DIAGNOSIS AND PREDICTORS OF TREATMENT OUTCOMES IN MENINGIMAS WITH ATYPICAL OR ANAPLASIC HISTOLOGY

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Introduction:
Meningiomas originate from specialized meningothelial cells called arachnoid cap cells and correspond about up to 26% of all intracranial lesions. According to the WHO classification, meningiomas are grouped in grade I (benign), grade II (atypical), and grade III (anaplastic) . Atypical corresponds to 4.7 to 20% of all meningiomas, while anaplastic for 1–2.8%. The standard treatment of grade II and grade III meningiomas involve total/radical resection, respecting Simpson score, followed by adjuvant therapy with irradiation and, eventually, chemotherapy. With the continuous improvement of molecular and immunochemistry analysis, the paradigm for treatment of these tumors has been changing.

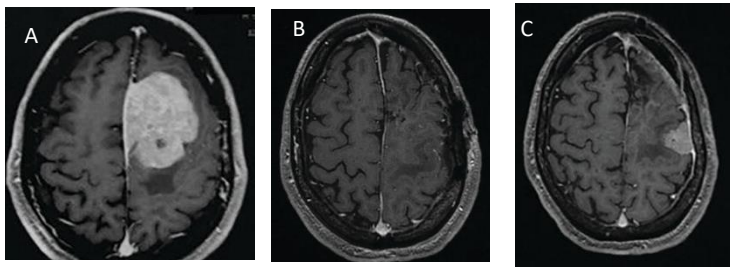
Objectives:
Discuss the current management of aggressive/malignant meningiomas focusing on the new discovers in genetic/molecular and radiotherapy.

Methods: Revision of all meningiomas operated between 2012 and 2017 in our institution to describe the epidemiologic characteristics of atypical and anaplastic subtypes. Also, literature was reviewed based on the WHO (2016) classification guided through genetic/molecular findings.

Results:
A total of 170 newly diagnosed patients with intracranial meningiomas underwent microsurgical resection at the Neurological Institute of Curitiba (INC) between January 2012 and June 2017. Only six (3.5%) patients had atypical/anaplastic tumors with mean age of 53 years (Table 1). Simpson grade I resection was achieved in all patients with malignant histology, and radiotherapy was reserved for progression. Only one patient with atypical meningioma received upfront radiotherapy because of high Ki-67 index. Any case of skull base meningioma exhibited progression to malignant subtypes in this series.

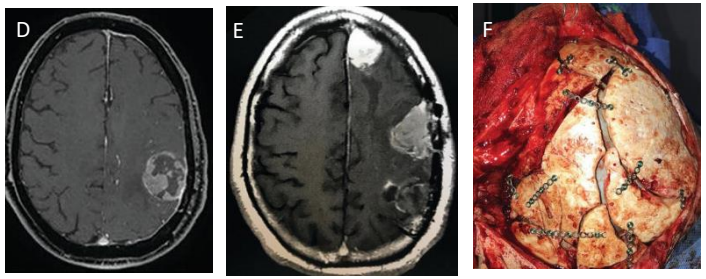
	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6
Gender	F	M	M	F	F	F
Age	57	58	36	62	65	44
Topography	Parasagittal	Parasagittal	Convexity	Convexity	Convexity	Parasagittal
Histology at 1st resection (WHO)	Grade I	Grade I	Grade I	Grade I	Grade I	Grade I
1st resection (Simpson)	Grade I	Grade I	Grade I	Grade I	Grade I	Grade I
Time to evolution	7m (anaplastic)	26m (anaplastic)	9m (anaplastic)	-	-	16 yrs (atypical)
Radiotherapy modality after anaplastic diagnosis	EBRT	EBRT	EBRT	-	EBRT	EBRT

Conclusions:
Malignant meningiomas remain a challenge pathology and no effective treatment is current available. Against literature evidence, we presume that the biological signature of this specific tumor is more important for evolution than previous reported prognostic factor. In this scenario, new studies aiming objective analyses of immunohistochemistry patterns and genetic profile of meningiomas are probably the next step for comprehension of such complex neurosurgical pathology.



Ilustrative case: 58-year-old male has sporadic new onset headache and MRI evidences enhanced parasagittal homogenous mass tumor (A). Simpson grade I resection (B) was achieved at surgery, and histopathology confirmed atypical meningioma with Ki-67 index of 70% in hot spots. Adjuvant external beam radiotherapy (EBRT) was added to the treatment.

One year follow-up evidenced recurrence of the lesion and another gross total resection was necessary (C).Histopathological analyses confirmed again an atypical histology. At this time, chemotherapy with octreotide was introduced without response.



2 years follow-up another recurrence was seen(D). After another Simpson grade I tumor removal, progression to anaplastic meningioma was confirmed with an increase in Ki-67 index from 70 to 90% of the cells.
Tumor recurred in two more occasions in an interval of 8 months (E). Progressive neurological impairment and seizures due to motor cortex/eloquent area involvement/gliosis were seemed, and tumor resection with extensive dural removal was performed both times (F). The patient underwent salvage irradiation. Two months after adjuvant treatment, the patient evolved with neurological worsening, dying due to clinical complications.

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