

# MULTIPLE INTRACRANIAL MENINGIOMAS

## Diagnosis, biological behavior and treatment

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**Abstract** – Multiple intracranial meningiomas (MIM) are a rare pathology when not associated with neurofibromatosis. The prevalence rate of those tumors varied from 2.3 to 8.9% of all intracranial meningiomas. **Objective:** To present, analyze and discuss the cases of seven patients diagnosed with multiple intracranial meningiomas, describing their clinical and histological characteristics, as well as their biological behavior. **Method:** The patients records, surgical descriptions, imaging studies and the histopathological exams were retrospectively reviewed. This is the largest series of MIM published in Brazil. **Results:** This sample consists of five women and two men. The age varied from 42 to 84 (average 53.8). Twenty-two meningiomas were identified and varied from 1.5 to 192 cm<sup>3</sup>, with an 62.8 cm<sup>3</sup> average volume. The number of procedures varied from 1 to 5 per patient. No surgical death occurred in this series. **Conclusion:** Despite the multiplicity of tumors, number of recurrences, the new tumors, repeated operations and re-operations, radiotherapy and a number of postoperative complications, the patients experienced a long survival in conjunction with a fairly good quality of life.

**KEY WORDS:** brain tumors, meningiomas, multiple intracranial meningiomas, microneurological surgery.

### Meningiomas intracranianos múltiplos: diagnóstico, comportamento biológico e tratamento

**Resumo** – Os meningiomas intracranianos múltiplos são tumores raros quando não associados a neurofibromatose, correspondem de 2,3 a 8,9% de todos os meningiomas intracranianos. **Objetivo:** Apresentar, analisar e discutir 7 pacientes com diagnóstico de meningioma intracraniano múltiplo, descrevendo as características clínicas, histológicas e o comportamento biológico desses tumores. **Método:** Trata-se de revisão retrospectiva incluindo a análise dos prontuários, das descrições cirúrgicas, dos estudos de imagem e do material histopatológico. Esta série é a maior série de meningiomas intracranianos múltiplos publicada no Brasil. **Resultados:** A casuística é composta de 5 mulheres e 2 homens. A idade oscilou entre 42 e 84 anos, com média de 53,8 anos. Identificamos 22 meningiomas que variaram de 1,5 a 192 cm<sup>3</sup>, com volume médio de 62,8 cm<sup>3</sup>. O número de procedimentos oscilou de 1 a 5 por paciente. Não ocorreu mortalidade cirúrgica. **Conclusão:** Apesar de vários tumores, de recorrências, do surgimento de novas neoplasias, de várias cirurgias, re-operações, do tratamento com radioterapia e de inúmeras complicações pós-operatórias, esses pacientes obtiveram uma longa sobrevida com boa qualidade de vida.

**PALAVRAS-CHAVE:** tumor cerebral, meningiomas, meningiomas intracranianos múltiplos, microneurocirurgia.

Meningiomas are tumors originated from arachnoidal cells present in the villi, in the granulations, in the stroma of the perivascular spaces and in the choroid plexus; corresponding to 13 to 20% of all intracranial tumors<sup>1-3</sup>.

Multiple intracranial meningiomas (MIM), when not associated with neurofibromatosis, are a rare event, which corresponding to 2.3 to 8.9% of all intracranial meningiomas<sup>4-11</sup>.

The multiple intracranial meningiomas terminology should be used only when two or more meningiomas occur either simultaneously or sequentially in different loca-

tions. It is important to establish the difference between this pathology and tumor recurrence or diffuse meningiomas<sup>1,3,4,7-10</sup>.

Our study aims presenting, analyzing and discussing 7 patients diagnosed with multiple intracranial meningiomas, describing their clinical, radiological, and histological characteristics, as well as their biological behavior. It also highlights the fact that, although the patients underwent a number of surgeries and have faced innumerable complications, they lived long, and with a good quality of life.

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Table. Demographic, clinical histological data.

Case	Age-sex	Location	Radio. Post	Radio. Pre	Vol (cm <sup>3</sup> )	Nº of operations	Histology
1	48-Fe	Parag. F (2) F F F P	Yes	No	48	5	Grade I Transitional
					3		
					7.5		
					6.7		
					6		
					8		
2	50-M	FP Tent R FR S Caver FL TR	No	Yes	192	3	Grade I Transitional Fibroblastic
					24.3		
					8		
					2		
					4		
3	42-Fe	Sph R and L	Yes	No	175	2	Grade I Transitional
					150		
4	55-Fe	F R and L	No	No	115.5	3	Grade I
					127.5		
5	56-M	FR and L	Yes	No	130	2	Grade II Meningoteliomatous
					150		
					125		
6	42-Fe	FR Sph	No	No	6	1	Grade I Meningotelial
					12		
7	84-Fe	Parag R and L	No	No	72	1	Grade I Fibroblastic
					1.5		

Cav, cavernous; F, frontal; Fe, female; FP, fronto-parietal; L, Left; M, male; Parag, parasagittal; Post, postoperative; Pre, preoperative; R, right; Radio, radiotherapy; S, sinus; Sph, sphenoidal; T, temporal; Tent, tentorial; Vol, volume.

## METHOD

Between 1986 and 2006, 7 patients with multiple intracranial meningiomas were diagnosed and treated at Servidores do Estado Hospital and at Copa D'Or Hospital (RJ). The present study carried out a retrospective review, which included analysis of patients' records, surgical descriptions, imaging studies, and histopathological material reviewed by a sole pathologist, confirming the diagnosis of meningioma in all the cases.

## RESULTS

The patients' follow-up lasted from 1 to 21 years, (average of 11.7 years). This sample consisted of 5 women and 2 men, at a proportion of 2.5 women/1 man. The age varied from 42 to 84 (average 59). Twenty-two meningiomas of different sizes were identified, they varied from 1.5 to 192 cm<sup>3</sup>, with an average volume of 62.8 cm<sup>3</sup>. Eleven specimens were cortical, seven parasagittal, two meningiomas were located in the sphenoid wing, one of these penetrated the cavernous sinus. Other was tentorial and another derived from the sphenoid wing.

The number of tumors varied from 2 to 5 per patient. Microsurgical techniques were utilized to operate those

tumors that needed surgical treatment. The number of procedures varied from 1 to 5 per patient. No surgical death occurred in this series. A 84-years-old female (case 7) died 3 months after surgery due to pneumonia. Case 2 had postoperative meningitis and 5 developed intracranial abscess. This case study showed, a high frequency rate of postoperative infections (16.6%). We believe, this is due to the large number of surgeries and radiotherapy undergone by some patients, which causes deterioration of skin vascularization and of the bone flap (atrophic scar). It is also due to low immunity caused by the pathology itself or by continuous administration of corticosteroides. This finding was not acknowledged in literature. During this period, 3 cases of recurrence were observed

The demographic, clinical, histological data are presented in the Table.

### Significative cases

**CASE 1** – A 48-year-old woman had been operated on to remove a left frontal parasagittal meningioma 5 years before our first evaluation. After two years, there was a local tumor recurrence. She was re-operated for a subtotal re-

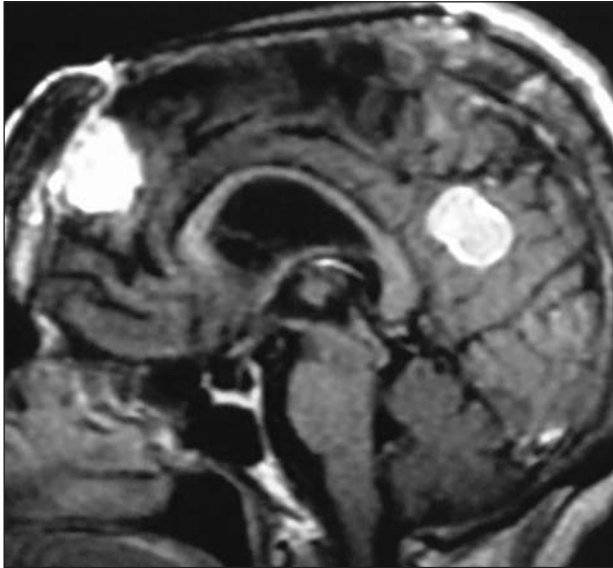


Fig 1. Patient 1. Post contrast T1 weighted imaging showing one frontal and one parietal meningiomas, away from the previous craniotomies.

removal of the lesion, and following she underwent radiotherapy treatment. Three years later, she developed right hemiparesis. MRI detected bilateral parasagittal meningiomas, leading to complete occlusion of the superior longitudinal sinus. A new surgery removed the two lesions together with the superior sagittal sinus. Postoperative MRI confirmed the total removal of the lesions. Two years later, MRI revealed two new tumors in the right frontal area, distant from the implantation site of the previous meningiomas. With a frontal craniotomy, performed anterior to the previous craniotomies, a new thorough removal of both lesions was achieved. The patient's response was again satisfactory, as she could return to her daily house duties. Five years after the last intervention, two other meningiomas were identified. For the fifth surgery to be made, rotation of a pedicle flap was necessary due to poor vascularization of the surgical site and atrophic scar. The lesions were once again thoroughly removed. The postoperative follow-up was extended. At the moment, the patient presents light hemiparesis, which does not prevent her from living a normal life for her age. The last MRI showed the presence of two new meningiomas (Fig 1).

**CASE 2** – A 50-year old man presented left hemiparesis with crural predominance. He informed that, when he was around 8- years- old, he underwent radiotherapy to treat *tinea capitis*. MRI revealed extra cerebral expansive process with clearly-defined contours, hyperintense, com heterogenic capitation of the contrast agent, located in the right parasagittal frontoparietal region and a second minor tumor implanted at the tentorium (Fig 2). A right fronto parietal craniotomy was performed, with the use

of microsurgical techniques a complete removal of the tumor was achieved including the tumor implantation. The follow-up of the tentorial lesion with annual MRI, showed a progressive increase of the meningioma. A new surgical procedure was performed through a right occipital craniotomy, with complete removal of the lesion, and coagulation of the implantation site. He had meningitis in the early postoperative period and needed intravenous antibiotics treatment. When discharged from the hospital he had recovered from meningitis, but presented left homonymous hemianopsia. MRI performed approximately 3 years after the last surgery revealed frontal tumor recurrence and new tumor located in the cavernous sinus. He underwent right fronto-parietal craniotomy in the same surgical site of the previous one, and a complete removal of the lesion was again achieved (Fig 2). At the moment the MRI shows unchanged cavernous sinus lesion and two minor lesions appeared, in the left frontal and right temporal regions, with no surgical prescription at the moment.

## DISCUSSION

The first description of a multiple intracranial meningioma was presented by Anfimov and Blumenau<sup>12</sup>, in 1889, but Cushing and Eisenhardt<sup>1</sup> were the ones to create a theoretical construct for this pathology. The multiple intracranial meningioma terminology should be used only when two or more meningiomas occur either simultaneously or in a sequence in different locations, but not necessarily of the same histological subtype. It is important to establish the difference between this pathology and tumor recurrence or diffuse meningiomatosis<sup>3,7,8</sup>.

Intracranial meningiomas incidence rate varies from 13 to 20%. But MIM's are rare, when not associated with neurofibromatosis<sup>4-11,13</sup>.

The first quotations reveal an incidence of only 1 to 2%. With the introduction of CT and MRI this incidence increased to 5.4 to 10.5%<sup>4-9</sup>. The incidence rate in our series was of 8.9%, according to the figures found in the literature. None of our patients showed any sign of neurofibromatosis.

Meningiomas are rare during childhood and adolescence periods. They are more common during adult life<sup>1,2,3,6</sup>. In this case study, age varied from 42 to 84 (average of 57.5 years).

According to Black et al. there are some factors that are important in the developing of the meningiomas<sup>14</sup>.

### Relevant etiological factors

**GENETICS** – Deletion of the chromosome 22 in patients with type 2 neurofibromatosis and in up to 50% of solitary meningiomas are connected with the appearance of multiple meningiomas.

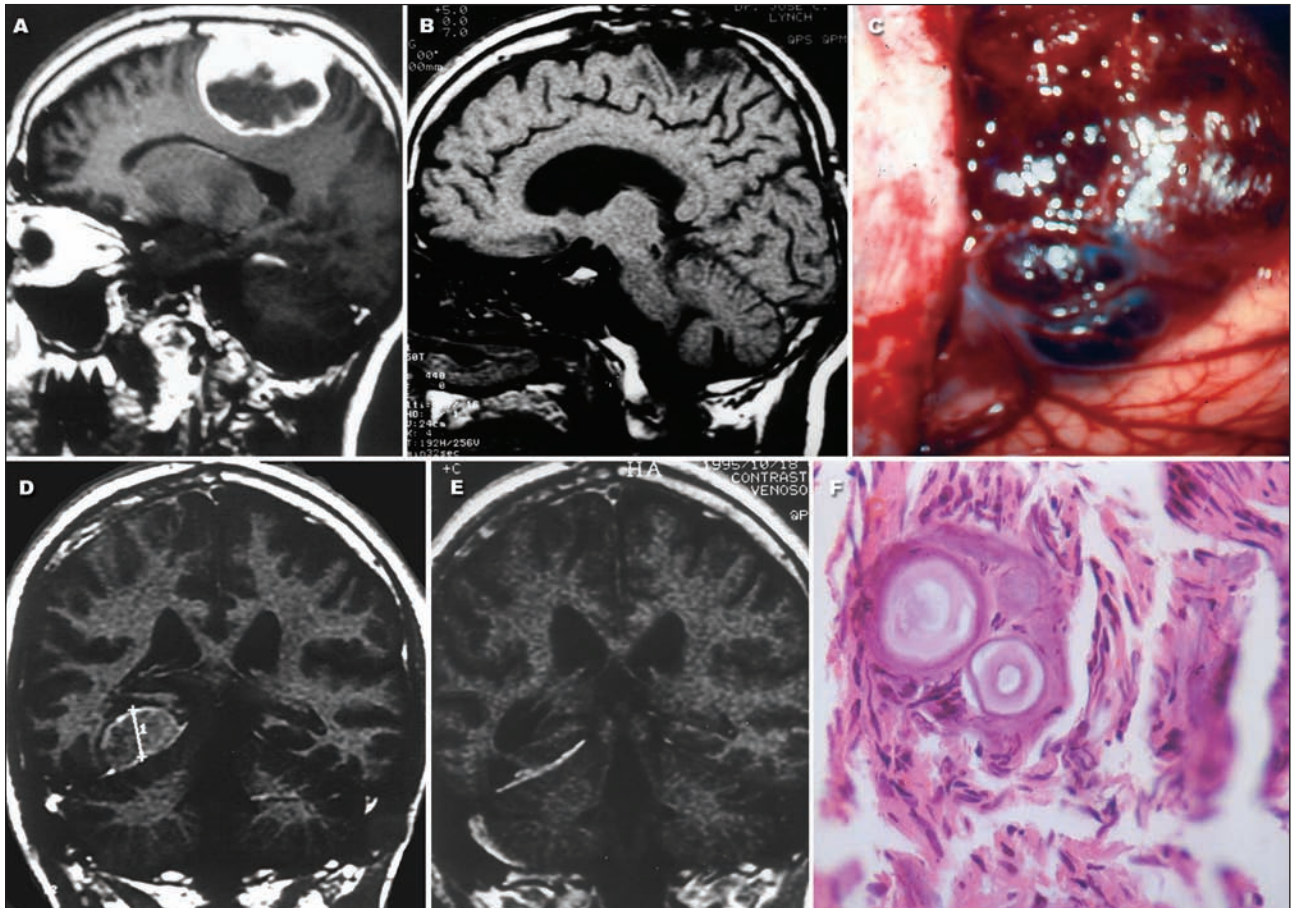


Fig 2. Patient 2. (A) Sagittal T1 post contrast image revealing heterogenic right parasagittal tumor. (B) Intraoperative photograph showing compressed brain parenchyma, a dark red tumor and duramater folded over superior sagittal sinus. (C) Postoperative image confirming total tumor removal (Simpson 1). (D) Coronal T1 post contrast image demonstrating a tentorial meningioma. (E) Postoperative coronal T1 post contrast image confirming a complete tumor removal. Note the dural tail (Simpson 2). (F) Histology showing a benign meningioma (Grade I) with a psammoma body in the center of the picture (HE x 120).

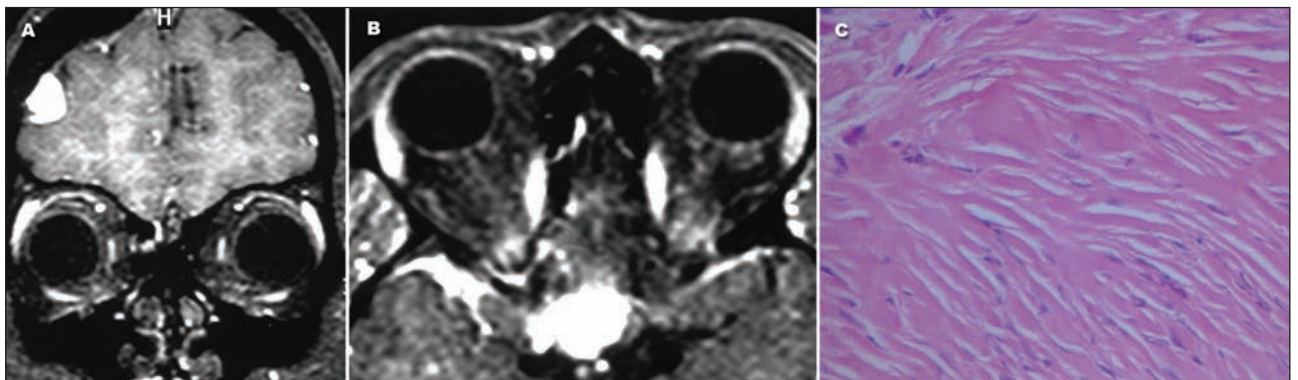


Fig 3. Patient 6. (A) Coronal post contrast T1 MRI demonstrating a small, frontal meningioma. (B) Axial post contrast T1 imaging revealing a planun sphenoidal meningioma compressing the right optic nerve. Both tumors were removed through a single craniotomy. (C) Histology showing a benign meningiomas of fibroblastic subtype. (HE x 120).

**IRRADIATION** – There are a number of reports revealing the appearance of meningiomas after radiotherapy treatment. Approximately 30% of the cases presented by Harrison et al. were multiples meningiomas<sup>15-18</sup>. Even with a low-dose therapy, as the one used for children, for *tinea capitis* treatment<sup>19</sup>. This occurred with our patient 2, who developed 5 meningiomas in adult life, after having undergone radiotherapy for *tinea capitis* treatment during childhood. Patient 1 underwent postoperative radiotherapy treatment after a partial meningioma removal. Some years later, she developed 4 successive recurrences. Aware of this risk, the use postoperative radiotherapy to inhibit tumor growth was prescribed exclusively for cases of partial removal with recurrence, as for example, meningiomas that invade the cavernous sinus, where total removal is rarely achieved and when so, is accompanied by morbidity, as it occurred with patient 3<sup>14,20,21</sup>.

**HORMONES** – A number of papers show a higher frequency rate of meningiomas in women. One factor associated is the action of progesterone in progesterone receptors found in 80% of meningiomas, leading to an increase during the luteal phase of the menstrual cycle and during pregnancy<sup>22-26</sup>. A proportion of 2.5 women to 1 man was observed in the present series.

**TREATMENT** – Each tumour should be individually assessed. Surgery is planned and performed aiming at total removal of the symptomatic lesion. An asymptomatic small meningioma without cerebral edema should be followed-up with MRI every 6 or 12 months, mainly if the patient is more than 65 years old. Surgery should be prescribed exclusively for cases with tumor expansion, symptoms appearance or cerebral edema<sup>6,14,27</sup>. The above described strategy was utilized to the patients involved in this study.

If, otherwise, both tumors are located close to each other and can be approached by a single craniotomy, it is advisable that both lesions be removed, including the asymptomatic tumor, as it occurred with Patient 6<sup>7,9,22</sup> (Fig 3). The meningiomas surgical treatment should always aim at their complete removal, as well as their dural implantation, thus decreasing recurrence possibilities, and improving the patient's chances of healing<sup>2,7,8</sup>. This above concept originates from Simpson et al. conclusions<sup>28</sup>, which established a correlation between tumor removal extension and recurrence.

Our department's elected procedure is always to plan and perform surgery aiming at total exeresis of the meningiomas and of their dural implants. When this is not possible, bipolar coagulation at the implant site is performed with the objective of achieving grade II of Simpson's classification. The grade I or II was achieved with all

the tumors, except for a meningioma which invaded the cavernous sinus (Patient 3).

Another important factor related to tumor recurrence and prognosis is the histological classification defined by World Health Organization (WHO). The grade of the histological classification has implications for tumor invasion and recurrence. The following grades were established by the WHO:

- Grade I: Benign meningiomas (85-90%) include meningoendotelial, fibroblastic, transitional, psammomatous, angiomatous, microcystic, and metaplastic meningiomas. These characteristics of the sub-group are not relevant for the prognosis. They are mere descriptions of different histology.
- Grade II: Atypical meningiomas (5-10%), more aggressive.
- Grade III: Malignant meningiomas (3-5%).

Except for one tumor (Case 5) classified as atypical, all the other meningiomas fit in Grade I WHO's histological scale. Three tumor recurrences were observed in these series.

Aiming at assessing the treatment results, we used Glasgow's outcome scale. There was no operative mortality in this series. There was one death, due to pneumonia, 3 months after surgery. All the other patients showed a positive response to the treatment performed, and were classified in grade 4 or 5, according to the Glasgow outcome scale. Follow-up varied from 1 to 21 years, (average of 11.7 years).

In conclusion, multiple intracranial meningiomas are a rare pathology. The multiple intracranial meningioma terminology should be used only when two or more meningiomas occur either simultaneously or sequentially in different locations. The goal of surgical treatment is to achieve grade I or II of Simpson's classification. Despite the multiplicity of tumors, number of recurrences, and the novo tumors, repeated operations and reoperations, radiotherapy and a number of postoperative complications, the patients experinced a long survival in conjunction with a fairly good quality of life.

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