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Case Report

Uncommon metastases to the brain: Frontal lobe myoepithelial carcinoma

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ABSTRACT

Background: Myoepithelial tumors have been widely described as a rare form of salivary gland neoplasm, although currently soft-tissue phenotypes have also been identified. These are tumors composed entirely of myoepithelial cells that exhibit a dual epithelial and smooth muscle phenotype. The occurrence of myoepithelial tumors within the central nervous system is also extremely rare, with only a few cases reported. Treatment options include surgical resection, chemotherapy, radiotherapy, or a combination of these approaches.

Case Description: The authors present a case of soft-tissue myoepithelial carcinoma with an unusual brain metastasis, rarely described in the literature. The purpose of this article is to present an update on the diagnosis and treatment of this pathology when affecting the central nervous system, through the review of the current evidence.

Conclusion: However, despite complete surgical resection, there is about a significative high rate of local recurrence and metastasis. Careful patient follow-up and staging is essential for better characterization and understanding of this tumor's behavior.

Keywords: Brain neoplasms, Intracranial, Myoepithelioma, Neuro-oncology, Pathology

INTRODUCTION

Myoepithelial tumors are rare neoplasms arising from myoepithelial cells. Most tumors arise from the salivary glands, but usual sites of presentation include the oral cavity and pharynx. However, there have been reported cases seen in soft tissue, upper respiratory tract, breast, skin, and gastrointestinal tract.[16] Primary intracranial myoepithelial neoplasms also have been described and are even rarer with around ten cases reported, according to literature.[11] Myoepithelial tumors can be classified as either benign myoepitheliomas or malignant myoepithelial carcinomas. The former has a better prognosis with complete resection, even though they can recur. Myoepithelial carcinomas are rarer and more aggressive, accounting for 1–2%,[17] and may metastasize to distant sites in up to 30–50% of patients.[2] Due to the rarity of this malignancy, consensus on appropriate treatment remains poor.

CASE PRESENTATION

A 43-year-old male, with a smoking history (3 pack-years), attended the soft-tissue surgery department presenting a lesion in the plantar area of the first metatarsal of the left foot (12 × 12 cm). On the

surface, the lesion appeared ulcerated and deeply infiltrated soft tissues and contacted with the base of the first phalanx, demonstrated by magnetic resonance imaging (MRI). A biopsy reported: Malignant mixed tumor (myoepithelial carcinoma), ulcerated. The patient was scheduled for amputation of the first toe + inguinal lymphadenectomy, with pathological analysis confirming the initial diagnosis and metastasis 1/2 lymphatic nodes examined. Subsequently, the patient received radiotherapy on the inguinal area, total dose 66 Gy.

Three months after completing adjuvant therapy, the patient presented to the emergency department with headache and cognitive impairment. A contrast-enhanced brain MRI revealed an intra-axial single lesion located in the deep white matter of the right frontal lobe. Hypointense and heterogeneous in T1 and T2 sequences, with irregular edges and significant vasogenic edema conditioning compression and displacement of the anterior horn of the lateral ventricle [Figure 1]. The findings on routine laboratory studies were unremarkable and no other lesions suggestive of mestastases in another part of the body were found in the chest and abdominal tomography imaging studies. With these findings, the patient was scheduled for craniotomy and total excision of the lesion [Figure 2], with a pathology report of metastatic myoepithelial carcinoma [Figure 3]. After this, the patient received whole-brain radiation therapy with a total dose of 30 Gy.

The patient did well for 7 months (Karnofsky index of 100), integrating himself into daily activities. He is currently under control but has returned to present headache and cognitive impairment (Karnofsky index of 60), a control MRI seven months after surgery evidenced a significant tumor recurrence in the frontal area accompanied again by perilesional edema and important mass effect [Figure 4]. Due to the functional and oncological status of the patient, and the biological behavior of the tumor, the case was presented to the institution's tumor committee to discuss available therapeutic modalities. The patient refused the possibility of surgery and reirradiation was not considered, being sent to supportive care.

DISCUSSION

Myoepithelial tumors are a rare form of salivary gland neoplasms composed entirely of myoepithelial cells that exhibit

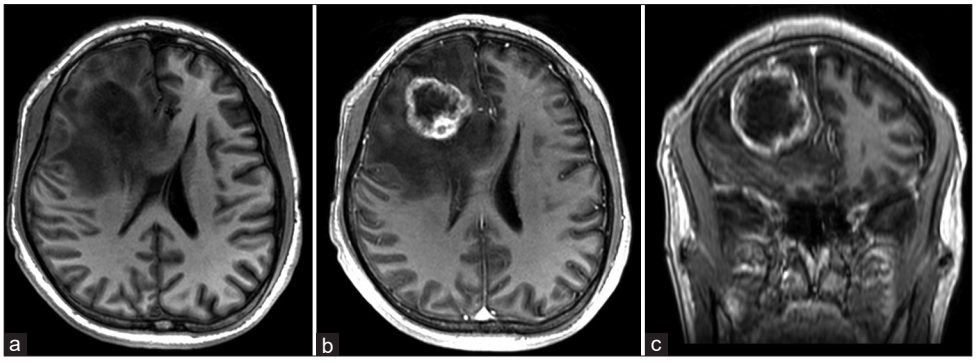

Figure 1: (a) T1-weighted axial magnetic resonance imaging (MRI) and (b) contrast-enhanced T1-weighted MRI showing a tumor within the frontal lobe with irregular peripheral enhance causing significant mass effect and midline shift; (c) contrast-enhanced T1-weighted coronal MRI showing tumor extension on the underlying brain parenchyma.

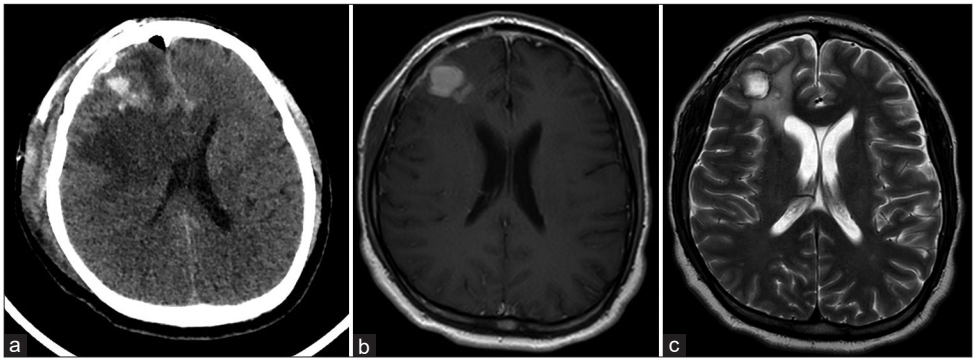

Figure 2: (a) Computed tomography scan in the immediate postoperative period; (b) and (c) contrast-enhanced T1-weighted and T2 magnetic resonance imaging sequences 2 months following surgery, showing no evidence of residual tumor.

a dual epithelial and smooth muscle phenotype. Furthermore, the spectrum and classification of these tumors is diverse and complex. Although extensively described as a salivary gland tumor, soft-tissue phenotypes have been sparsely described. They are now increasingly being recognized in varied anatomical sites including head and neck (tongue, paranasal sinuses, pharynx, and larynx), breast, skin, vulva, respiratory, and gastrointestinal tract.[2,16] The occurrence of myoepithelial tumors within the central nervous system is also extremely rare, with only a few cases reported.[1,2,4,11]

Most commonly these tumors present as benign myoepitheliomas, but malignant myoepithelial carcinomas have been known to metastasize to the lungs, bone, soft tissue, skin, liver, and brain. As reported by Ren *et al*.,[15] the mean metastatic rate can reach 47% and mortality 29%. Soft-tissue myoepithelial carcinoma has a male gender predominance with a wide age range distribution. The most frequent soft-tissue sites are the extremities and limb girdles.[7]

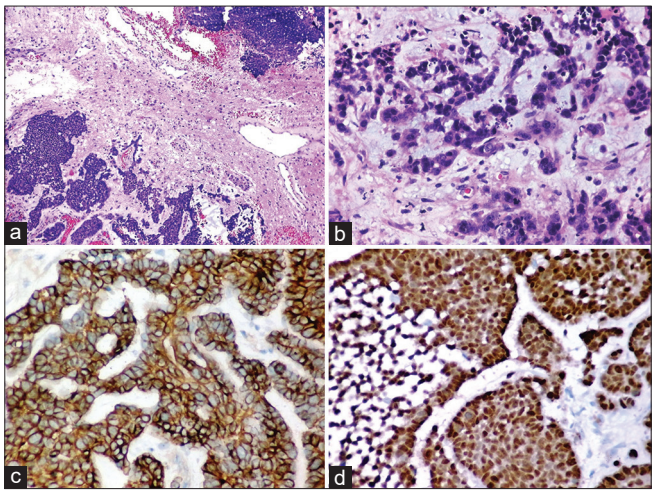

Figure 3: (a) Myoepithelial carcinoma invading the brain parenchyma. Hematoxylin and eosin (H&E), × 20; (b) cords of malignant cells immersed in myxoid stroma. H&E, ×40 (c) Diffuse, cytoplasmic CKAE1/AE3 positivity immunohistochemistry (IHC), ×40; (d) SOX 10 diffuse, nuclear positivity (IHC), ×40.

Preoperative diagnosis is difficult due to nonspecific clinical manifestations and imaging characteristics; thus, diagnosis can only be made based on histopathological and immunohistochemical analysis. Microscopically, these tumors exhibit a wide range of morphological heterogeneity, with the need for immunohistochemical analysis for accurate diagnosis. Furthermore, the accurate diagnosis is particularly important considering the high mortality related to tumor metastasis. Studies have described myoepithelial tumors with various morphological cellularities including spindle, epithelioid, plasmacytoid, clear, and stellate.[6,8] The presence of significant atypia, atypical mitotic figures, hemorrhage, and necrosis has been considered features of malignancy.

Overall, in immunohistochemistry, most of the antibodies used to detect myoepithelial neoplasm target myofilament and keratin.[3] It is advised that this must include a tumor panel with all antibodies to broad-spectrum keratins, high-molecular-weight keratins, and myofilaments. These tumors frequently stain positive for EMA, S100, p63, GFAP, cytokeratin (AE1/AE3), CD10, and myogenic markers including calponin and smooth muscle actin.[2,15] Interestingly, our patient presented negative staining for some of these markers (CK 20, HMB-45, SMA, EMA, S-100, GFAP, and calponin), with positivity for CAM 5.2, CK7, CK 5/6, broad-spectrum keratin, p63, and SOX10.

This particularity, as postulated by Ellens *et al*.,[2] is presumed due to the malignant nature of the tumor, demonstrated by its aggressive behavior (recurrence and distant spread), which may result in the increasing loss of expression of typical markers. Awareness by pathologists of these potential pitfalls and the appropriate use and interpretation of immunohistochemical markers in conjunction with the clinical history are useful tools in the diagnosis of these tumors with unusual staining patterns.

Because central nervous system is a rare site for malignant myoepithelioma development, we found only a few cases

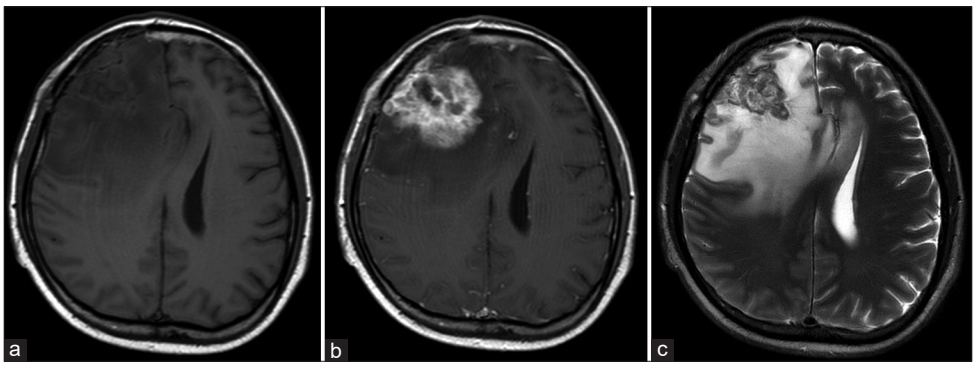

Figure 4: (a and b) T1-weighted axial magnetic resonance imaging with and without contrast showing extensive tumor recurrence 7 months after surgery with significant peripheral edema and compression of the lateral ventricle on T2 sequence (c).

reporting intracranial primary or metastatic malignant myoepithelioma with the help of PubMed. We found a compiled series of cases reported by other authors, where the most common sites of intracranial affection correspond to the sellar area, the cavernous sinus, the cerebellopontine angle, the dura, temporal lobe, and from direct extension from the orbital apex into the middle cranial fossa.[2,5] In addition, and as mentioned by these authors, all previously reported cases of intracranial myoepithelial tumors, whether benign or malignant, primary or metastatic, have presented as a single, solitary tumor.

The case illustrated herein is unique in some respects. Interestingly, the patient developed a single frontal lobe metastasis, being very unusual, and to our knowledge and due to the lack of data in the literature, the determination of this biological behavior and pattern of dissemination is challenging. Further, imaging did not show metastases elsewhere in the body.

Particularly due to its rarity, we did not find a consensus evidence-based treatment modality for intracranial malignant myoepithelioma.[13] Treatment options include surgical resection, chemotherapy, radiotherapy, or a combination of these approaches.[6] Total surgical resection is the mainstay treatment, although it may not always be feasible due to tumor extension or involvement of vascular structures. Radiotherapy and chemotherapy are considered after surgery; however, there is no consensus whether adjuvant therapy is even required, because the prognosis of this condition is still unclear.[6,10]

Radiation therapy is an important postsurgical adjuvant therapy, but evidence is not clear either, some authors report that is effective; however, other studies confirm the lack of effectiveness of this adjuvant treatment.[12,14,15] The overall prognosis of this type of tumor has been described as poor, with aggressive clinical behaviors for malignant forms.[2,6] We did not find specific data on the prognosis in intracranial involvement, whether primary or metastatic. Despite complete surgical resection, there is about a 43% rate of local recurrence and a 40–50% rate of metastasis.[7,9] Careful patient follow-up and staging is therefore essential for better characterization and understanding of this "tumor's behavior in the future.

Several factors have been postulated as possible prognostic markers: clinical stage, tumor location and size, high proliferative activity with extensive invasion of surrounding tissue, perineural permeation, abnormal presence of nuclear DNA content, and marked cellular pleomorphism.[2,3,5,10] However, the biological behavior of this type of tumor remains poorly understood, as in our case, for example, the patient presented a recurrence despite the apparent local and regional control of the disease.

CONCLUSION

Tumors with myoepithelial differentiation occurring either as dura-based lesions or within the central nervous system are exceedingly rare, and as such, seldom considered in the spectrum of differential diagnoses for intracranial/dura-based lesions. Metastatic intracranial myoepithelial carcinoma is an extremely rare tumor and may not possess many of the classic immunohistochemical features present in other myoepithelial tumors. At present, there is no standard therapy for these patients with metastatic spread of myoepithelial carcinoma to the central nervous system. Complete excision with tumor-free margin is always the preferred treatment, while adjuvant therapy is a suggestive treatment option, although this remains controversial. The prognosis of malignant myoepithelioma seems to be unfavorable; therefore, further information is needed to provide diagnostic and therapeutic recommendations for this rare intracranial lesion.

Search strategy and selection criteria

References for this Review were identified through searches of PubMed with the search terms "brain neoplasms," "intracranial," "neuro-oncology," "myoepithelioma," and "pathology" from 2000 to January, 2023. Articles were also identified through searches of the institution' own files. Only papers published in Spanish and English were reviewed. The final reference list was generated based on originality and relevance to the broad scope of this review.

Author contributions

The authors confirm contribution to the paper as follows: Study Conception and Design: César Chong, Xavier Wong Achi; Data Collection: Xavier Wong Achi, Marlon Pozo, Janio Pico; Analysis and Interpretation of Results: César Chong, Xavier Wong Achi, Marlon Pozo; Draft Manuscript Preparation: Xavier Wong Achi, Marlon Pozo. All authors reviewed the results and approved the final version of the manuscript.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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