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Case Report

Multidisciplinary approach to anaplastic and metastatic meningioma: A case report and review of the literature

Pablo Ajler[1], Emily Zoraida Guerra Davila[1], Pedro Plou[1], Florencia Casto[1], Silvia Christiansen[2], Luis Alejandro Boccalatte[3], Juan Larrañaga[4]

Departments of [1]Neurosurgery, [2]Pathological Anatomy, [3]Head and Neck Surgery, [4]Reconstructive Surgery, Hospital Italiano de Buenos Aires, Ciudad Autonoma de Buenos Aires, Argentina.

E-mail: Pablo Ajler - pablo.ajler@hospitalitaliano.org.ar; *Emily Zoraida Guerra Davila - emily.guerra@hospitalitaliano.org.ar; Pedro Plou - pedro.plou@hospitalitaliano.org.ar; Florencia Casto - florencia.casto@hospitalitaliano.org.ar; Silvia Christiansen - silvia.christiansen@hospitalitaliano.org.ar;Luis Alejandro Boccalatte - luisboccalatte@gmail.com; Juan Larrañaga - juan.larrañaga@hospitalitaliano.org.ar

***Corresponding author:**
Emily Zoraida Guerra Davila, Department of Neurosurgery, Hospital Italiano de Buenos Aires, Ciudad Autonoma de Buenos Aires, Argentina.

emily.guerra@hospitalitaliano.org.ar

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ABSTRACT

Background: Meningiomas are slow-growing neoplasms, accounting for 20% of all primary intracranial neoplasms and 25% of all intraspinal tumors. Atypical and anaplastic meningiomas are infrequent, representing fewer than 5% of all meningiomas. Unusually, they can show aggressive behavior, and extracranial metastases are extremely rare, representing approximately 0.1% of all reported cases.

Case Description: Fifty-six-year-old male patient diagnosed with atypical basal frontal meningioma with multiple resections, both endoscopic endonasal and transcranial. After hypofractionated radiosurgery, the patient showed new tumor recurrence associated to right cervical level II ganglionic metastasis. We opted for complete resection of the meningioma and reconstruction with anterior rectus abdominis muscle flap, as well as selective cervical ganglionectomy. Anatomical pathology showed neoplastic proliferation of meningothelial cells in syncytial cytoplasm, oval or spherical nuclei with slight anisocariosis and hyperchromasia, and intranuclear vacuoles, all compatible with anaplastic meningioma.

Conclusion: Due to a lack of consensus on how to treat a metastatic malignant meningioma, this pathology requires a multidisciplinary approach, and treatment needs to be adapted to each particular case. Complete resection of the lesion is the primary goal, and this requires complex procedures involving endocranial as well as extracranial surgeries, which result in composite defects difficult to resolve. Microvascular free flaps are considered the gold standard in reconstructions of large skull base defects, with high success rates and few complications.

Keywords: Anaplastic meningioma, Anterior rectus abdominis muscle flap, Deep inferior epigastric artery perforator flap, Metastatic meningioma, Skull base reconstruction

INTRODUCTION

Meningiomas are slow-growing tumors derived from the arachnoid "cap cells," accounting for 20% of all primary intracranial neoplasms and 25% of all intraspinal tumors.[8,25,27,28] The World Health Organization classifies them into three grades: benign (grade I), atypical (grade II), and anaplastic/malignant (grade III).[25,28] Grade II and III meningiomas have a more aggressive behavior and show a higher risk of recurrence, ranging from 29% to 52% and 50% to –94%, respectively.[3,8] Histological

grade, subtotal resection, young age, specific subtypes, brain infiltration, and a high proliferation rate are well-known risk factors for recurrence.[1,8,14,30]

Extracranial metastases of meningiomas are rare, accounting for 0.1% of all meningiomas.[3] The most common extra-axial sites of metastasis are the lungs (60%),[21] followed by the liver, lymph nodes, and bone.[13,34] Due to the fact that these metastases are extremely rare, there are no established management protocols, and prognosis varies.[3,13]

Despite advances in radiology and radiosurgery, the standard treatment of meningiomas is still surgical resection.[25,28] Surgical management of these tumors, when they affect the anterior skull base and invade adjacent structures, is a real challenge and may require a multidisciplinary approach among neurosurgeons, head and neck surgeons, reconstructive plastic surgeons, and oncologists.[19] These resections may lead to significant craniofacial defects. Therefore, in some occasions, it is required a reconstruction with local, regional, or microvascular free flaps. This type of reconstruction is performed to obliterate the dead space resulting from the absence of the skull base tumor, interposing a well-irrigated living tissue free from radiotherapy (RT), with the aim to prevent cerebrospinal fluid (CSF) fistulas, meningitis, pneumocephalus, and cutaneous esthetic defects.[10,20,33]

We present the case of a patient with recurrent invasive anaplastic meningioma and cervical metastasis, its surgical resection, and later reconstruction. Biological aggressiveness, the unusual presentation, the surgical challenge, and the skull base reconstruction make this case valuable. A review of the literature available on this topic was also performed.

CASE DESCRIPTION

Fifty-six-year-old male patient, with a history of Chagas-Mazza disease, diagnosed in 1996 with anterior skull base meningioma due to headaches without any other accompanying symptoms. He underwent surgery in a different center before reaching our institution in 2016, with a recurrent meningioma with intranasal and right orbit invasion [Figures 1a and b]. Complete exeresis was performed by double surgical approach: transcranial and endoscopic transnasal [Figures 1c and d]. Due to the defect of the anterior skull base, an anterolateral thigh (ALT) flap was performed and anastomosed to the temporal vessels with an internal saphenous vein graft. The histopathologic analysis revealed an atypical meningioma [Figures 2a-c]. In January 2017, hypofractionated radiosurgery was performed, with a total dose of 25 Gy (5 Gy/day during 5 days), which was well tolerated. In this case, hypofractionated radiosurgery was chosen due to the tumor's location and short distance from the optic pathways and other critical

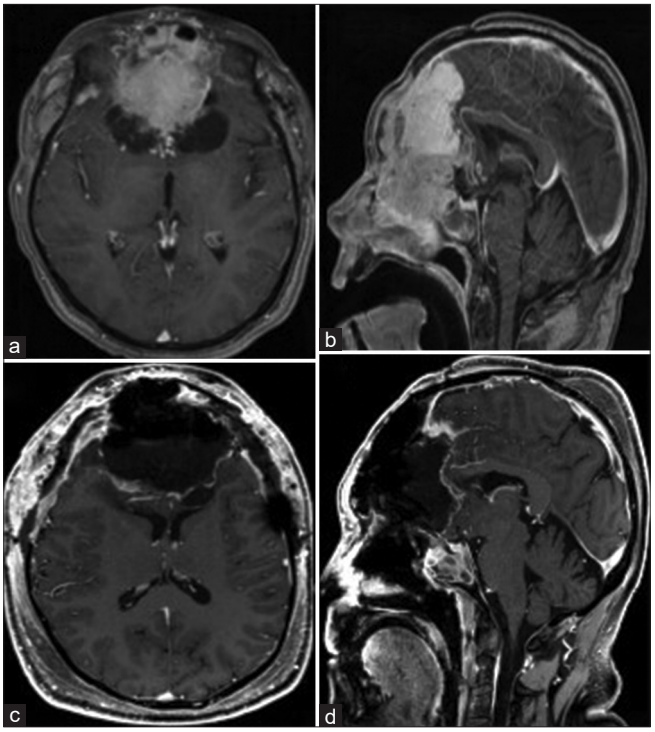

Figure 1: Preoperative (a and b) and postoperative (c and d) gadolinium-enhanced T1-weighted magnetic resonance imaging of the first surgery (in 2016) in our institution. (a and b) Voluminous polylobulated expansive brain tumor with skull base compromise, orbital and nasal invasion. (c and d) Imaging control of gross total resection of the tumor.

structures. One year later, the patient presented with anterior skull base tumor recurrence and nasal skin infiltration, as well as pial and brain parenchyma infiltration, associated to right level II cervical lymphadenopathy [Figures 3a-d]. The latter was biopsied and confirmed lymphatic metastasis of meningioma, Ki-67 labeling index was 20%. Chest and abdomen contrast tomography was performed to exclude any other metastasis; brain computed tomography showed typical bone erosion [Figure 4]. We decided to perform total resection of the meningioma and subsequent microsurgical reconstruction. The histopathologic analysis confirmed the recurrence of an atypical meningioma [Figures 5a-e]. Total lesion resection included superior orbital rim, nasal dorsum, medial orbital wall, nasi proprium bone, upper portion of the medial wall of the maxillary sinus, ethmoidal cells, and vomer bone. Intraoperative frozen sections of margins were negative. CSF loss was reported after resection of part of the tumor attached to the ALT flap from the previous surgery. We performed a primary closure of the defect. Reconstruction was planned with a free anterior rectus abdominis muscle flap. However, due to the lack of adjacent adequate vascular pedicles, this flap was transformed into a deep inferior epigastric artery perforator (DIEP) flap with an 8 × 4 cm skin paddle. In a chimeric fashion, we included a segment

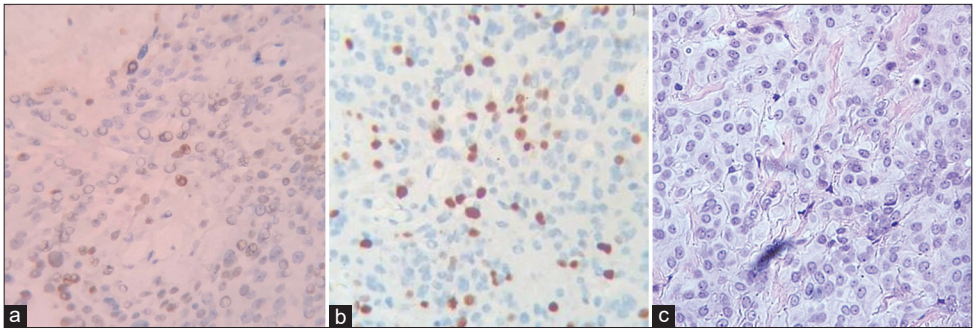

Figure 2: Anatomical pathology images of the first surgery in 2016 (a-c). (a) Focal positivity for progesterone receptor (Immunohistochemistry, ×40). (b) Increase in cellular kinetics (Ki 67 immunohistochemistry. ×40). (c) Cells with syncytium formation and conspicuous nucleoli. Mitosis figures are observed (Hematoxylin and eosin stain, ×40).

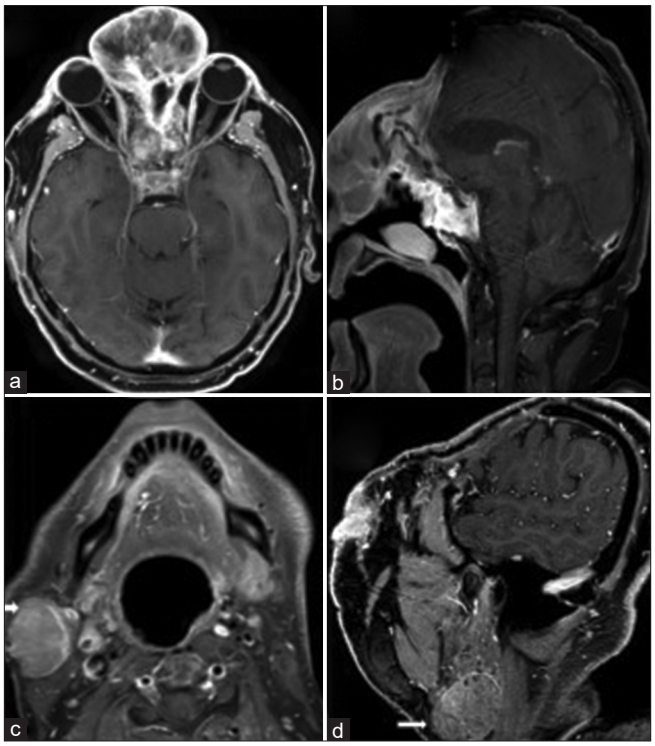

Figure 3: Gadolinium-enhanced T1-weighted magnetic resonance imaging of the tumor recurrence and the neck metastasis in 2018. (a and b) A more extensive component of the expansive nasoethmoidal and orbital wall lesion can be observed. The lesion compromises the subcutaneous tissue of the nose. (c and d) Right laterocervical adenopathy compatible with metastasis (white arrow).

of anterior rectus abdominis muscle based on the external branch of the epigastric artery. In this way, the pedicle was extended to 10 cm to reach the neck, where vascular anastomosis with the facial artery and the thyrolinguofacial trunk was performed without resorting to a vein graft [Figures 6a-d]. Later, selective resection of the right cervical level II was performed [Figure 7]. The patient spent the first postoperative 48 h in an intensive care unit. The flap was clinically controlled by checking temperature, skin color, and type of bleeding by puncture every 4 h. He did not present postoperative complications and was discharged on the 8th postoperative day. Subsequently, on the 15th postoperative day, it was found that the flap was vital and healing, so we decided to remove the stitches. The reconstruction gave a good cosmetic outcome. 3 months later, the patient returned to the consult with less inflammation and the facial defect was well covered. It persisted with a mild hypopigmentation and the sensory recovery was satisfactory. There were no donor-site morbidities and the imaging controls until this instance did not show recurrence of the tumor. Even though radiant therapy was indicated at this stage, the patient refused it and finally returned to his hometown. He passed away a year later due to pneumonia.

DISCUSSION

Meningiomas grades II and III are characterized by a more aggressive behavior and a high recurrence rate, ranging from 29% to 52% and 50% to 94%, respectively.[8,28] Even though surgical resection is still the treatment of choice for all types of meningiomas, combined strategies are usually applied to maximize progression-free survival and to reduce postoperative neurological deficits.[7,17,34] Current standard treatment consists of gross total resection (GTR), subsequent radiosurgery for grade III lesions, and optional for grade II lesions.[16,17] The latter showed 74–100% progression-free survival rates at 5 years with GTR and RT, while the percentages for grade III meningiomas are 47–61%.[4,18,22] Some studies show that adjuvant radiotherapy has reported improvement in progression-free survival and provides local control. However, there is limited evidence regarding overall survival.[2,4,34] Furthermore, RT doses of more than 54 Gy might be associated to decreased survival.[4] According to Smith *et al*., hypofractionated radiosurgery ranging from 22.5 Gy to 30 Gy divided in five fractions in intracranial meningiomas provides satisfactory tumor control and

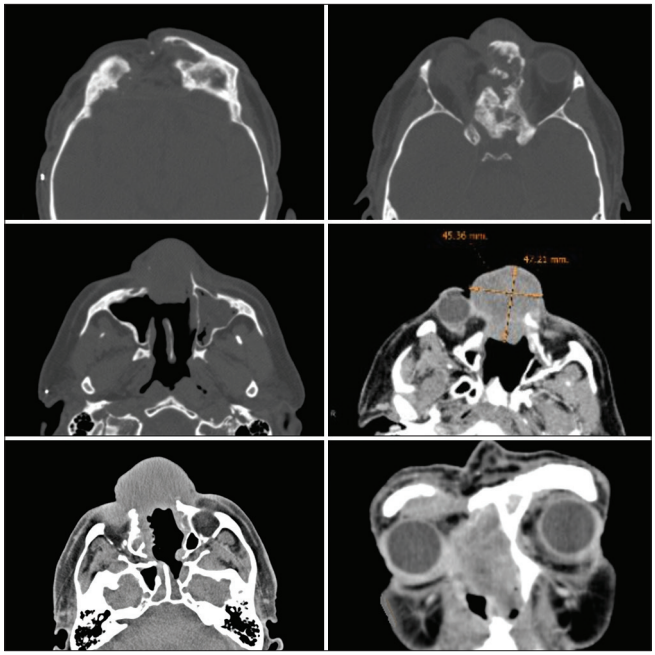

Figure 4: Brain computed tomography of anterior skull base and paranasal sinus with thin cuts where bone erosion of the tumor can be seen. Yellow lines show measures of the tumor (45.36 × 47.21 mm).

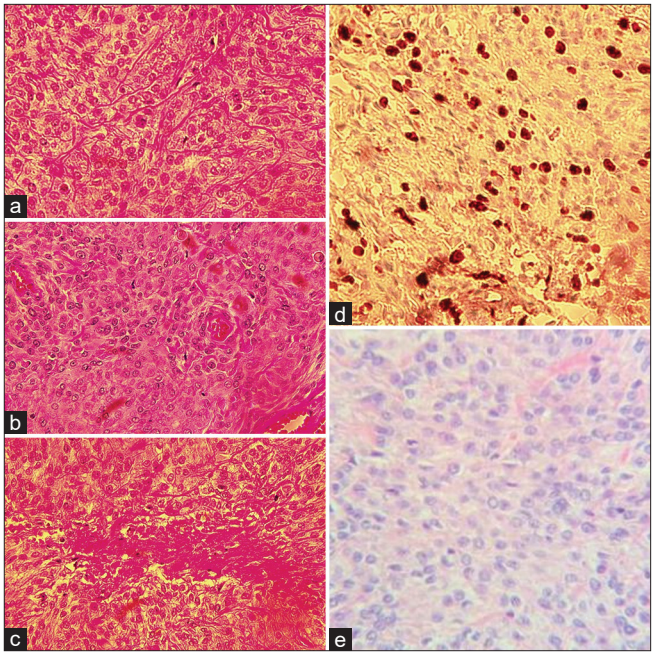

Figure 5: Anatomical pathology images of the second surgery in 2018 (a-e). (a) Syncytial arrangement, moderate nuclear pleomorphism (H&E, ×40). (b) Nuclear pleomorphism, evident nucleoli and marked vascularization (H&E, ×40). (c) Areas of tumor necrosis and nuclear pleomorphism with some pyknotic nuclei (H&E, ×40). (d) Increase of cellular kinetics with "hot spots" of 12% with Ki67 (Immunohistochemistry, x40). (e) Neoplastic infiltration in lymph node. Note the presence of intranuclear vacuoles in the center of the field (H&E, ×40).

a low rate of side effects, even in large tumors (> 9 cm). Also, symptoms seem to improve or ameliorate in >66%.[29] Compared to a conventional treatment, hypofractionated radiosurgery has the advantage of treating larger tumors, even those close to sensitive neurological structures. There are few high-level studies supporting the use of hypofractionated radiosurgery for intracranial meningiomas, although it is a widely accepted and used treatment.[26]

Metastatic meningioma is a rare clinical entity, with an estimated prevalence ranging from 0.1% to 0.76% of all patients with meningiomas according to different reported series.[3,14,21] The metastatic rate for grade II meningiomas ranges from 1.3% to 2%, and around 8% for grade III meningiomas, according to different authors.[14,23] The most frequent extracranial sites of metastases are pulmonary and pleural, followed by the intra-abdominal organs, especially the liver, lymph nodes, long bones, pelvis, skull, vertebrae, and other visceral organs.[5,6,15,21,23] Although physiopathology is not known exactly, one of the strongest hypotheses suggests that the main dissemination pathway is hematogenous, since the most affected organs are lungs and liver.[13,14,31] In turn, surgical resection might lead to an increased risk of iatrogenic metastasis of histologically aggressive meningiomas.[3] Other possible routes of dissemination are through CSF and also lymphatic, since meningiomas gain access to the lymphatic system as they spread in the skull and scalp or to the lymphatics around the cranial nerves, for instance in the cavernous sinus, ending in the cervical lymph nodes.[23,24] Factors correlated with metastasis include high cellularity, cellular heterogeneity, high mitotic rate, necrosis, and blood vessel invasion.[13]

In our case, after several surgical resections, the patient presented with recurrence at the level of the anterior cranial fossa with invasion of the superior meatus of the nasal cavity, medial orbital wall, and nasal subcutaneous tissue. Although the hematogenous route is the best known for metastatic meningiomas, our patient presented with lymphatic spread, since histopathologic findings confirmed that a cervical lymph node was infiltrated by neoplastic cells, compatible with metastasis.

There is no standard protocol to treat metastatic meningiomas.[23,24] Different studies describe cases treated with chemotherapeutic agents including hydroxyurea, doxorubicin, vincristine, cyclophosphamide, and temozolomide, together with targeted therapies such as apatinib and sunitinib.[10,16] These are frequently used when there is unreported lymph node capsule perforation. However, there is little evidence of the effectiveness of these treatments. Although some of them report improvement, there are also cases of disease progression; thus, there is no conclusive evidence in this respect.[27]

Figure 6: Preoperative (a and b) and postoperative (c and d) picture of the patient in 2018. (a and b) There is a more exophytic component of the expansive nasoethmoidal and orbital lesion. (c and d) Reconstruction with free microvascular pediculated flap of anterior rectus abdominis muscle.

Due to tumor aggressiveness, high cellularity, and presence of metastasis, we opted for total resection with negative surgical margins, later reconstruction with a microvascular free flap, and selective ipsilateral metastatic cervical lymph node drainage. Even though most reconstructions for large skull base defects are secondary to resections of locally aggressive malignant lesions, surgical resolution of locally aggressive benign tumors may also cause large defects that must be repaired.[32,33] The main objective of microvascular free tissue transfer, in this case DIEP, is to facilitate the restoration of a hermetic barrier capable of separating intra- and extracranial structures by means of RT-free tissue transfer. This allows the sealing of the cranial defect and reduces complications, including persistent CSF leak and infectious sequelae such as meningitis,[20] which may seriously compromise the patients' health. Restoration of facial aesthetics and function are secondary objectives, which can be accomplished by means of free flap transfer.[33] Due to the anatomical and functional complexity of the anterior cranial fossa, there are several descriptions of reconstructive techniques with microvascular free flap following en bloc resection of anterior skull base tumors.[11,32] To choose the flap,

Figure 7: Intraoperative image, where metastatic right laterocervical adenopathy is observed.

two essential points need to be considered: (a) defect size once the tumor has been resected and after obtaining intraoperative frozen section analysis of negative surgical margins and (b) type of tissue to be reconstructed (bone, muscle, skin, etc.). Other factors, such as patient comorbidities, previous surgeries, available vascular pedicles, and pedicle length provided by the chosen flap, among others, are also worth considering.[6]

Literature frequently mentions the free rectus abdominis muscle flap as the most widely used in microvascular free tissue transfer reconstruction of the skull base, due to its reliable anatomy and vascularity, its irrigation by the inferior epigastric artery, and a branch of the external iliac artery.[6,12] Its advantages include its tendinous intersections, which help facilitate fixation to the skull base; adequate volume, which allows obliteration of complex dead spaces given the significant volume of soft-tissue transfer; and the versatility to use it with or without cutaneous panniculus, depending on volume demand.[11,32] The main disadvantage of this type of flap includes donor-site morbidities, which may lead to eventration.[9,12]

CONCLUSION

Due to a lack of consensus on how to treat metastases of a malignant meningioma, we believe that this pathology must have a multidisciplinary approach, and treatment needs to be adapted to each particular case. Total resection is the primary goal for the treatment of this disease since adjuvant therapies are not highly beneficial. Microvascular free flaps are considered the gold standard in large skull base reconstructions, with high success rates and minor complications.

Declaration of patient consent

Patient's consent not required as patient's identity is not disclosed or compromised

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Conflicts of interest

There are no conflicts of interest.

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