CASO CLÍNICO/CASE REPORT

Tumor-to-Tumor Metastasis: Breast Carcinoma Metastasis to Meningioma.

Metástase de Tumor-em-Tumor: Metástase de Carcinoma da Mama em Meningioma.

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Abstract

The management of a dural-based nodule in patients with history of malignancy is challenging. Tumor-to-tumor metastasis is a rare phenomenon that should be considered in the differential diagnosis along with metastasis and meningioma. Imaging is often unspecific and histological examination remains the only reliable diagnostic method whenever an accurate diagnosis is critical for clinical management. We describe an unusual case of an asymptomatic dural-based nodule in a breast cancer patient, discovered during follow-up. Pathological examination revealed a breast carcinoma metastasis within a meningioma. Due to the risk of neurocognitive impairment, post-operative radiotherapy was not performed. The patient died one year later, with brain metastases, but no evidence of local recurrence at the resection site. There is no consensus regarding adjuvant treatment in this setting and this case reinforces the need for surgical resection of single dural-based nodules in patients with history of malignancy, even if a meningioma is imagiologically suspected.

Resumo

A gestão clínica de um nódulo na dura-máter num doente com história de neoplasia maligna é desafiante. A metastização de tumor-em-tumor é rara e deve ser considerada no diagnóstico diferencial juntamente com metástase e meningioma. A imagiologia é frequentemente inespecífica. A avaliação histológica é fundamental sempre que um diagnóstico preciso seja essencial para a decisão clínica. Descreve-se um caso raro de um nódulo na dura-máter, numa doente assintomática, com antecedentes de carcinoma da mama. O exame anátomo-patológico revelou uma metástase de carcinoma num meningioma. Pelo risco de défice neurocognitivo não foi realizada radioterapia pós-operatória. A doente faleceu um ano depois, com metástases cerebrais, mas sem evidência de recorrência no local de ressecção. Não há consenso quanto à melhor forma de proceder após excisar estas lesões. Este caso reforça a necessidade de excisão de nódulos únicos na dura-máter em doentes com história de neoplasia maligna, mesmo que imagiologicamente suspeitos de meningioma.

Informações/Informations:
Caso Clínico, publicado em Sinapse, Volume 19, Número 3-4, julho-setembro · outubro-dezembro 2019. Versão eletrónica em www.sinapse.pt
Case Report, published in Sinapse, Volume 19, Number 3-4, july-september · october-december *2019. Electronic version in www.sinapse.pt*

Keywords:
Breast Neoplasms;
Meningeal Neoplasms;
Meningioma;
Neoplasm Metastasis;
Neoplasms;
Multiple Primary.

Palavras-chave:
Meningioma;
Metástases;
Neoplasias da Mama;
Neoplasias Meníngeas;
Neoplasias Primárias Múltiplas.

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Recebido / Received: *2019-08-13*
Aceite / Accepted: *2019-10-29*
Publicado / Published: *2019-11-12*

Introduction

The differential diagnosis of a dural based nodule in patients with a history of malignancy, includes meningioma, dural metastasis, and much less likely tumor-to-tumor metastasis,[1] a well-recognized although rare phenomenon. There are less than 100 intracranial cases recorded, 34 of which of breast carcinoma metastasis to meningioma[2] which is the most common intracranial tumor to harbor cancer metastases. Lung and breast are the most frequent sources.[3] We describe the pathological features of a patient with a breast cancer metastasis within a meningioma and its clinical course.

Case Report

A 51-year-old woman with stage IV breast cancer presented with a dural based nodule in the left frontal region. The patient had undergone radical surgery in 2013 for bilateral invasive breast cancer with lymph node metastasis (pT2 N2a and pT1b N0(sentinel lymph node - sn)). The primary tumors were a moderately differentiated and a well differentiated invasive carcinoma of no special type, both hormone receptor positive (estrogen receptor - ER 100%, progesterone receptor-PR 80%-100%) and human epidermal growth factor receptor 2 (ERBB2) negative. Postoperative adjuvant chemotherapy, radiotherapy and hormonotherapy were performed. Bone metastases were diagnosed in 2016 and 2017, for which the patient was treated with hormonotherapy and radiotherapy. In June 2018, a brain magnetic resonance imaging (MRI) revealed an asymptomatic dural based, left frontal, heterogenous nodule measuring 18x19x19 mm (Fig. 1), reported as suspicious for either meningioma or dural metastasis. The lesion was completely resected for histological evaluation (Fig. 2) which revealed two different morphologies: 1) a meningothelial proliferation with syncytial and focally whorling pattern, composed of monotonous cells with oval nuclei, powdery chromatin, and inconspicuous nucleoli, without mitosis or anaplasia. Psammoma bodies were focally present; and 2) an epithelial component with predominant glandular architecture. By immunohistochemistry the meningothelial cells showed diffuse epithelial membrane antigen (EMA) expression, focal PR expression (<10%) and low Ki-67 (<1%); the epithelial component showed diffuse cytokeratin (CAM 5.2), mammaglobin and gross cystic disease fluid protein 15 (GCDFP15) expression, focal ER expression (5%) and no PR or ERBB2 expression. The final diagnosis was transi-

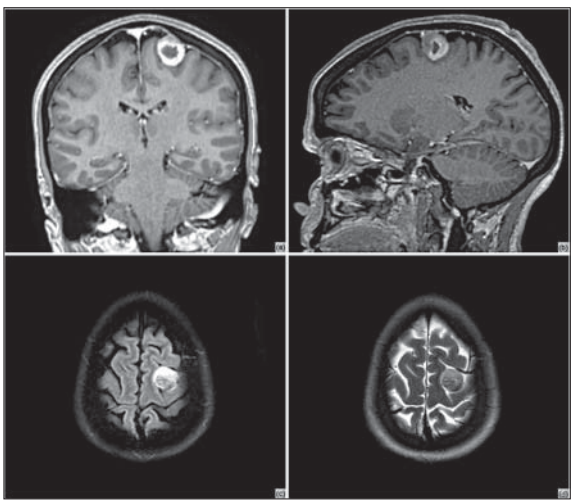

Figure 1. Gadolinium-enhanced T1-weighted magnetic resonance imaging displaying a left frontal extra axial, dural based nodule with peripheral contrast enhancement on coronal (a) and sagittal (b) planes; There was no significant perilesional edema on axial FLAIR sequence (c) and T2-weighted imaging denoted an heterogeneous lesion (d).

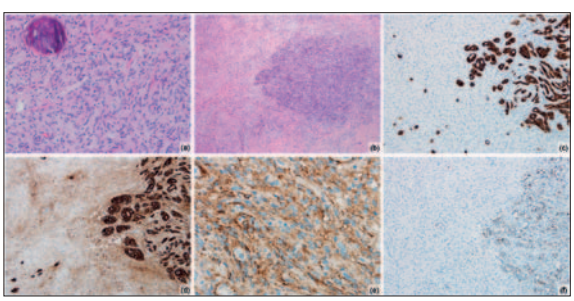

Figure 2. Meningothelial proliferation, hematoxylin and eosin x200 (a); Epithelial neoplasia with glandular architecture infiltrating a meningothelial proliferation, hematoxylin and eosin x100 (b); Diffuse positivity of Cam 5.2 in the epithelial component x100 (c); EMA positivity in the epithelial and meningothelial components, x100 (d); Diffuse positivity of EMA in the meningioma (e); Ki-67 labeling index in both components (f).

tional meningioma (Grade I, WHO) infiltrated by an adenocarcinoma of likely breast origin. There are currently no clinical guidelines regarding adjuvant treatment after complete surgical removal in this particular situation of a metastasis surrounded by a benign tumor. In the absence of a formal recommendation towards adjuvant focal radiotherapy and taking in account the patient's major concerns regarding the neurocognitive safety profile of radiotherapy, this option was delayed until tumor recurrence. After approximately 1 year of imagiological surveillance, the patient developed multifocal brain parenchyma metastases with extensive leptomeningeal dissemination, but no imagiological evidence of local recurrence at the site of the meningioma. She refused additional treatment and died shortly after.

Discussion

Central nervous system metastases are present in 15%–30% of patients with metastatic breast cancer during the course of the disease.[4] The most frequent intracranial metastatic site is the brain parenchyma and less often the meninges.[5] Interestingly, in this case, the meningioma was the first intracranial site to harbor a metastasis, before subsequent parenchymal dissemination. Tumor-to-tumor metastasis is a rare event that occurs when one tumor metastasizes into another. Campbell[6] and Pamphlett[7] proposed the most widely accepted diagnostic criteria. Campbell's criteria are: (1) at least two primary tumors must exist; (2) the host tumor must be a true neoplasm; (3) the metastatic focus must show established growth inside of the host tumor, and must not be the result of contiguous growth; and (4) the host tumor cannot be a lymph node involved by leukemia or lymphoma. Pamphlett added two criteria: (1) the metastatic focus must be at least partially enclosed by a rim of histologically distinct host tumor tissue; and (2) the existence of the metastasizing primary carcinoma must be proven and compatible with the metastasis. Our case fulfills all these diagnostic criteria.

Several hypotheses addressing possible mechanisms of meningioma receptivity to metastases have been proposed. Meningiomas are highly vascular tumors, which renders them susceptible to hematologic metastases.[3] Their high collagen and lipid content and modest metabolic profile may also provide a nutrient replete microenvironment to metastatic tumor growth.[1,2] E-cadherin expression may also contribute the processes of homing malignant cells. E-cadherin binds to E-cadherin on other cells. In doing so, it enables the adhesion of cancer cells to each other until some cells downregulate its expression prior to metastasis, enabling the escape from the primary tumor mass. Metastatic cells resume E-cadherin expression upon seeding their destination, which allows them to grow into a secondary tumor mass.[8] Both meningiomas and breast invasive carcinomas of no special type are known to have ubiquitous expression of E-cadherin.[9] Signaling through progesterone receptors, mutually expressed by some breast carcinomas and meningiomas, may also mediate tumor-to-tumor interactions.[2] In addition, local inflammatory infiltrates in meningiomas are rare, creating a permissive environment for metastases.[3]

Breast cancer and meningioma have a strong epidemiological association and women with either meningioma or breast cancer have a higher risk of being diagnosed with the other condition.[10] In a breast cancer patient without evidence of disseminated disease, the likelihood of a solitary dural nodule being a meningioma is much greater than the likelihood being an isolated metastasis. However, even when there is metastatic disease, as in our case, it may be impossible to differentiate a metastasis from a meningioma using conventional MRI. Although MRI provides excellent soft-tissue resolution, many intracranial pathologies share similar radiologic features, making a definitive diagnosis difficult.[11] Discernment of meningioma from metastasis is clinically relevant because complete surgical resection may be curative for the former,[12] while radiotherapy would be typically employed for the latter.[13] Histological examination is crucial for this purpose. There are, however, no guidelines addressing the optimal management of a patient with a breast cancer metastasis within a meningioma after surgical removal, making it important to gather information about the clinical course of these patients.

In conclusion, clinicians and pathologists should be familiar with the possibility of intrameningioma metastases. Given the challenges in differentiating a meningioma from cancer metastasis in imaging alone, surgical resection should be considered in patients with history of breast cancer presenting with a dural based nodule. ■

Responsabilidades Éticas

Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.

Fontes de Financiamento: Não existiram fontes externas de financiamento para a realização deste artigo.

Confidencialidade dos Dados: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.

Consentimento: Consentimento para publicação obtido.

Proveniência e Revisão por Pares: Não comissionado; revisão externa por pares.

Ethical Disclosures

Conflicts of Interest: The authors have no conflicts of interest to declare.

Financing Support: This work has not received any contribution, grant or scholarship.

Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of data from patients.

Consent: Consent for publication was obtained.

Provenance and Peer Review: Not commissioned; externally peer reviewed.

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