

Multiple spinal and cranial meningiomas: A case report and review of literature

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Article information	Abstract
Key words <i>craniospinal, meningioma, multiple meningiomas, NF2</i> <i>Received: 30-09-2024</i> <i>Accepted: 23-12-2024</i> <i>Available: 28-01-2025</i>	Though meningiomas are common neoplasms of the nervous system, the occurrence of multiple meningiomas in different neuraxial compartments is rather rare. We report a case of A 28-years old girl presented to neurosurgery outpatient clinic of National Cancer Institute, Misurata - Libya complaining of headache, increased attacks of convulsions (she has been on anti-convulsant since childhood , valproic acid) and unsteadiness. She walks with assistance and has a history of bowel and bladder dysfunction and right eye visual loss. Her Cranial and spinal magnetic resonance imaging (MRI) revealed multiple homogenously enhancing lesions in the left parieto-temporal region ,craniometrical junction, lumbar and sacral regions.. She underwent multiple surgeries including left side frontotemporal craniotomy, suboccipital craniotomy and spinal laminectomy in different sessions and total removal of thd tumors was achieved. Only about 19 cases of multiple cranial and spinal meningiomas have been reported, of which, only five cases have more than one spinal meningioma. The implication of the incidence of such multiple meningiomas in the same patient with relevance to investigations and decision making are discussed along with a brief review of literature of cases with multiple spinal and cranial meningiomas.

I) Introduction

Meningiomas are the most common primary non-glial brain tumors and comprise 13-19% of all primary intracranial neoplasm[1].

Spinal canal meningiomas account for about 25% of all spinal cord tumors[2].

With recent extensive use of neuroimaging, the incidence of meningiomas has increased and is estimated to occur in up to 1% of the population[3].

Multiple cranial meningiomas are more common than multiple spinal meningiomas.[4].

Multiple meningiomas occurring in different neuraxial compartments are distinctly rare,

Multiple meningiomas (MM), defined as the presence of ≥ 2 spatially separated synchronous or metachronous lesions, occur in <10% of patients with diagnoses of meningioma[5, 6]

Meningiomas are typically slow growing, and the vast majority remain asymptomatic, thus, 50% are diagnosed at autopsy.[7-9]

A) Importance of Study

With the rising incidence of meningiomas and the ubiquity of cross-sectional neuroimaging, more patients with multiple meningiomas (MM) are being identified. These patients have a higher disease burden, with limited possibility of cure, requiring multiple interventions understanding of MM epidemiology, etiology, management and outcomes of MM. It is well-established that MM represent a heterogeneous group of conditions with different etiologies and constitutes a distinct clinical entity posing special management challenges.

They can be sporadic, hereditary, or radiation-induced. Familial cases of MM can be attributed to numerous inherited cancer syndromes with germline mutations in genes thought to be related to meningioma initiation and progression (shown in parentheses), including NF2 (NF2), Cowden syndrome (PTEN), Gorlin syndrome (PTCH1, SUFU), Werner Syndrome (LMNA), Li Fraumeni syndrome (TP53/CHEK2), von Hippel–Lindau syndrome (VHL), and Multiple Endocrine Neoplasia type I (MEN1).[10] Radiation-induced meningiomas (RIM) are the most common radiation-induced neoplasm[11–13] and in the absence of a familial syndrome the presence of multiple lesions is suggestive of RIM.[14] The pathophysiology of MM is not clear, but there are 2 dominant theories. The first is that these tumors occur independently, are isolated sporadic neoplasms, driven by different key genetic events, arising in different locations. This hypothesis is supported by histologic and cytogenetic differences observed between different meningiomas in a single patient.[15,16,17,18–23]

Conversely, the monoclonal hypothesis proposes that MM originates from a single neoplastic transformed clone that subsequently spreads along the meninges to form multiple monoclonal meningiomas. This hypothesis is supported by the fact that most MM present the same histological features and molecular genetic analyses, including detection of a common NF2 gene mutation that strongly favors a monoclonal origin.[16,20,23–28] There is evidence that both theories might be true and applicable to different patients.[29] MM should be regarded as a chronic disease, and in many cases, the management goal is disease control as a cure is seldom feasible. Multiple interventions and lifelong surveillance are sometimes necessary. We aim to review the MM literature and create a comprehensive overview, including an evidence-based management paradigm.

MM may be associated with an NF2 alteration. Non-NF2-associated MM may occur as sporadic or familial cases[6] or radiation-induced or as the result of subarachnoid seeding spread of a single sporadic tumor.[30]

although meningiomas are common neoplasms of the nervous system, the occurrence of Multiple meningiomas occurring in different neuraxial compartments are distinctly rare, with only 19 well-documented cases reported in world literature,[31] of these, only six cases had more than one spinal tumor. Occurrence of such multiple meningiomas of spinal and cranial distribution in absence of neurofibromatosis is quite rare.

II) Case Report :

In 2023, a 28-year-old girl presented to neurosurgery outpatient clinic of National Cancer Institute, Misurata - Libya complaining of headach,increased attacks of convulsions (she has been on anticonvulsant since childhood on valproic acid), unsteadness and the need for assistance while walking.she had history of bowel and bladder dysfunction and right eye visual loss.she was conscious and oriented **glasgow coma scale**. (GCS) 15/15 ,On examination, she had spastic quadriparesis wih grade 3 power in the right upper and lower limbs and grade 4 power in left upper and lower limbs , increased tone, exaggerated reflexes at all limbs , Babinski's was positive bilateraly and Hoffman's sign was positive There were no multiple hypopigmented macules, neurofibromas, or other stigmata of neurofibromatosis.

Her Laboratory investigations were normal except for elevated liver function tests , ALT 553U/L and AST 295U/L other investigations were normal.

Magnetic resonance imaging (MRI) of the brain revealed[figure 1]7×5cm mass with multiple cystic changes and surrounding vasogenic edema seen in left pareito-temporal region with mild homogenous enhancement ,the mass is creating mass effect on the brainstem and ventricular system causing dilatation of contralateral ventricle and midline shifting . another extra-medullary heterogeneous lesion causing sever compression at cervico-medullary junction.

And magnetic resonance imaging of whole spine was revealed three well defined itra-dural homogenously enhancing mass lesions opposite to L2/L3 vertebrae and L3L4 disc space and L5/S1/S2 vertebrae,the largest measures 2.3×2.6×5.0cm with posterior scalloping of S1vertebrae.

The patient underwent left side frontotemporal craniotomy and complete removal of the lesion.

post operative patient improved ,the patient power is improved and she was able to walk without support after aweek,Histopathology revealed psammomatous meningioma.

then after tow weeks from cranial operation she underwent suboccipital craniotomy with posterior arch removal of the atlas and laminectomy of the axis and complete removal of craniocervical meningioma was achieved.histhopathology examination revealed meningotelial type.

post operative the patient doing well.MRI of the brain and spine showed complete removal of tumors and decompression of the cord.

Despite our detailed counseling, the patient and their relatives steadfastly refused surgery for lumbar and lumbo-sacral lesions,later on they accept the surgery after 5 months of cranial sugery,she underwent multiple level laminectomy and complete removal of all lesions from lumbar and lumbosacral region in two sessions surgery one week apart,, histopathology examination revealed psammomatous meningiomas.

patients discharged on day 4 post surgery in good general condition on antiepileptics and advised for physiotherapy and follow up in our out patient clinic.

Up to now October 2024 Our pateint are doing well walking alone without assistance, incomplete sphincter control.

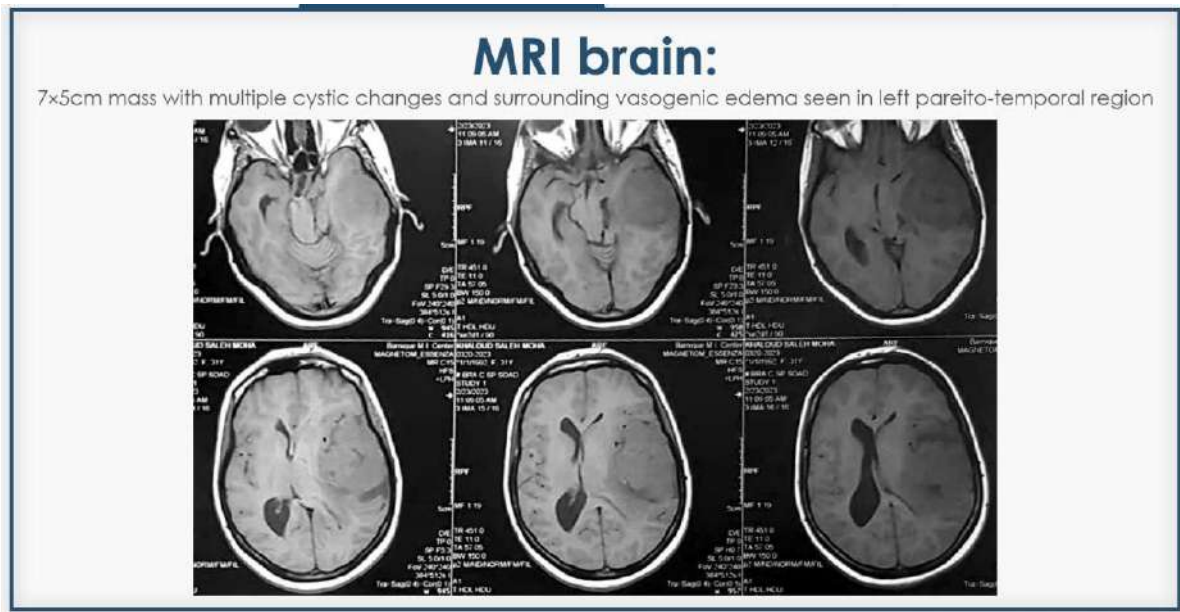


figure 1 preoperative MRI.

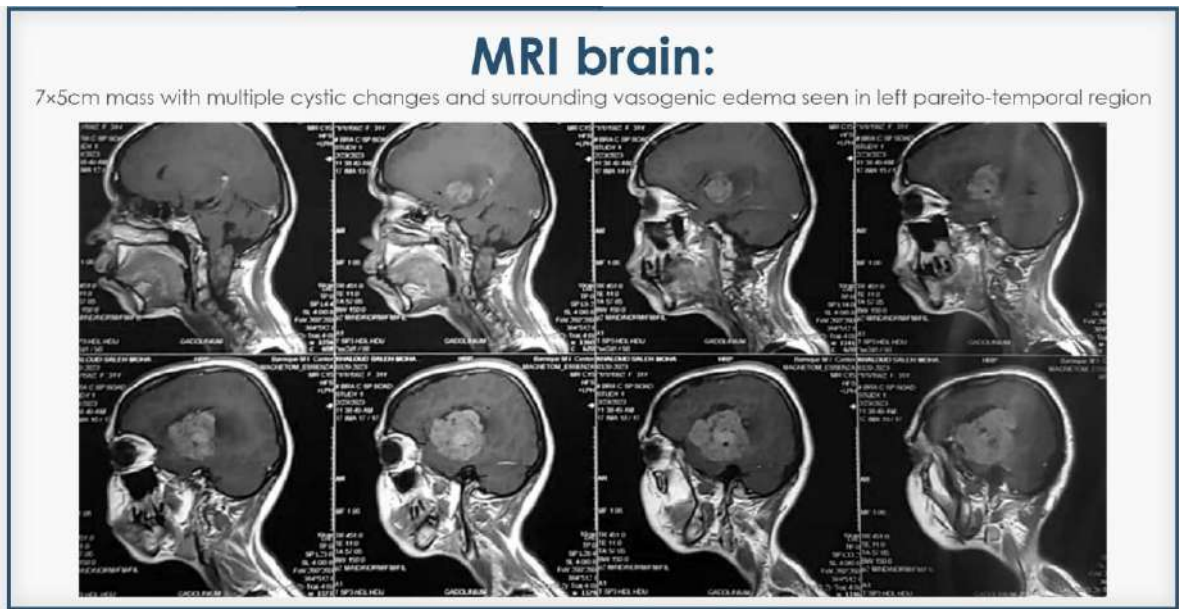


figure 2 preoperative MR



Figure 3

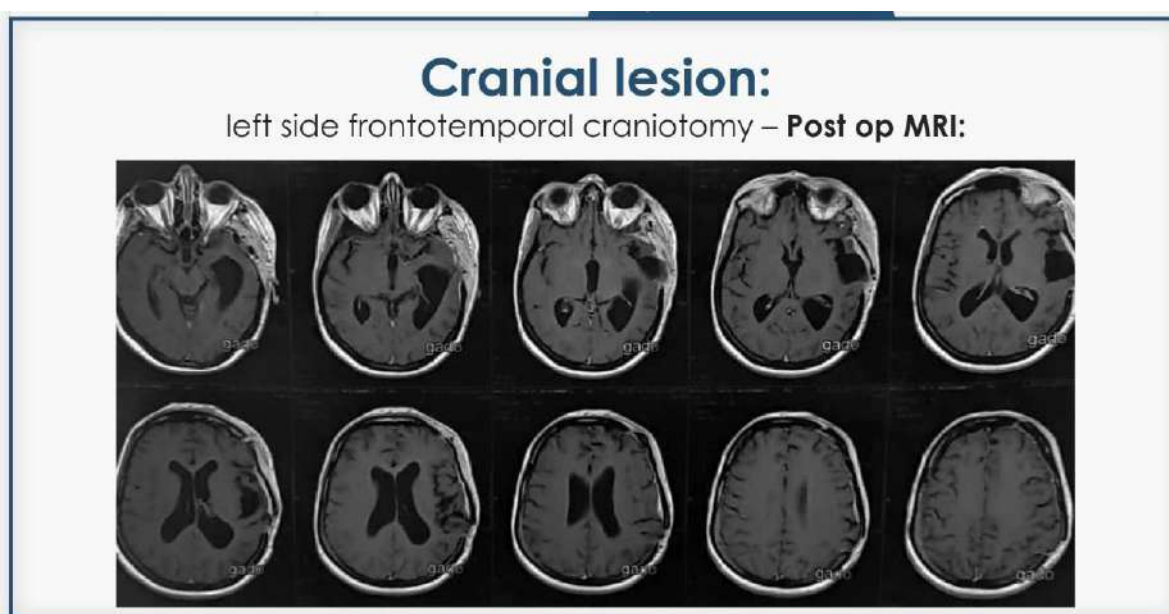


Figure 4 postoperative MRI Brain with Gad



Figure 5 preoperative craniocervical MRI.....

Figure 6 postoperative craniocervical MRI.....

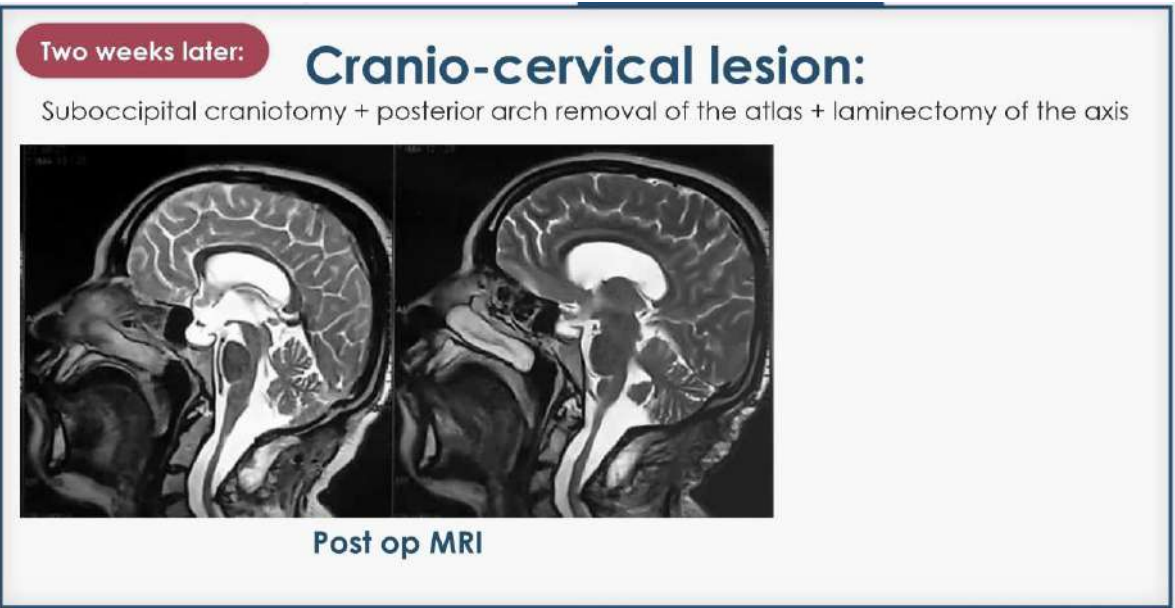
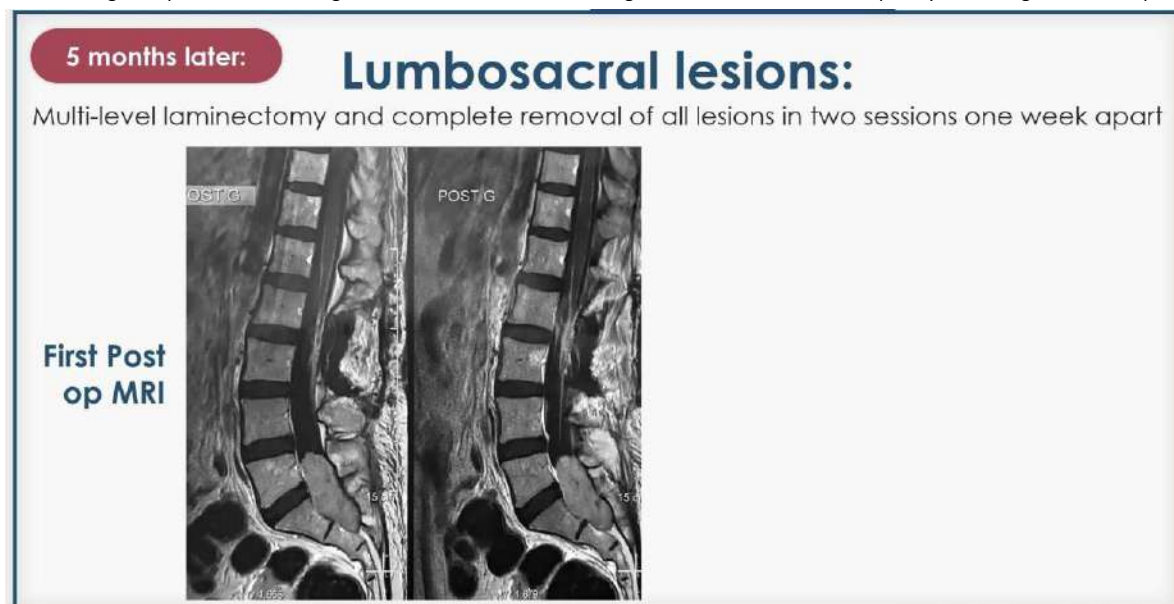


Figure 7 preoperative Lumbosacral MRI....



Figure 8 post lumbar meningioma resection ,the sacral meningioma also was resected completely undersurgical microscope.



III) Discussion

Multiple meningiomas are defined as at least two spatially separated meningiomas occurring simultaneously or more than two meningiomas arising sequentially from two clearly distinct regions[32]

Multiple spinal meningiomas are rarer than multiple cranial meningiomas. Multiple meningiomas occurring in different neuraxial compartments are rarer, with only six cases was reported having both multiple spinal and multiple cranial meningiomas[33].

the incidence of MM has been reported to range between 1% and 3%, based on 8 classical series with a total of 1769 cases.[34,16] After the introduction of computed tomography (CT), the number of imaging verified, but asymptomatic, cases increased. In the early CT era, Lusins et al (1981) reported a MM incidence of 8.9% in a series of 168 cases of meningioma studied by CT, and during the same year, Nahser et al (1981) reported an incidence of 5.9% in a cohort of 84 patients.[34,16] In the absence of larger studies, MM were most often reported in 1%–10% of patients.[35,29,36,15] However, in a recent multicenter study of 838 patients with meningioma, 11.46% had more than 1 lesion,38 and in the previously mentioned SEER study of 99 918 patients with meningiomas, 81 253 (82%) had SM, whereas 18 665 (19%) patients had 2 or more lesions.[36] Thus, the true incidence is likely much higher than previously thought.[11] However, this is not the first report of a higher incidence; Wood et al (1957) found an incidence of MM of 16% in their review of 100 intracranial meningiomas found incidentally at necropsy.[39]

The number of meningiomas per patient varies in the literature. with a 2019 systematic review reporting 3.1 per patient.[29,15,37] Those with RIM tend to have significantly more tumors than sporadic multiple meningiomas patients.[29,38]. no study shows a difference in WHO grades between MM and SM.[37,39,40] The Central Brain Tumor Registry of the United States (CBTRUS) 2013–2017 data reports that among 81.3% of reported meningiomas with grading, 80.3% of newly diagnosed meningiomas are WHO grade 1, 17.9% WHO grade 2, and 1.6% WHO grade 3.[41]

Several mechanisms could account for multiple meningiomas. Such meningiomas could arise from a single primary tumor via subarachnoidal spread of a benign or malignant nature. Alternatively, they could be atypical forms of neurofibromatosis type 2 or tumors with a multifocal origin as evidenced by the histological and cytogenetic differences between multiple tumors from the same patient [37].

Of the intracranial meningiomas, one percent are multiple, usually in neurofibromatosis. The most common locations are Falx and parasagittal, convexity, sphenoid, and olfactory groove[34]. In the spinal canal, the preferred location for meningiomas is in the dorsal region followed by the cervical region, and finally, the lumbar region[16].

The radiological features are similar to isolated meningiomas. Well described features include well defined extra axial lesions that enhance uniformly on contrast administration, enhancement of the dural attachment and little or no perilesional edema.

Operative management of multiple meningiomas occupying both cranial and spinal compartments poses special problems. A decision is made regarding which lesion, or lesions should be removed initially keeping in mind that histologically, each of these tumors may be a different variant of meningioma. Small or asymptomatic tumors may be followed-up with serial imaging.

The majority of multiple meningiomas (80-90%) are benign and classified as World Health Organization (WHO) grade 1.[42] Regarding the cases of spinal canal multiple meningiomas, the psammomatous type predominate. Usually, multiple meningiomas are circumscribed and show slow growth and have a good post surgical prognosis. On the other hand, the

meningiomas that occur in younger patients might have an aggressive behavior and an unfavorable prognosis from surgery. Regardless of the eventual management decision, such patients must be kept under close follow-up.

Table shows Number in superscript in author column indicate the relevant reference number, number in parentheses in cranial/spinal column indicate number of tumors excised

Year reported	Author	Age/sex	Cranial location	Spinal location	Histopathology
1973	Sedzimir et al.	13/m	Tuberculum sellae	Cervicall Dorsall	Cranial-not resected Spinal-psammomatous
1992	Roda et et al	50/m	Suprasellari Falcinet	Dorsal	Cranial and spinal-meningotheliomatous
2003	Bhatoe HS	35/f	Multiple supra and infratentorial	Dorsal	Cranial-transitional, meningothelial Spinal-fibroblastic, atypical
2011	Stachowicz-stencelT et al.	13/f	Multiple supra and infratentorial	Lumbosacral multiple	Cranial-psammomatous Spinal meningioma
2011	Shukla et al.	13/f	Left frontoparietal	Dorsal Lumbar	Spinal-predominantly meningotheliomatous
2011	Present case	62/f	Multiple bilateral supratentorial	Dorsal Lumbar	Spinal-psammomatous

In Our present case in 2020 28 years old girl, cranial supratentorial was psammomatous meningioma and infratentorial was meningothelial type, while two spinal meningiomas were psammomatous type.

A. Genetics of Multiple Meningiomas

The genetic features of sporadic meningiomas have been reviewed extensively elsewhere and include frequent initiating mutations, deletions, or epigenetic silencing of NF2 and 4.1B (Table 2).[10,43] It is difficult to delineate meningioma initiating genes from those purported to increase the aggressiveness of tumor growth, so-called “progressor” genes, though numerous genomic alterations common among higher grade meningiomas signal the possible loci of such progressor genes. Losses on 1p, 10q, 14q, 6q, and 18q, and gains on 1q, 9q, 12q, 15q, 17q, and 20q are associated with higher grade meningiomas with multiple genes implicated at each locus (table 2).[10]

Multiple meningiomas may be both sporadic and familial, with these groups likely representing unique disease processes. Familial MM can be attributed to numerous inherited cancer syndromes, with germline mutations in genes thought to be related to meningioma initiation and progression (shown in parentheses), including NF2 (NF2), Cowden syndrome (PTEN), Gorlin syndrome (PTCH1, SUFU), Werner Syndrome (LMNA), Li Fraumeni syndrome (TP53/CHEK2), von Hippel Lindau syndrome (VHL), and Multiple Endocrine Neoplasia type I (MEN1).[10] In contrast, present evidence suggests sporadic MM arises from new somatic mutations, although germline mosaicism is difficult to exclude.[19,26,27,28,44,45]

Meningiomas are the most common form of radiation-induced neoplasm, are frequently multiple,[13,54] and the first patient with a RIM was reported in 1953.[55] It has been reported that patients who received 1–2 Gy of radiation in childhood have a 9.5-fold increased risk of developing a meningioma,[56,57] To define a meningioma as radiation-induced, it must fulfill the following criteria: (i) the tumor must arise in the irradiated field; (ii) the histological features must differ from those of any previous neoplasm in the region; (iii) the tumor must occur after an interval sufficient to demonstrate that the neoplasm did not exist prior to irradiation (usually years); (iv) this type of tumor must occur frequently enough after irradiation to suggest a causal relationship; (v) this type of tumor must have a significantly higher incidence in irradiated patients than in an adequate control group; (vi) there must be no family history of a

phacomatosis; and (vii) the tumor must not be recurrent or metastatic.[11,13,54,58] RIM are often divided into 3 groups based on the radiation exposure:

(i) low dose (<10 Gy); (ii) moderate dose (10–20 Gy); (iii) high dose (>20 Gy), RIM are characterized by lower patient age at diagnosis, an increased rate of multiplicity and higher risks of recurrence after treatment and atypical or anaplastic histology, when compared to nonradiation-induced SM.[12,13,54] Furthermore, Gillespie et al (2021) reported that RIM demonstrates high absolute and relative growth rates, indicating an increased risk for clinical and radiological progression.[60]

Although higher doses of radiation of 22–87 Gy have been associated with RIM with latencies of 19.5 years, even lower doses of 1–2 Gy, such as used to treat tinea capitis and for dental X-rays can be associated with a 9.5-fold increased risk of RIM with latencies of 12–49 years.[12]

B. Neurofibromatosis Type 2 and Multiple Meningiomas

NF2 is a rare autosomal dominant familial disorder associated with MM,[46] and due to germline loss of the NF2 tumor suppressor gene. NF2 increases the risk of meningiomas, with approximately 50% of NF2 patients bearing MM.[10]The management of patients with NF2 is complex and out of scope. However, one of the most important differences in the management of sporadic and familial MM is the need for genetic counseling, which is relevant in NF2.

C. Treatment

The therapeutic modalities available for MM include surgery, stereotactic radiosurgery and fractionated external beam radiotherapy. However, many tumors do not require treatment, with studies reporting between 32% and 44% of tumors and 64% of patients requiring active treatment. [29,15]

Surgery	SRS/RT
Surgically accessible	Surgically unfavorable location
Young age	High age
Good clinical condition	Poor clinical condition
Large tumor, peritumoral oedema	Multiple tumors requiring treatment

Figure 2. Factors affecting choice of treatment modality. RT, fractionated radiotherapy; SRS, stereotactic radiosurgery.

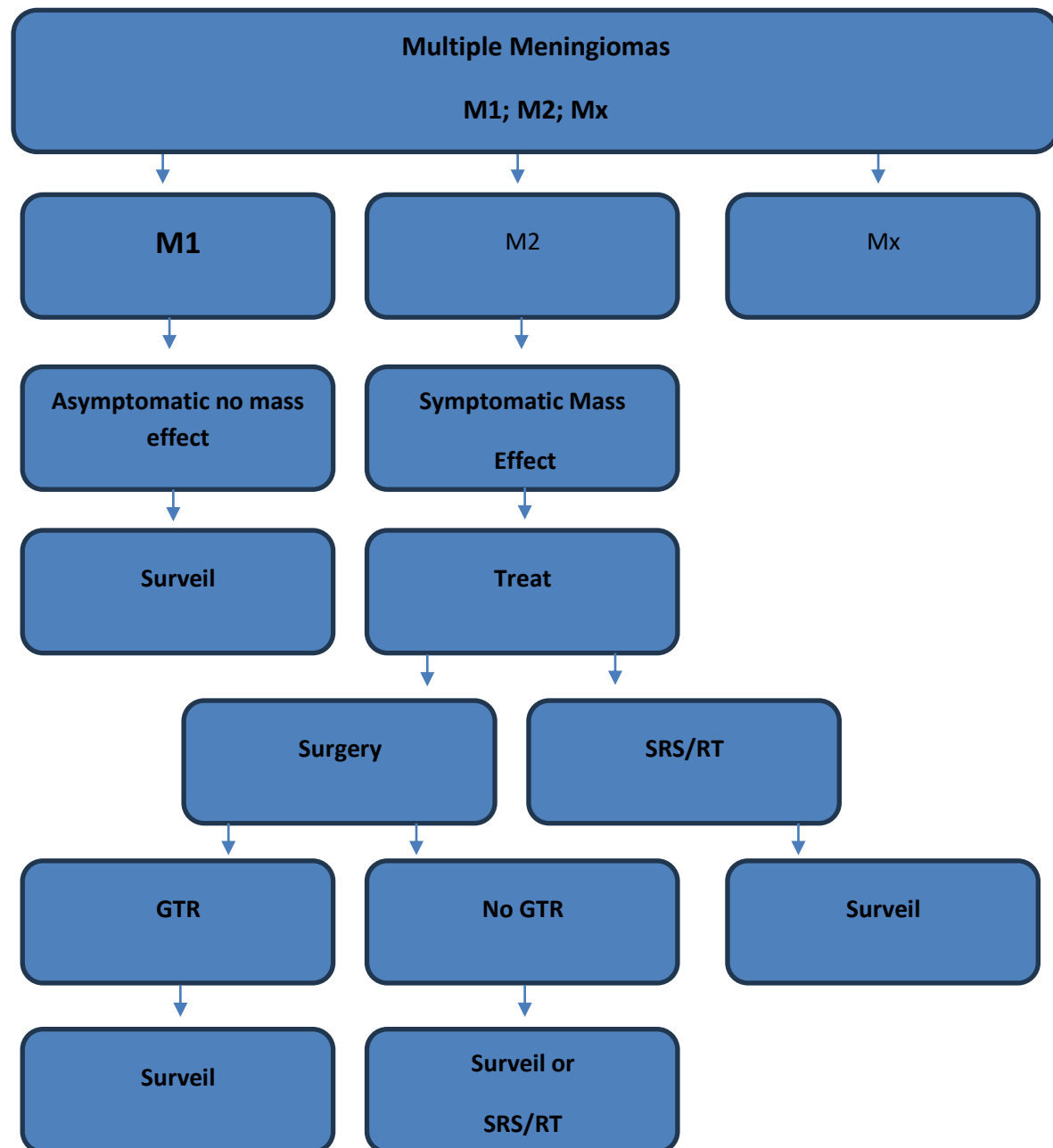


Figure 3. Management recommendations for multiple meningiomas. Surveillance: annual MRI scans for 5 years, thereafter interval can be doubled. GTR, gross total resection; RT, fractionated radiotherapy; SRS, stereotactic radiosurgery.

The overall goal of treatment is tumor control, as surgical removal of all tumors is seldom possible, and it is necessary to have the perspective of chronic disease.

Before the surgery, it is vital to discuss with the patient the surgical goals, as well as the surgical risks. In patients with MM, it is important to clearly explain the goals of treatment, particularly where not all tumors can be removed, and disease control is the aim. The patient should be prepared for multiple treatments and lifelong surveillance.

Multiplicity brings challenges, including localizing the symptomatic lesion or lesions, choosing the most suitable treatment modality, avoiding treatment risks, and predicting the behavior of individual untreated tumors. It is crucial to consider that a patient with MM might need repeated treatments over their lifetime (Figure 1). An important consideration is the likely growth rate of any tumor. The natural history and growth rate of MM were investigated by Wong et al 2013. They analyzed 55 tumors in 12 patients with an average follow-up of 61 months (range 24–101 months).[35] They reported an average growth rate of 0.46 cm³/year (range 0.57–2.94

cm³/year), which is similar to that reported for incidental found SM.[35,61] The relationship between tumor multiplicity and growth rates was also analyzed, but no correlation between the number of meningiomas per patient and growth rate was observed.[35]

The European Association of Neuro-Oncology (EANO) has updated its meningioma treatment guideline in 2021.[62] Specific recommendations regarding MM are not discussed in these guidelines but are warranted. To the best of our knowledge, this is the first attempt to present management guidelines for MM (Figures 2 and 3).

D. Prognosis

the 2020 SEER study is the first survival analysis of a large cohort of patients with MM and showed that the number of lesions, age at diagnosis, and sex influence OS in MM patients.[37] The median survival was 180 months for patients with SM and 94 months for patients with MM. The analysis showed a progressive decrease in OS for every additional lesion. Patients treated with radiation had a longer OS compared to patients who didn't receive radiation. Female patients had a longer OS. Analysis of the male cohort showed that MM reduced OS starting at age [40], with shorter OS for every added decade. A similar analysis of the female cohort showed that MM reduced OS starting at age [52], with shorter OS for every added decade. As these results represent a single study, the applicability is limited and should be applied with caution.[37]

IV. CONCLUSION :

Although meningiomas are one of the most common tumors encountered in neurological practice, multiple meningiomas still remain a rare event. Published data on MM is rare and mostly limited to case reports and small case series. The presented epidemiological data indicate that the true MM incidence is much higher than previously thought

Multiple meningiomas should be put in the mind of the surgeon to not be missed. Features that suggest the presence of multiple meningiomas include early age of onset, female sex or presence of neurofibromatosis. When silent meningioma is discovered not causing the symptoms of the patient, a careful decision is made taking into consideration the presenting features, age, sex, tumor biology, associated diseases and patients expectations from surgery. Regardless of the eventual management decision, such patients must be kept under close follow-up.

The management of patients with MM is complex, including multiple treatments, sometimes with different modalities, and lifelong surveillance. We advocate that MM should be regarded and managed as a chronic disease.

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