J Bras Patol Med Lab. 2021; 57: 1-4.

10.5935/1676-2444.20210018

Soft tissue myoepithelial carcinoma: is it a low-grade cancer?

Carcinoma mioepitelial de partes moles: um tumor de baixo grau de malignidade?

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ABSTRACT

Myoepithelial carcinoma is a rare neoplasm of very heterogeneous manifestation that represents a major challenge to the adoption of categorical prognostic criteria since, despite being classified as a low-grade cancer, it behaves very aggressively. While several studies have indicated complete surgical resection as the best treatment for myoepithelial carcinoma, adjuvant therapies have proven effective in preventing relapse. This study describes the case of a patient who developed myoepithelial carcinoma in the right thigh, affecting deep tissues, which were conducted as indicated in the current literature, however, presenting an unfavorable outcome. The available information comes from few studies; therefore, we emphasize the importance of gathering data on the subject, which are still scarce.

Key words: carcinoma; cell dedifferentiation; myoepithelioma; neoplasms of soft tissues; neoplastic metastasis.

RESUMO

O carcinoma mioepitelial é uma neoplasia rara, de manifestação muito heterogênea, que encerra um grande desafio na adoção de critérios prognósticos categóricos, uma vez que, apesar de ser classificado como tumor de baixo grau de malignidade, apresenta comportamentos muito agressivos. Enquanto vários estudos indicam a ressecção cirúrgica completa como o melhor tratamento para carcinoma mioepitelial, terapias adjuvantes têm-se revelado efetivas na prevenção da recidiva. Este estudo descreve o caso de uma paciente que desenvolveu carcinoma mioepitelial em coxa direita, acometendo partes profundas, o qual foi conduzido como indica a literatura atual, contudo, apresentando desfecho desfavorável. As informações disponíveis provêm de poucos estudos, logo, ressaltamos a importância de reunir dados a respeito do tema, que ainda são escassos.

Unitermos: *carcinoma; desdiferenciação celular; mioepitelioma; neoplasias de tecidos moles; metástase neoplásica.*

RESUMEN

El carcinoma mioepitelial es una neoplasia rara, de manifestación muy heterogénea, que encierra un gran desafío para la adopción de criterios pronósticos categóricos, puesto que, a pesar de ser clasificado como tumor de bajo grado de malignidad, muestra comportamientos muy agresivos. Mientras varios estudios indican la resección quirúrgica completa como el mejor tratamiento para el carcinoma mioepitelial, terapias adyuvantes se han revelado efectivas para prevenir la recidiva. Este estudio describe el caso de una mujer que presentó carcinoma mioepitelial en muslo derecho, afectando partes profundas, lo cual fue conducido como indica la literatura actual, sin embargo, con un resultado desfavorable. Las informaciones disponibles son producto de pocos estudios, por ello, destacamos la importancia de reunir datos acerca del tema, que aún son escasos.

Palabras clave: *carcinoma; desdiferenciación celular; mioepitelioma; neoplasias de los tejidos blandos; metástasis de la neoplasia.*

First submission on 01/27/20; last submission on 03/02/20; accepted for publication on 03/02/20; published on 03/20/21

INTRODUCTION

Myoepithelial carcinoma, or malignant myoepithelioma, is a rare, low-grade tumor, composed of specialized basal cells, presenting in salivary glands, respiratory epithelium, breasts, and sudoriferous glands. It has no predilection for sex; in relation to the age group, there are still controversies in the literature regarding its predominance[1]. However, it is known that malignancy frequently occurs in the pediatric population[2]. Morphologically and immunophenotypically, these tumors are similar to their counterparts in the salivary glands and can differ bilaterally, having both epithelial and myogenic features. They were first characterized in 1997 by Kilpatrick *et al*., in a case study[3].

More than 90% of myoepithelial carcinomas occur in the salivary glands[4] and correspond to less than 1% of all salivary gland tumors. Myoepithelial soft tissue carcinomas are extremely rare and 75% of cases affect the limbs, especially the lower limbs[5].

In the present study, we describe the clinical case of a patient who developed myoepithelial carcinoma in the right thigh, affecting deep tissues; we reviewed the literature to assess the actions taken in relation to the outcome of the case, highlighting the malignant potential of this tumor and the importance of gathering data on the topic, which are still scarce[3].

CASE REPORT

Female patient, 36 years old, black, with no history of smoking or alcoholism, presents with a tumor in the middle third of the lateral aspect of the right thigh. She states that the palpable mass was firm, immobile, and painless; it appeared in 2009 and had a progressive growth until reaching 5 cm in diameter, in 2016. In the same year, the first surgical procedure for complete excision of the lesion was performed. The result of immunohistochemistry (**Table 1**) led us to conclude that the lesion was a poorly circumscribed multilobular neoplasia with stromal sclerosis foci, associated with myoepithelioma, with no malignancy criteria. However, its characteristics of a multilobular infiltrative pattern and significant foci of cellularity could be related to a greater potential for recurrence, as well as dedifferentiation, requiring close clinical monitoring.

In 2017, after about eight years of evolution, the patient reports recurrence of the tumor in the same area, however, now painful. In April 2019, she claimed the presence of "blood" in her mouth, at random times of the day, without the occurrence of coughing or vomiting, as well as a of retrosternal burning feeling of 9/10 intensity, with no irradiation, worsening during movement, and improvement in dorsal decubitus, unrelated to organic functions. After these symptoms, she sought medical service at the Emergency Room (ER), and was referred to the General Public Hospital of Palmas [Hospital Geral Público de Palmas (HGPP)]. Conventional radiography (X-ray) and computed tomography (CT) of the chest were performed; such examinations showed multiple nodules with soft tissue attenuation randomly distributed in both lungs, the largest measuring 1.8 cm.

Ten days after carrying out the imaging tests, surgery was performed to remove tumors from one of the lungs. The immunohistochemical test showed mesenchymal neoplasia with evidence of myoepithelial differentiation in pulmonary parenchyma; the features are described in the **Table 2**.

TABLE 1 – Immunohistochemical results of the soft tissue lesion (right thigh)

Moderate-to-low epithelioid cell type in a linear and reticular arrangement in myxoid stroma
Absence of mitosis
Low Ki-67 proliferative index
Focal S100, Caldesmon, HHF-35, and SOX-10 immunoexpression

TABLE 2 – Immunohistochemical results of the lung lesion

Well-differentiated, non-encapsulated, intraparenchymal tumor with multilobulated aspect
Morphological pattern with moderate-to-low cellularity of epithelioid type in linear and reticular arrangement in myxoid stroma
Mitotic activity, eight mitoses/10 HPF associated with Ki-67 proliferative index of from 5% to 8%
Focal p63 and SOX-10 immunoexpression, with no other significant expressions

HPF: high-powered field.

The aspects found in the biopsy of the pulmonary nodules were similar to those found in the previous examination of the right thigh, it is the same neoplasm. Therefore, the current sample (pulmonary) would correspond to metastatic neoplasia from the previous (2016) lesion of the right thigh. In the previous sample, there was co-expression of S100 protein and myogenic antigens, characterizing myoepithelial differentiation. In the recent sample, there was no expression of myogenic antigens possibly due to the process of dedifferentiation from the primary neoplasm.

The neoplasm was better classified as metastatic malignant myoepithelioma (soft tissue myoepithelial carcinoma) to the lung. On July 22, 2019, the patient started chemotherapy treatment at the HGPP (**Figures 1** and **2**).

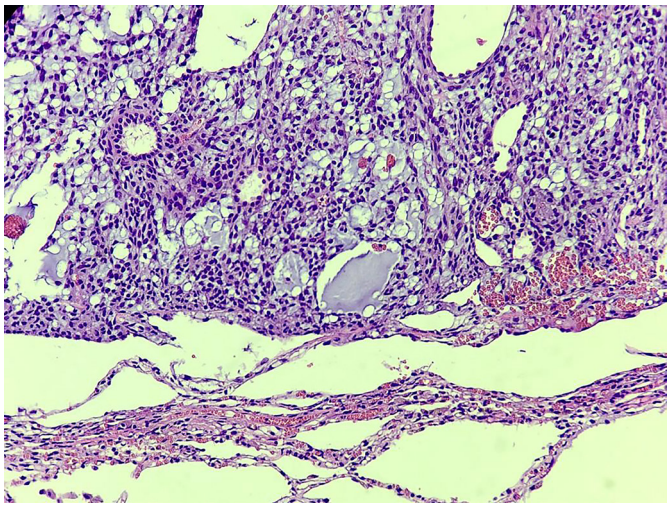

FIGURE 1 – *Microscopic image (100×) of metastasis to the lung, showing mucin lake*

Courtesy of Dr. Plínio Medeiros, Sicar Laboratory, Palmas, Tocantins, Brazil.

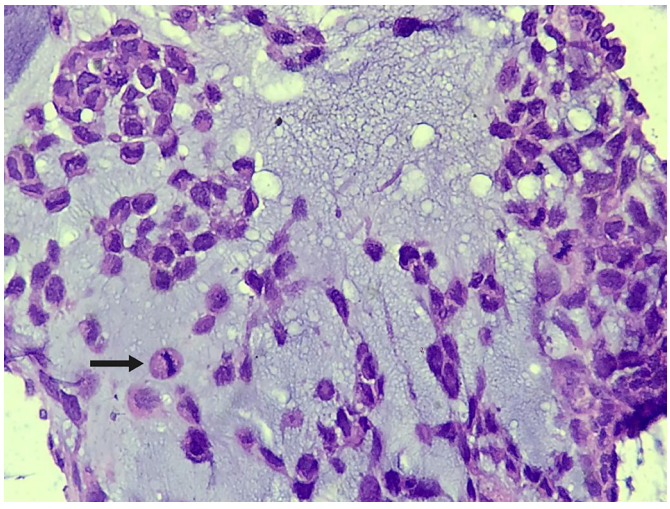

FIGURE 2 – *Microscopic image (400×) of metastasis to the lung, with cytologic features of the neoplasm, containing mitoses (arrow)*

Courtesy of Dr. Plínio Medeiros, Sicar Laboratory, Palmas, Tocantins, Brazil.

DISCUSSION

Myoepithelial carcinoma is a rare neoplasm with a very heterogeneous manifestation, and the data currently available are insufficient for a holistic understanding of this disease. The adoption of categorical prognostic criteria is one of the most important challenges in its investigation and, considering the overly aggressive behavior of myoepithelial carcinoma, it is very important to establish a diagnosis as soon as possible. Pathological features such as myxoid areas and cytopleomorphism, or immunohistochemical analysis would be very useful tools to achieve accurate diagnosis[6].

Some studies report the average age of 38 years at the time of diagnosis and the peak incidence, which occurs between the third and fifth decades of life, and also show that the rate of involvement is the same for men and women[2]. The average duration of symptoms, as well as that of this study, is, on average, 4 years, but with a wide margin of duration (two weeks to 20 years). Hornick *et al*. (2003)[2] still report that the main signs and symptoms are: painless or painful mass, pain without the presence of a mass, edema, and paresthesia; they also found that malignant tumors were significantly larger than benign tumors, however, there is no data to strongly support this situation with a prognostic criterion.

Regarding the microscopic aspect, it is believed that myoepithelial carcinoma is well-circumscribed or surrounded by a fibrous pseudocapsule. It may manifest focal infiltration; in some cases, it is not possible to properly assess the edges of the tumor. The architecture is often lobulated or multinodular, and most of the tumor have a predominantly reticular growth pattern, with strands that intersect epithelioid, ovoid or spindle cells, separated by chondromyxoid or collagen stroma[5].

The study by Hornick *et al*. (2003)[2] used these cytological elements to classify tumors according to malignancy: benign tumors showed little atypia, with small nucleus and more uniform elements, with little variation in cells size; moderate atypia pattern and vesicular or thick chromatin, prominent nucleus, usually large or nuclear pleomorphism, determine the malignant tumors. Once classified as high-grade soft tissue myoepithelioma, its malignancy is known, and the tumor must be treated as such.

Microscopic analysis of this clinical case revealed, in a primary lesion, a poorly circumscribed multilobular structure, with stromal sclerosis foci, and low epithelioid cell type in a linear and reticular arrangement in myxoid stroma, these findings are consistent with myoepithelioma. Although the malignancy criteria were not initially verified, the infiltrative multilobular pattern with high cellularity foci revealed a greater potential for local recurrence, including dedifferentiation. Thus, strict follow-up and evolutionary monitoring with clinical research for possible residual neoplasia were indicated, aiming at the complete excision of the lesion.

Regarding the immunohistochemical findings, more than 90% of myoepitheliomas express broad-spectrum keratins, protein S100 and calponin, in addition to other markers that guide the analysis. The findings of the present study were also consistent with myoepitheliomas, showing focal immunoexpression of S100, caldesmon, HHF-35 and SOX-10, and low Ki-67 proliferative index.

Most patients with high-grade lesions findings undergo complete excision, the goal of which is healing; however, the establishment of malignancy is complex in myoepitheliomas that do not present atypia, and many low-grade myoepithelial

carcinomas have quite aggressive behaviors[2]. Although many authors describe complete surgical resection as the only and the best treatment for myoepithelial carcinoma, adjuvant radiotherapy can be effective in preventing recurrence[7].

Due to the high trend of local recurrence, in addition to possible metastasis, the follow-up of these patients is essential, and a long period of surveillance is necessary, even in clinically early-stages tumors and submitted to complete surgical resection with negative margins[8]. Regarding our study, despite the excision of the lesion performed at the first moment, recurrence occurred after one year; in three years, neoplasia in the lung parenchyma corresponding to the metastatic lesion of the previous lesion was observed.

Currently, although a low grading malignancy is attributed to myoepithelioma, the information available in the literature suggests a poor long-term prognosis for patients with malignant lesions. Thus, the malignant potential of this tumor is evident, with a recurrence rate of 17% to 50% and a metastasis rate of 8% to 48%[1]. The most common foci of metastases include lungs, lymph nodes, bone metastases and other soft tissues[5].

CONCLUSION

Studies available in the literature are scarce, despite the increasing number and recognition of cases at an early stage. Therefore, it is essential that there is a considerable effort to collect information in a data file and unify them for an accurate determination of the prognosis and the correct follow-up of this neoplasm.

REFERENCES

1. Rastrelli M, Fiore PD, Damiani GB, et al. Myoepithelioma of the soft tissue: a systematic review of clinical reports. Eur J Surg Oncol. 2019; 45(9): 1520-6.

2. Hornick JL, Fletcher CD. Myoepithelial tumors of soft tissue a clinicopathologic and immunohistochemical study of 101 cases with evaluation of prognostic parameters. Am J Surg Pathol. 2003; 27(9): 1183-96.

3. Jo VY, Fletcher CDM. Myoepithelial neoplasms of soft tissue: an updated review of the clinicopathologic, immunophenotypic, and genetic features. Head Neck Pathol. 2015; 9(1): 32-38.

4. Silvers A, Som B, Brandwein M. Epithelial-myoepithelial carcinoma of the parotid gland. Am J Neuroradiol. 1996; 17: 560-62.

5. Fletcher CDM, Bridge JA, Hogendoorn PCW, Mertens F, editors. WHO classification of tumours of soft tissue and bone. Pathology and genetics of tumours of soft tissue and bone. 4 ed. Lyon: IARC Press; 2013.

6. Yokoshe C, Yokoshe C, Asai J, et al. Myoepithelial carcinoma on the right shoulder: case report with published work review. J Dermatol. 2016; 43(9): 1083-7.

7. Canon J, Alexander C, Kader H. Am J Clin Oncol. 2017; 40(3): 318-22.

8. Fonte D, Águas LN, Alves L, Sotto-Mayor C, Pinto G. Carcinoma epitelial-mioepitelial da parótida: um tumor de baixo grau de malignidade? Acta Med Portuguesa. 2011; 24: 675-80.

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