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Case Report

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Myoepithelial Carcinoma arising from a Parotid Pleomorphic Adenoma A Case Report

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ABSTRACT

Myoepithelial carcinoma is a rare neoplasm, accounting for less than 2% of all salivary gland carcinomas and can arise de novo or secondary to a previous pleomorphic adenoma, as in the case presented here. The presence of mitoses, foci of necrosis, characteristic histomorphology, and exclusive proliferation of myoepithelial cells identified by immunohistochemistry confirm the diagnosis. The gold standard of therapy is surgical resection with clear margins; however, the risks of local recurrence and distant metastasis are 35% and 22%, respectively. Our case corresponds to a 65-year-old patient who underwent surgery for a pleomorphic adenoma, which recurred after 5 years. She presented to our clinic with a myoepithelial tumor of 2 months' evolution with involvement of the facial nerve and soft tissues. Due to its rapid growth, this is an unusual presentation.

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Introduction

Myoepithelial carcinoma is an uncommon salivary gland neoplasm that can arise de novo or on a previous pleomorphic adenoma in 50% of cases [1-4]. The term myoepithelial refers to the fact that it is predominantly composed of myoepithelial cells and may exhibit focal ductal formation and squamous differentiation [1] The first case was described in 1972 by Donath and the malignant component of myoepithelioma was described by Stromayer in 1975 [5-7].

The World Health Organization defines carcinoma ex pleomorphic adenoma as an epithelial and/or myoepithelial neoplasm that develops in the context of a previous primary or recurrent pleomorphic adenoma (ICD-O Code 8941/3) [4,8,9].

It accounts for 0.4 - 0.6% of tumors of all salivary glands and less than 2% of all carcinomas [1,4,5,12]. The most affected gland is the parotid (76.9%) and there is no sex predilection [4,8,12]. The age range is wide, from 14 to 86 years of age [1,8].

It has an infiltrative growth pattern into surrounding tissues and vessels [1,8]. Diagnostic criteria include myoepithelial differentiation and malignancy, with infiltration of the affected gland and invasion of neighboring tissues [1].

Treatment consists of wide surgical resection and may be combined with postoperative chemotherapy or radiotherapy [1,13] [1,2,4].

Case

65-year-old female with 10 years evolution of non insulin dependent type 2 diabetes, without other comorbidities, who presented with a multinodular formation of 6 centimeters in diameter in the right parotid gland of several years of evolution and slow growth. An ultrasound was performed, which showed a solid multinodular lesion. With normal pre-operative findings, she underwent surgery under general anesthesia, and a superficial lobe parotidectomy was performed without functional alteration of the facial nerve. She evolved without complications and the pathology report stated: parotid mass of 5 x 7 x 5 cm, with abundant basophilic myxoid matrix including typical tubules and typical myoepithelial cells. Periphery with preserved salivary gland. Diagnosis "pleomorphic adenoma" with free margins.

Five years later, she presented with tumor recurrence of 8 cm in diameter in the parotid gland, with rapid growth over 2 months. Clinically, there was evidence of trunk-type facial nerve involvement. An ultrasound was performed again, which showed a heterogeneous multinodular lesion without regional adenopathy. With normal pre-operative findings, she underwent surgery under general anesthesia. Excision of the formation with resection of the deep lobe of the parotid gland was performed, and involvement of the facial nerve was noted, so it was resected

along with surrounding soft tissues. Figure 1 (A,B,C and D).

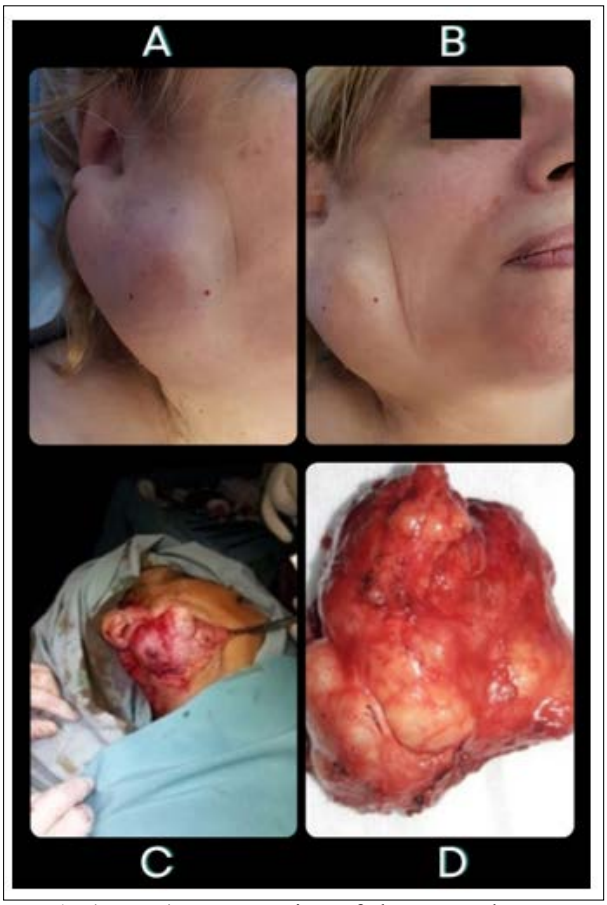

Figure 1: (A y B) Preoperative of the Second Surgery. (C) Intraoperative. (D) Surgical Specimen.

The pathology reported stated parotid tumor formation of 8 x 5 x 4.7 cm, whitish with areas of mucoid appearance and central cystic degeneration, with a multinodular growth pattern, infiltrative margins, consisting exclusively of myoepithelial cells with foci of squamous differentiation, which were immersed in a chondromyxoid stroma. More than 5 mitoses were seen in 10 high-power fields (HPF) and foci of necrosis. The neoplasm infiltrated the dermis and extraparotid soft tissues. Immunohistochemical staining was performed automatically with Ventana Bench Mark Ultra equipment: Smooth muscle actin (clone 1A4 BioGenex) focally positive, P63 (clone 4A4) diffusely positive. Calponin (clone CALP, Cell Marque) negative, Cytokeratin Cocktail (clone AE1/AE3/PCK26) positive in foci of squamous differentiation, Ki67 (clone 30-9) greater than 30%, P53 (clone DO-7) WT (non-mutated pattern), HER2 (EP3 - Cell Marque) negative, CD117 (c-kit, YR145 - Cell Marque) negative. Diagnosis: Myoepithelial carcinoma arising from a pre-existing pleomorphic adenoma. Pathological staging based on American Joint Committee on Cancer pT4a pNx. Figure 2 (A, B, C, and D).

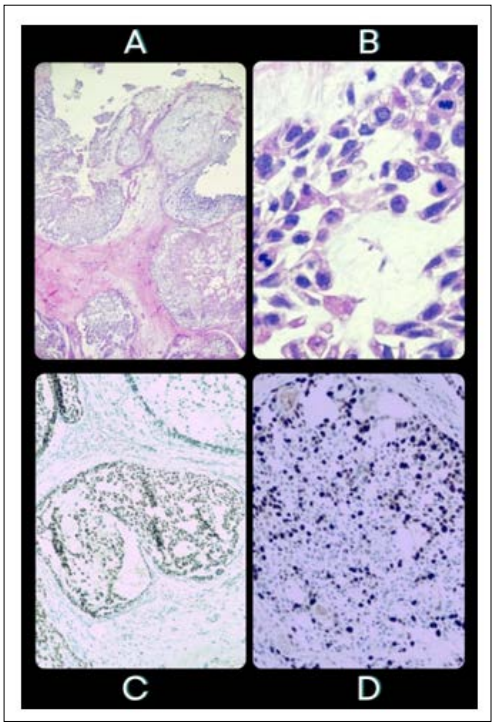

Figure 2: (A) H&E 4x Neoplasm composed exclusively of myoepithelial cells immersed in a chondromyxoid background with focal squamous differentiation. Infiltrative multinodular growth pattern. Diagnostic key: hypercellular peripheral areas and hypocellular center with foci of necrosis. (B) H&E 40x Frequent mitotic figures. (C) Immunohistochemistry for p63: Neoplasm composed exclusively of myoepithelial cells. (D) Immunohistochemistry for Ki-67: High cellular proliferation index (greater than 30%).

The patient evolved favorably in the postoperative period, and was discharged 24 hours later. Due to trunk-type facial paralysis, a gold implant in the upper eyelid, Kuhnt Zymanowski blepharoplasty, and tensor of the labial commissure were performed under local anesthesia 7 days later. Six months postoperatively, she is still under follow-up by Oncology, free of disease.

Discussion

Myoepithelial carcinoma accounts for 0.4 to 0.6% of salivary gland tumors and less than 2% of all carcinomas, with the most common location being the parotid gland [4,14]. Myoepithelial cells are found in normal salivary glands, between the basal membrane of the acini and the plasma membrane of the secretory cells, and have contractile functions in salivary secretion [4]. During embryonic development, they take part in the branching process of the salivary glands [4]. Myoepithelial carcinoma is an infrequent, malignant neoplasm that can arise as a first instance in the salivary gland or on a pre-existing pleomorphic adenoma[4,15]. Initially described in 1972 by Donath, the malignant component of myoepithelioma was described by Stromayer in 1975 [4,16] [6,7]. Today, there is still controversy surrounding myoepithelial cells because their functions are poorly defined, and their structures are complex [8]. Donath suggested that it could be due to the fact that the originating cells came from the intercalated ducts and according to other authors, this would motivate the integration of both, the epithelial and myoepithelial components of this type of tumor [8]. Myoepithelial carcinomas were included in the second edition of the World Health Organization's histological classification of salivary gland tumors in 1991 [1,6,16,17].

The tumors can appear de novo or appear in an ex pleomorphic adenoma, in which case, they are suspected when there is a long history of a benign salivary tumor or multiple recurrences with rapid growth and/or local infiltration. It has been reported that 50% of myoepithelial carcinomas develop in an ex pleomorphic adenoma and this is the second histological subtype after salivary duct carcinoma [4,18,19].

Clinically, it may manifest as an asymptomatic, non-painful, and generally slow-growing tumor, although cases of rapid progression and facial paralysis due to involvement of this nerve, the presence of pain, and adhesion to deep planes have been described. Macroscopically, these tumors are commonly a single mass, but they can also be multilobulated, irregular with areas of necrosis and haemorrhage [1,7]. Some authors cite that the tumor remains small for a period of time and then makes an abrupt growth, similar to what happened in our case, where a rapidly growing mass is evident 5 years after surgery for a pleomorphic adenoma and in the initial consultation, the patient cites a mass of no more than 2 months' evolution, with facial paralysis and local involvement of soft tissues [1,7].

Histologically, it is characterized by a great morphological heterogeneity with several cell types (fusiform, epithelioid, plasmacytoid and clear cells) and different architectural patterns (solid, trabecular and reticular), with abundant hyaline or myxoid matrix and metaplastic changes, whether squamous, sebaceous or chondroid. Our presentation refers to a tumor with necrosis, foci of squamous differentiation and areas of cystic degeneration [20].

Different authors cite that the most frequent cell subtype is epithelioid [4,21].

The criteria for evaluating malignancy are based on histological characteristics, cytological atypia, infiltration, and mitotic index [1,4,16]. Considering the tumor's invasion of the fibrous capsule, it is classified as non-invasive, minimally invasive (1.5 mm penetration) or invasive (more than 1.5 mm infiltration) [4,22]. Other characteristics include frequent mitoses and necrosis, currently more than 7 mitoses per 10 high power fields or a proliferative index by immunostaining with Ki 67 greater than 10% [1]. When the morphological characteristics of malignancy, such as infiltrative growth or cytological atypia, are obvious, the malignant nature of the tumor can be easily recognized. However, this neoplasm often presents low-grade cytological features. The tumor we present showed monomorphic cells with frequent mitotic figures, foci of necrosis, a high cellular proliferation index (Ki67 greater than 30%), and although it did not present perineural invasion, it totally and circumferentially engulfed it; it also did not present angiolymphatic emboli but did infiltrate the dermis and extraparotid soft tissues.

Currently, there is no well-defined and widely accepted classification system: some consider the presence of tumor necrosis as a characteristic of high-grade myoepithelial carcinoma with an impact on survival, on the contrary, cytological atypia does not seem to influence the prognosis of this neoplasm [23].

Immunohistochemistry confirms the diagnostic suspicion and positivity for Smooth Muscle Actin, S100, Calponin and p63 in tumor cells, evidencing their myoepithelial nature [11]. The Ki-67 cellular proliferation index would be used to confirm the malignant nature of the neoplasm and to evaluate the possibility of recurrences [4,13,24].

Most carcinomas arising from ex pleomorphic adenomas are high-grade adenocarcinomas and excretory duct carcinomas, mucoepidermoid carcinoma, adenoid cystic carcinoma, or myoepithelial carcinoma [4,25]. The neoplasm we present has a tendency for local recurrence and distant metastasis with a rate of 8.1 to 80% [2,7,13]. There is a series of published cases in which it is mentioned that distant metastasis is more frequent than to cervical lymph nodes or local relapse; skin metastases are very infrequent and the reported metastases are to the lung, pleura, liver, spine, peritoneum, brain, inguinal lymph nodes, and ribs [1,13,24].

Differential diagnoses to be considered include adenoid cystic carcinoma, polymorphous adenocarcinoma, epithelial-myoepithelial carcinoma, acinic cell carcinoma, adenocarcinoma, plasmacytoma, mucoepidermoid carcinoma, sarcomatoid squamous carcinoma, and metastatic tumors, especially clear cell tumors, among others [13,18]. Its main differential diagnosis is a benign neoplasm such as pleomorphic adenoma, since both tumors share histological characteristics such as low-grade cytology and myxoid stroma, constituting a diagnostic challenge [2].

There are studies that demonstrate a more aggressive behavior of myoepithelial carcinomas arising from a pleomorphic adenoma compared to de novo tumors [2]. At the molecular level, it has been observed that rearrangements in the PLAG1 and HMGA2 genes are the most common genetic events in ex pleomorphic adenoma carcinomas, including myoepithelial carcinomas. On the contrary, these anomalies are not found in de novo myoepithelial carcinomas. The presence of these genetic anomalies correlates with an aggressive behavior and has an impact on survival [1,2].

Fine needle aspiration has a sensitivity of 91 to 98% for parotid masses, however, myoepithelial carcinoma is difficult to identify by cytological puncture and rarely gives a definitive diagnosis preoperatively. (1) Neither computed tomography nor magnetic resonance imaging are relevant for diagnosis, being totally nonspecific [17].

Treatment is based especially on the role of a complete and wide excision of the tumor lesion, with safety margins. Cervical lymphadenectomy is indicated in cases of cervical lymph node invasion observed and verified during the surgical procedure or diagnosed by paraclinical studies in the preoperative period [25,26]. Based on the ability to recur and metastasize to distance, different authors cite a mortality rate of 40% [2,3,7].

The use of radiotherapy or chemotherapy is not yet defined and is controversial in the literature, with no conclusive data [1,6]. Postoperative oncology therapies are sometimes used when the margins are questionable or as an attempt to prevent recurrences [6,27].

Facial paralysis is a sign of malignancy and carries a severe aesthetic and motor disorder, as it makes it impossible to close the eye, exposing the cornea to possible ulcers with lagophthalmos and epiphora due to eversion of the lower eyelid; for this reason, it is common practice to place a gold weight on the upper eyelid, favoring its closure, and blepharoplasty to reduce ectropion [28,29].We performed both procedures in our case one week after the second parotid surgery; at the same time, we placed a lip tensor to elevate the commissure, which also falls due to post-denervation muscle hypotonia [30,31]. Given the latency in the probability of recurrences and metastases, control and follow-up should be very long-term [27].

Conclusion

Myoepithelial carcinoma arising from an ex pleomorphic adenoma is predominantly located in the parotid gland and often presents with rapid growth and local infiltration.

Although it is a rare neoplasm, it is currently believed that its incidence is higher due to the fact that it is a poorly recognized tumor because it presents histomorphological overlap with other benign tumors.

Recognizing this histological subtype of carcinoma in correlation with immunohistochemistry is essential to reach a definitive diagnosis.

Surgery is the elective treatment, aiming for complete resection with a safety margin.

Due to the small number of cases, the evolution and long-term prognosis are still controversial, so strict control and monitoring are recommended.

The authors have no potential conflicts of interest.

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