

Multiple Extracranial Metastases from a Rhabdoid Meningioma: A Case Report

Metástases Extracraniais Múltiplas de um Meningioma Rabdoide: Relato de Caso

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Abstract

Meningiomas are among the most common intracranial primary tumors, and generally have a benign behavior. The incidence of extracranial metastasis of this pathology is low. There are different variants of them, with a wide variety of aggressiveness and potential to metastatic spread. Among the malignant meningiomas (1–3% of total), the rhabdoid variant is known for its aggressive biological and clinical behavior. It is also known that some histological subtypes are inherently prone to recur or spread, as the latter. In the latest World Health Organization classification, extracranial metastases are not currently considered a pathological criterion for malignancy, and, when present, they are most commonly found in the lung, liver, lymph nodes, and bone. Treatment is usually surgical resection of the metastases, but there is still no consensus about it. Owing to its poor prognosis, the rhabdoid subtype is commonly treated aggressively. Patients are submitted to local radiotherapy to prevent recurrence. Extracranial metastases of meningiomas are rare, but should always be remembered, especially in cases of local recurrence and malignant histology, as the rhabdoid variant. We report one case of extracranial metastases in a patient diagnosed with rhabdoid subtype of meningioma, and discuss the literature on this pathology.

Keywords

- ▶ meningioma
- ▶ metastatic meningioma
- ▶ rhabdoid meningioma

Resumo

Meningiomas estão entre os tumores intracranianos primários mais comuns, e geralmente possuem comportamento benigno. A incidência de metástases extracranianas desta patologia é baixa. Existem diversas variantes, com uma ampla variedade de agressividade e potencial para disseminação metastática. Entre os meningiomas malignos (1–3% do total), a variante rabdoide é conhecida por seu comportamento agressivo clínico e biológico. Também é sabido que alguns subtipos histológicos são propensos à recidiva e disseminação, como o supracitado. Na última classificação da Organização Mundial de Saúde, metástases extracranianas não são consideradas como critério patológico para malignidade, e, quando presentes, são geralmente

Palavras-chave

- ▶ meningioma
- ▶ meningioma metastático
- ▶ meningioma rabdoide

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encontradas nos pulmões, fígado, linfonodos e ossos. O tratamento é geralmente a ressecção cirúrgica das metástases, embora não há consenso. Devido ao seu prognóstico pobre, o subtipo rabdoide é comumente tratado de forma agressiva. Os pacientes são submetidos à radioterapia local para prevenção de recidivas. As metástases extracranianas de meningiomas são raras, mas sempre devem ser consideradas, especialmente em casos com recidiva local e histologia maligna, como a variante rabdoide. Relatamos um caso de metástases extracranianas em um paciente com o subtipo rabdoide de meningioma, e discutimos a literatura a seu respeito.

Introduction

Meningioma is one of the most common intracranial primary tumors, with different variants, a wide variety of aggressiveness, and potential to metastatic spread. The rhabdoid variant is known for its aggressive behavior. Only 130 cases of extracranial metastases of meningiomas have been reported to date. We report a case of a patient diagnosed with rhabdoid meningioma with multiple metastases to lung and liver, and discuss the literature on this subject.

Case Report

A 21-year-old Caucasian woman presented to medical assistance complaining of a moderate headache, associated with vomiting, bradypsychism, worsening of general condition, and daily low fever. Furthermore, she had ventilatory-dependent thoracic pain, mild dyspnea, and abdominal pain in right hypochondrium. In the past, the patient was submitted to neurosurgical procedures for intracranial tumors. The first surgery was performed in childhood, and after that, the patient was operated several times, receiving the diagnosis of a grade I meningioma according to the World Health Organization (WHO).

Initially, we performed a new oncological staging. Chest X-ray showed one single lesion in the right lung. Abdominal ultrasound also evidenced a solitary lesion in the liver and the blood tests showed leukocytosis, anemia, and high inflammatory markers. In addition, computed tomographic (CT) scan and magnetic resonance imaging (MRI) of the brain revealed recurrence of the tumor in the left frontal region, associated with perilesional edema, homogeneous contrast enhancement, and the presence of obstructive hydrocephalus. CT scan of the thorax and abdomen evidenced multiple nodular lesions in both lungs (► **Fig. 1**), with the largest lesion in the right lower lobe and a nodular lesion in the liver.

Considering the clinical and radiological aspects presented, the patient underwent a new neurosurgical procedure to reduce the intracranial hypertension and to provide another sample to pathological investigation. Lung biopsy was performed to rule out a primary tumor of the respiratory system. The definitive pathological and immunohistochemistry features of intracranial and pulmonary lesions were suggestive of a rhabdoid meningioma.

The patient did not show major improvement in her condition, and after a long period of hospitalization and infectious complications, she had no clinical conditions to proceed with the systemic treatment of her disease. The patient died after 4 months of hospitalization.

Discussion

Meningiomas originate from meningotheial cells of the arachnoid and are the most common primary extra-axial tumors of the central nervous system (CNS) in adults,¹ representing approximately 20% of all primary intracranial tumors, the majority of benign histology. They are more prevalent from fourth to sixth decades of life (the patient in question is much younger if compared with literature),^{2,3} and have a higher incidence in women (ratio of 2:1 to men).³ The malignant variant has almost equal incidence among both genders,⁴ with a peak incidence in the seventh decade.^{5,6} In addition, metastatic meningiomas have a higher incidence among men,^{3,7} which differs from our case.

The major risk factor for meningiomas is exposure to ionizing radiation, although there are assumptions about genetic inheritance and hormonal factors.⁸ Considering metastatic meningiomas, the main predisposing factors are previous intracranial surgery,^{1,3} local recurrence, dural venous sinus invasion, malignant grading, and papillary morphology.³

Meningiomas may be located in any region where arachnoid cells are present, but are more prevalent near dural venous sinuses. They are classified into three grades according to the WHO: grade I (> 80% of total), consisting of benign meningiomas, with several subtypes, slow growth, and low potential for recurrence after treatment; grade II (7–20%), called *atypical meningiomas*, characteristically intermediate among the others, with greater potential for recurrence; and grade III (1–3%), the anaplastic/malignant meningiomas.^{1,8,9} Grades II and III are characterized by cellular malignancy, invasion of brain tissue, necrosis, numerous mitotic figures, and potential to cause metastasis. Nevertheless, in the latest WHO classification, extracranial metastases are not currently considered a pathological criterion for malignancy.⁸

The histological tumor grade of the meningioma is the most important predictor for a recurrence or metastases.¹⁰ The 2007 WHO classification states that more than 90% of grade III tumors exhibit aggressive behavior (local invasion

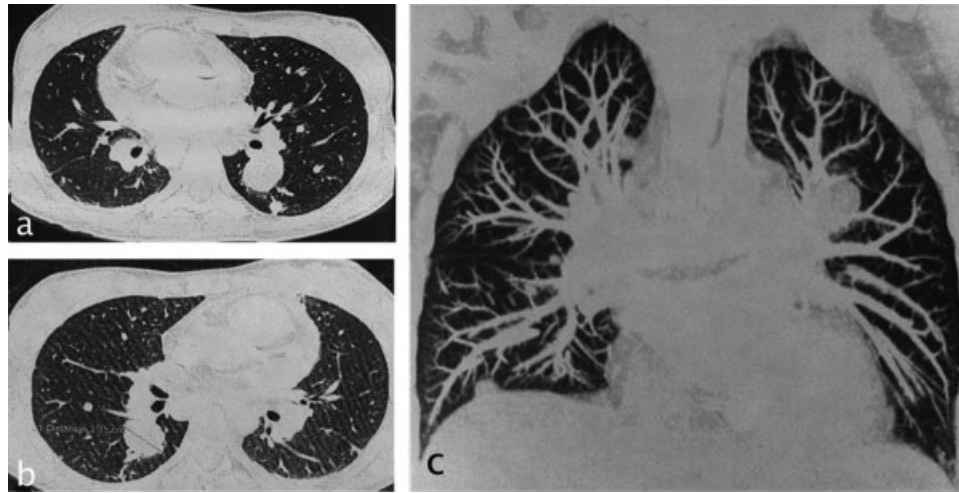


Fig. 1 (a, b) Computed tomography (CT) of the chest (axial view), showing bilateral lung metastatic lesions, the largest on the right side, measuring 2.85 cm. (c) CT of the chest (coronal view), detailing the bronchial architecture and its relation with the tumors.

and/or distant metastases).¹⁰ The latter happens in approximately 0.1% of the cases,^{6,8,10,11} although some authors reported a higher overall rate (1% of total).^{1,9,12} Figueroa et al found only 0.01% of metastatic spread outside the CNS.^{13,14} There are even reports of remote metastases by histologically benign meningiomas.^{11,15} In addition, it is known that a previously benign meningioma can change to a higher grade,^{10,16} as happened to our patient.

The term “rhabdoid meningioma” was used by Perry et al to describe a distinctive, highly aggressive meningotheelial tumor resembling malignant rhabdoid tumor of the kidney.^{17,18} Rhabdoid morphology has evolved to denote a distinctive, rare variant, aggressive primary tumor of meningotheelial origin and is classified as a variant corresponding to grade III in the 2000 revision of WHO classification.^{17,19} Kepes first introduced the rhabdoid transformation of a meningioma, associated with an aggressive biologic and clinical behavior.^{16,17,19} Also, some histological subtypes are inherently prone to recur or spread, as the rhabdoid and papillary variants.¹⁰ Among these, the papillary variant carries the highest risk of late distant metastases.^{3,10,20}

Although it can happen, distant metastases of an anaplastic meningioma are rare. Proposed mechanisms for the low frequency are strong cohesion among tumor cells, lack of intracranial lymphatic system, and the absence of sites prone to deposition of malignant cells.^{3,21} When present, metastases are commonly found in the lung (61%) followed by liver, lymph nodes, and bone (particularly spine).^{1,3,6,10,11,13,22} Rarer sites include kidney, bladder, thyroid, breast, thymus, heart, skin, vulva, and adrenal gland.^{2,3} Metastases can also be found as a iatrogenic spreading in the operative route, especially in the subcutaneous tissue and periosteum.¹¹

The exact mechanism of metastatic spread is undetermined,²³ but is believed to be hematogenous in up to 75%, by microembolization,^{3,6} or invasion of venous sinuses or large vessels.¹¹ Spinal metastases, probably due to cerebrospinal fluid route, have also been described.^{11,24} The average time

between diagnosis of primary tumor and metastasis is approximately 6.4 years.³ Of particular interest is that the tumors are more likely to metastasize and at least one tumor recurred at the primary site,^{3,10,16} as in the patient in this report.

The clinical picture depends on the location of the lesion, displacement of structures by the tumor, and perilesional edema. In the case of lung metastases, they are usually found incidentally,¹ and in about half of the cases they are multiple. In almost 40% of patients, the diagnosis is made only during the autopsy.^{3,4,6}

Diagnosing these metastases can be challenging,¹ and relies mainly on imaging, particularly CT or MRI brain features, which provide data on the lesion size, location, dural adhesion, invasion of bony structures, nerves, and blood vessels, as well as features related to atypical or malignant subtypes.⁸ Because virtually 100% of meningiomas, in culture and in vivo, contain somatostatin receptors, and because some of these receptors (SSTR2, SSTR5) bind octreotide, a somatostatin analog, the ¹¹¹In-octreotide scintigraphy, can be used to identify intracranial meningiomas with high sensitivity (90–100%). Alexandru et al suggested its use for the detection of meningioma metastasis.^{1,13} Also, whole-body diffusion-weighted image (DWI) is a useful technique in cancer imaging, improving tumor detection and characterization, and monitoring response to treatment. DWI is an efficacious method to detect osseous and extraosseous metastases.¹¹

Immunohistochemical stain may also be helpful not only in the diagnosis but also in the evaluation of aggressiveness of the tumor (►Fig. 2).^{3,8,17} The positivity for epithelial membrane antigen (EMA) is characteristic of meningiomas, with a sensitivity of 100%.²⁵ Desmin is usually negative in these tumors,²⁶ but can be positive in rhabdoid variants. The positive immunostaining of tumor cells for vimentin and EMA may aid in the diagnosis of the rhabdoid variant too.²⁷ Also, as in our patient, INI-1 was positive, a characteristic of malignant extrarenal rhabdoid

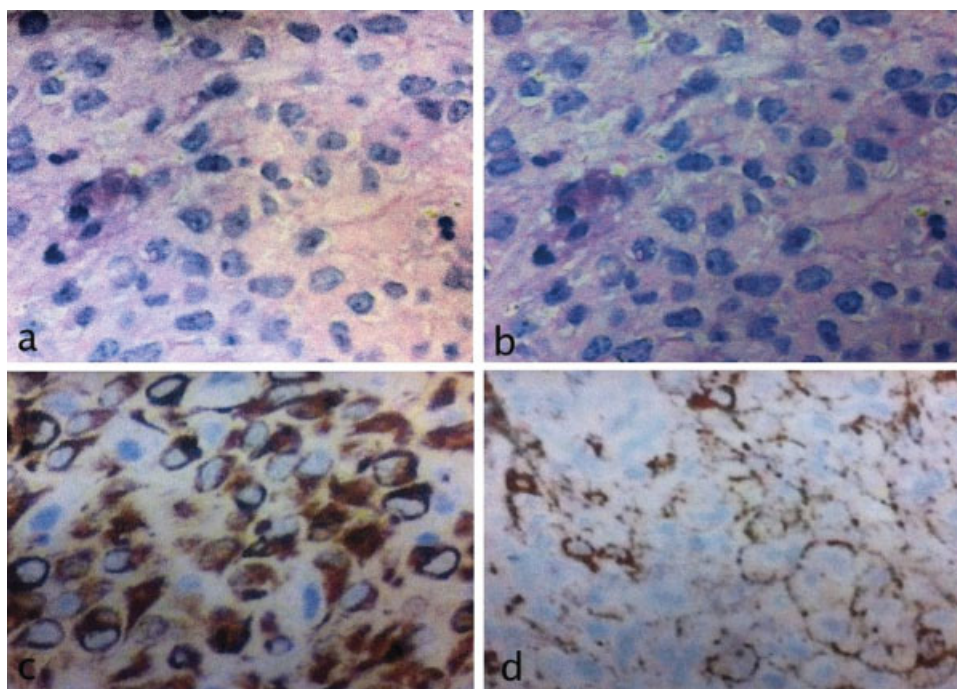


Fig. 2 (a, b) Hematoxylin and eosin stain, showing the features of the metastatic lesion. (c) Desmin positivity, suggesting a rhabdoid variant. (d) EMA positivity, characteristic of meningiomas.

tumors, with a sensitivity of up to 100%.²⁸ In the present case, synaptophysin was also positive, as reported in some other series.²⁹ The Ki-67 index (MIB-1) is a marker of cell proliferation, has been used to assess the proliferative potential of a wide range of tumors, and is shown to correlate with the histologic grade of meningiomas.^{17,30,31} MIB-1 staining index of 3% or more has a significantly higher risk of recurrence. It can also predict recurrence, independent of Simpson surgical resection grade.⁸ The Ki-67 index has been identified as an independent predictor for both survival and tumor recurrence in meningiomas.^{8,10} In other words, a positive Ki-67 predicts aggressiveness.^{3,8} In general, an MIB-1 index of more than 10% delineates malignant meningeal tumors.^{17,30,31}

Treatment of choice is surgical resection of the metastasis, but there is still no consensus about it.^{10,16} The rhabdoid subtype of meningioma has a poor prognosis and must be treated aggressively.¹⁹ Patients are usually submitted to local radiotherapy to prevent recurrence. They can also receive chemotherapy, according to the degree of resection and histology, as well as radiosurgery in selected cases.^{1,8} Prognosis is directly related to the degree of resection, histological pattern, and the presence of metastases. The mean survival time after initial diagnosis is around 7 years,^{3,4} but in cases of anaplastic histology, it is less than 2 years.^{6,8,32}

Conclusion

Extracranial metastases of meningiomas are rare, but should always be remembered in patients with this diagnosis,

especially in cases of local recurrence and malignant histology, as the rhabdoid variant.

Conflict of Interest

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this article.

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