclei and clear cytoplasm.

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Highlights:

Clear cell myoepithelial carcinoma of the parotid gland is defined as a rare and aggressive tumour, exhibits a propensity for distant metastasis more than for regional lymph node metastasis, with an ability by most tumors for extensive local growth, infiltration, and destruction. Distant metastasis has been seen to the lungs (most commonly), bone, liver, peritoneum, pleura, kidneys, brain, and skin.

Diagnosis of clear cell salivary neoplasms encompasses a broad range of possibilities, including clear cell myoepithelial carcinoma (CCMEC), primary salivary clear cell tumors (CCC), epithelial-myoepithelial carcinoma (EMEC), and, as well as clear cell variants of other salivary tumors, including acinic cell carcinoma, oncocytoma and mucoepidermoid carcinoma.

In our case report, a more extensive treatment is proposed for such malignancy, mostly in big, relapsing tumours, notwithstanding cytological diagnosis, consisting in parotidectomy and lymphadenectomy. On the other hands, we also considered a more conservative treatment following guidelines, as this case was lacking metastases and lymphatic involvement, considering that application of guidelines, surgical and clinical expertise and appropriate technology can contain potential medicolegal implications.