Clinics of Oncology

Review Article ISSN: 2640-1037 | Volume 7

Advancements in the Management of Meningioma: A Comprehensive Review of Current Treatment Modalities

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Received: 16 May 2024
Accepted: 20 June 2024
Published: 25 June 2024
J Short Name: COO

Citation:

Dimitrios P, Advancements in the Management of Meningioma: A Comprehensive Review of Current Treatment Modalities. Clin Onco. 2024; 7(11): 1-8

1. Abstract

Meningiomas, which are derived from the meninges, are a significant category of brain tumors that present with a wide range of symptoms, from mild headaches to severe neurological deficits. Recent epidemiological studies have highlighted their prevalence, particularly among women aged 20-60 years. Diagnostic advancements, notably in MRI and CT imaging, have enhanced the precision of meningioma characterization and localization, facilitating improved treatment planning. The management of meningiomas has evolved to include surgical resection, stereotactic radiosurgery, and preoperative embolization. Surgical techniques remain central, especially for resectable tumors, while stereotactic radiosurgery and fractionated radiotherapy have become pivotal for managing small or inoperable tumors. Despite these advances, challenges remain, particularly in managing incidental findings, assessing the long-term efficacy of treatments, and addressing healthcare disparities. This review explores the classification, prognostic factors, and treatment modalities for meningiomas, emphasizing the integration of surgical, radiotherapeutic, and emerging treatment approaches to optimize patient outcomes.

2. Introduction

Meningiomas, which originate from the meninges, particularly the arachnoid layer, represent a significant subset of brain tumors. They present a spectrum of symptoms, ranging from mild headaches and vertigo to severe neurological deficits, such as seizures, visual disturbances, or motor impairments [1]. Despite their predominantly benign nature, meningiomas vary in size and anatomical location, posing challenges in their management [2].

Epidemiological studies continue to shed light on the prevalence and distribution of meningiomas. Recent data suggest that these tumors account for approximately 13– 26% of primary intracranial tumors in adults and 0.4–4.6% in children, with a higher incidence observed in women aged 20–60 years. However, geographical and temporal variations in incidence rates underscore the need for a nuanced understanding of meningioma epidemiology to tailor treatment approaches effectively [3,4]. Advances in diagnostic imaging, including magnetic resonance imaging (MRI) and computed tomography (CT), have revolutionized meningioma diagnosis and characterization. These imaging modalities allow for precise localization, assessment of tumor vascularity, and identification of anatomical relationships, guiding treatment planning and decision-making [5]. The therapeutic landscape for meningiomas has evolved significantly in recent years, driven by innovations in surgical techniques, radiation therapy, and minimally invasive procedures [6]. Although surgery remains the cornerstone of treatment for resectable tumors, stereotactic radiosurgery has emerged as a viable option for small, deep-seated lesions, particularly in elderly or medically unfit patients. Additionally, preoperative embolization has gained prominence as a means to reduce intraoperative bleeding and optimize surgical outcomes [7]. However, challenges persist in meningioma management, including the optimal management of incidental findings, the impact of age and comorbidities on treatment decisions, and the long-term efficacy and safety of emerging therapies. Moreover, disparities in access to specialized care and treatment outcomes underscore the importance of addressing broader healthcare system issues to ensure equitable

access to optimal care for all patients.

3. Classification and Prognosis

3.1. Meningioma Grading

The categorization of meningiomas has evolved significantly, mirroring advancements in our comprehension of tumor biology. Presently, the histological grading of meningiomas adheres to the latest WHO classification, as shown in Table 1 [8]. The majority, approximately 90%, are classified as WHO grade I, which is indicative of their benign nature. Nonetheless, a subset of meningiomas classified as atypical (WHO grade II), constituting 5–7% of cases, and anaplastic variants (WHO grade III), accounting for 1–3%, exhibit distinct histological features that distinguish them [9,10].

Table 1: WHO grading criteria and frequency of meningiomas

WHO grade	Description	Frequency
Grade I	Low mitotic rate, < 4 per 10 HPFs	80–85%
	Absence of brain invasion	
	Nine histologic subtypes	
Grade II atypical	Mitotic rate 4–19 per 10 HPFs or Brain invasion or more than three or five histologies:	15-20%
	• Spontaneous or geographic necrosis	
	• Patternless sheet-like growth	
	• Prominent nucleoli	
	• High cellularity	
	• Small cells with high n:c ratio	
Grade III anaplastic (malignant)	Mitotic rate > 20 per 10 HPFs or papillary or rhabdoid	1–2%

Footnote: HPFs = High-power field

3.2. WHO Grade I

Meningiomas exhibit a diverse histological spectrum, with approximately 80% of cases characterized as slow-growing tumors. Among the most frequently encountered histological variants are the meningothelial, fibrous, and transitional subtypes [11]. Histologically, WHO grade I meningiomas are typified by neoplastic cells forming conjunctivae, encased within delicate collagenous septa. This category manifests various architectural patterns, with tumor cells expressing epithelial membrane antigen[8]. Despite these similarities, fibroblastic and transitional meningiomas often harbor mutations in the NF2 gene in a substantial portion of patients, estimated at up to 80%. However, the detection rate of NF2 mutations in meningothelial meningioma patients is notably lower, encompassing only approximately 25% of patients. Secretory meningiomas, histologically characterized by glandular metaplasia and pseudopsammoma bodies, exhibit rare occurrences of NF2 mutations[12].

3.3. WHO Grade II

Atypical meningioma and other variants classified as WHO grade II represent a notable subset, comprising 15–20% of meningioma cases. The recurrence rate for atypical meningiomas is estimated to be approximately 40%, a figure that increases with prolonged follow-up periods. Consequently, close postoperative monitoring is imperative for patients diagnosed with atypical meningiomas [13]. Histologically, increased mitotic activity, defined as four or more mitoses per ten high-power fields, serves as a reliable indicator of recurrence risk. However, in the absence of elevated mitotic activity, other histological features are also indicative of recurrence risk and thus contribute to classification. Numerous studies have identified prominent nucleoli, sheet-like growth, cellular atypia, necrosis, and/or nuclear pleomorphism as factors associated with an increased risk of recurrence in patients with atypical meningiomas [10,14,15]. The presence of three out of the five aforementioned criteria may warrant the diagnosis of atypical meningioma: increased cellularity, high nuclear to cytoplasmic ratio (small cells), prominent nucleoli, uninterrupted or sheet-like growth pattern, and foci of spontaneous necrosis (not induced by embolism). Distinct histological subtypes within the WHO Grade II category include chordoid meningiomas, characterized by areas histologically reminiscent of chordomas, featuring cords of small epithelioid neoplastic cells with eosinophilic cytoplasm or cytoplasmic vacuoles embedded in a basophilic, mucin-rich matrix. Furthermore, clear-cell meningiomas exhibit a predilection for the spinal cord and posterior cranial fossa, whereas choroidal meningiomas are predominantly located in the supratentorial region [16]. Compared with Grade I tumors, WHO Grade II tumors exhibit a higher recurrence rate, ranging from 29% to 40%, which typically ranges from 7% to 20%. This discrepancy in recurrence rates is particularly pronounced following subtotal resection procedures [9].

3.4. WHO Grade III

Anaplastic meningiomas, constituting 1–3% of all cases, often exhibit irregular shapes and demonstrate a greater relative cerebral blood volume than WHO grade I and II tumors [17]. These aggressive tumors manifest clinical features akin to those of other malignancies, penetrating extensively into adjacent tissues and forming

metastatic solid masses. Following surgical resection, anaplastic meningiomas are associated with recurrence rates ranging from approximately 50% to 80%, underscoring their formidable nature. Certain meningioma subtypes exhibit malignant behavior and are accordingly classified as Grade III tumors. Papillary meningiomas, which typically affect pediatric patients, demonstrate brain infiltration and the involvement of other local structures in approximately 75% of patients, with 55% of patients experiencing recurrence and 20% experiencing metastasis [18,19]. Histologically, papillary meningiomas exhibit incoherent growth, resulting in a perivascular pseudopapillary pattern, often accompanied by pseudo-rosettes reminiscent of structures found in ependymomas.

Another highly aggressive histological variant of meningioma is rhabdoid meningioma, which is characterized by rod-shaped cells with abundant eosinophilic cytoplasm, eccentrically placed nuclei, and nuclei enclosed within whorled bundles of intermediate filaments. Both papillary and rhabdoid features typically emerge during recurrence and gradually increase in prominence over time [20].

3.5. Clinical Prognostic Factors

Despite being predominantly benign tumors, meningiomas are associated with shorter survival compared to the general population, with survival rates significantly declining according to WHO grade. The 10-year survival rates for patients with WHO grade I, II, and III meningiomas are reported to be 97%, 90%, and 30%, respectively, while the median survival time for patients with malignant meningiomas is approximately 4.1 years [21,22]. Prognostic indicators span a spectrum of clinical and pathological variables, including age, sex (with a notable adverse prognostic implication for males), Karnofsky performance status, tumor grade, mitotic rate, degree of surgical excision, and critical anatomical structures such as the optic nerve [23]. Although somatic metastases are rare, isolated cases have been reported for recurrent Grade II and III meningiomas, particularly in parasagittal locations conducive to venous diffusion through the superior sagittal sinus. Emerging evidence suggests that genetic and epigenetic subtypes may offer more accurate prognostication, especially in complex cases. Notably, ionizing radiation exposure to the skull, particularly therapeutic radiation for head and neck neoplastic conditions, is a well-established risk factor for meningioma development [24]. Hormonal influences, such as the correlation with postpubertal women, fluctuations in the incidence ratio during reproductive years, and the expression of hormone receptors (e.g., progesterone receptors) in benign meningiomas, underscore the intricate interplay between hormones and meningioma pathogenesis. Conversely, factors such as head trauma, smoking, and cellular phone usage do not appear to confer an increased risk for meningioma development.

3.6. Management

The management of meningiomas involves careful consideration of various factors, including symptomatology, patient demographics, and tumor characteristics [25]. A key aspect of treatment is achieving maximal safe resection, which entails complete tumor removal while preserving neurological function. The Simpson grading system, introduced in 1957 (Table 2), provides a framework for assessing the extent of resection and predicting recurrence rates [26]. Patients who undergo Simpson grade 1 resection, involving complete tumor removal with resection of the involved dura and adjacent bone, typically have a lower 10-year recurrence rate of approximately 9%. In contrast, patients who underwent Simpson grade 3 resection, indicating incomplete excision with residual tumor remnants, had a higher 10-year recurrence rate of approximately 29%. Beyond the extent of resection, survival outcomes are influenced by factors such as histological grade and subtype, patient age, and tumor location [27]. Moreover, data suggest higher 5-year recurrence rates following gross total resection in Grade I, II, and III meningiomas, reported as 7–23%, 50–55%, and 72–78%, respectively. Subtotal resection substantially increases the likelihood of disease progression. Notably, analysis revealed enhanced recurrence-free survival at 5 years (ranging from 37% to 62%) following Simpson grade 4 resection in Grade I tumors compared to Simpson grade 1–3 resection [28–30]. This finding underscores the importance of maximal safe resection for optimizing therapeutic outcomes and reducing disease recurrence, particularly in Grade I meningiomas.

Table 2: The Simpson grading system.x

Simpson's grade	Completeness of resection	10-year recurrence (%)
Grade I	Macroscopic complete removal including resection of underlying bone, associated dura, and venous situs, where involved.	9
Grade II	Macroscopic complte removal and coagulation of dural attachment.	19
Grade III	Macroscopic complete removal of intradural tumor w/o resection or coagulation of dura/dural attachments.	29
Grade IV	Partial removal or subtotal resection leaving macroscopic intradural tumor.	40
Grade V	Simple decompression, with or without biopsy.	100

3.7. Surgery

Surgery is the primary treatment for most symptomatic and enlarging meningiomas, aiming not only to remove the tumor and alleviate mass effects but also to improve neurological function and control seizures swiftly [31,32]. The gold standard is complete tumor resection while minimizing neurological morbidity for long-term control or cure. However, factors such as tumor location, the involvement of critical structures, and patient health status can influence surgical decisions and outcomes [33]. The surgical management of meningiomas hinges on a meticulous assessment of neuroanatomical location and individual tumor characteristics. While convexity meningiomas offer relatively straightforward access for resection, they represent a minority of cases. Conversely, parasagittal tumors present heightened challenges due to their intricate relationship with the sagittal sinus, entailing risks of complications such as air embolism and sinus thrombosis [34,35]. Tumours located in complex regions, such as the sphenoid wing, olfactory groove, tuberculum sella, cerebellopontine angle, and petroclival area, necessitate meticulous surgical planning to manipulate critical neurovascular structures while minimizing brain injury.

Advancements in surgical techniques, particularly endoscopic approaches and minimally invasive keyhole surgeries, have significantly broadened the surgical armamentarium for meningioma resection. Endoscopic technologies, with their enhanced visualization and manoeuvrability through narrow corridors, have facilitated the removal of select meningiomas, particularly those located at midline anatomic sites [36,37] However, challenges persist for tumors extending laterally or involving critical structures such as the carotid artery or cranial nerves, underscoring the importance of thoughtful surgical approach selection based on individual patient characteristics and tumor features [38]. Central to meningioma surgery is the principle of maximal safe resection, emphasizing meticulous attention to detail throughout the surgical process. Techniques such as embolization of feeding arteries, central tumor debulking, and preservation of the arachnoid plane play pivotal roles in safeguarding neurovascular structures while optimizing resection outcomes [39]. Despite the challenges posed by factors such as venous sinus involvement and skull base invasion, the overarching goal remains complete tumor removal to mitigate the risk of recurrence and optimize long-term outcomes[40].

3.8. Radiotherapy

For many years, radiation therapy (RT) has been a cornerstone in the management of tumors that are not amenable to surgical resection. It is frequently employed as an adjuvant therapy following surgical resection and for treating recurrent meningiomas.

3.9. Radiation Therapy for WHO Grade I Meningiomas After Subtotal Resection (STR)

Gross total resection (GTR) remains the ideal treatment for WHO Grade I meningioma. However, GTR is often unachievable in approximately 30% of patients due to the location of the tumor or its proximity to vital neurological or vascular structures [41,42]. This difficulty is particularly true for meningiomas involving the sphenoid ridge, posterior fossa, parasellar area, and optic nerve sheath. Following subtotal resection (STR), the 5-year local progression rate ranges from 37% to 62%, with the 10-year local progression rate potentially reaching 52% to 100% [43,44]. To improve outcomes after STR, fractionated stereotactic radiotherapy (FSRT) or stereotactic radiosurgery (SRS) is employed and has shown excellent local control rates. Preliminary data from a series of more than 1,100 patients indicate local control rates exceeding 92–100% at five years and 88–95% at ten years, although longer follow-up is necessary to confirm these findings [45,46]. Patients typically receive FSRT in fractions of 1.8–2 Gy to a total dose of 50.4–54 Gy, or SRS in a single fraction of 13–16 Gy. Observational studies have consistently demonstrated the benefit of fractionated external beam radiation therapy (EBRT) in the adjuvant setting following STR for benign meningioma [47,48]. The progression-free survival rate after STR without adjuvant treatment ranges from 18% to 52%. In contrast, adjuvant radiation therapy significantly improves local control, with 68–100% of patients remaining free from progression during extended follow-up [46,49].

3.10. Radiation Therapy for WHO Grade II and III Meningiomas

Adjuvant radiation therapy plays a critical role in managing WHO Grade II (atypical) and Grade III (anaplastic/malignant) meningiomas, aiming to prevent progression to higher-grade malignancy and reduce the risk of recurrence. These higher-grade meningiomas have a significantly elevated risk of recurrence even after gross complete resection [8,50]. For Grade II meningiomas, recurrence rates after Simpson Grade 1 or Grade 1–2 surgical resection are alarmingly high, with 5-year recurrence rates of 50% and 71%, respectively. For patients with Grade III tumors, the situation is even more concerning, with 5-year progression-free survival rates of 0% following subtotal resection and 28% following gross total resection without RT [51,52]. Advances in radiotherapy techniques, including intensity-modulated radiation therapy (IMRT) and proton beam therapy, have further refined the precision and effectiveness of treatment, minimizing damage to surrounding healthy tissue [53,54]. These innovations have expanded the therapeutic arsenal, providing options that can be tailored to the individual patient's needs based on tumor characteristics and location [55,56].

3.11. Radiosurgery

Radiosurgery encompasses several advanced technologies, with Gamma Knife and Linear Accelerator (LINAC) being the most prominent. Single-fraction stereotactic radiosurgery (SRS) is generally reserved for tumors smaller than 30 mm in diameter or approximately 10 cm^3 in volume, particularly when these tumors are

not adjacent to or compressing radiation-sensitive structures such as the optic chiasm [46,57]. The efficacy of SRS is significantly influenced by tumor size. For instance, a study by DiBiase et al. demonstrated that patients with meningiomas smaller than 10 cm^3 achieved a 91.9% 5-year disease-free survival rate, whereas those with larger tumors had a substantially lower rate of 68% [58]. Additionally, the risk of toxicity is closely related to tumor size. In a 22-year study, Pollack and colleagues reported complication rates of 4.8% for tumors less than 3.2 cm^3 and 22.6% for tumors larger than 9.6 cm^3. Notable complications included cranial nerve deficits, headaches, hemiparesis, new or worsened seizures, cyst formation, and stroke [59]. For larger tumors or those in proximity to critical structures such as the optic nerves and chiasm, fractionated radiation therapy is often preferred. Fractionated therapy allows for the delivery of radiation in smaller, more controlled doses over multiple sessions, thereby reducing the risk of damage to surrounding healthy tissues [60,61]. Emerging technologies and ongoing research continue to refine radiosurgical techniques, aiming to improve outcomes and minimize complications. Innovations in imaging and treatment planning, as well as the development of new radiosurgical platforms, hold promise for the enhanced management of meningiomas through precise, targeted treatment protocols [62,63].

3.12. Hormonal Treatment

Meningioma growth may be influenced by hormonal factors, as suggested by epidemiological data indicating a higher prevalence among female patients and biochemical studies showing that approximately 70% of meningiomas express progesterone receptors, while 30% express estrogen receptors. Additionally, approximately 60% of meningiomas exhibit resistance to prolactin receptors [64].

Despite these associations, clinical trials investigating the efficacy of hormone receptor inhibitors and analogues for therapeutic purposes have not demonstrated significant clinical benefits in treating meningiomas [65].

4. Treatment of Meningiomas by WHO Grade

4.1. WHO Grade I Meningioma

For asymptomatic and incidentally discovered WHO Grade I meningiomas, management often involves careful observation with annual clinical and MRI evaluations following an initial observation period of six months. The primary goal of surgery for symptomatic meningiomas is complete tumor resection, including resection of the involved dura, known as gross total resection (GTR) or Simpson grade I resection [66]. The negative predictive factors for achieving GTR include the presence of symptoms at presentation, skull-base location, and bone invasion. The extent of resection should be confirmed intraoperatively and verified by postoperative MRI within 48 hours or after three months to avoid artefacts [67,68]. For elderly patients (over 65 years), patients with tumors that are not safely accessible by surgery, or patients with incomplete surgical resection, stereotactic radiosurgery (SRS) can be an effective alternative for treating small tumors (less than 30 mm in diameter) [62,69]. If the tumor volume precludes single-fraction treatment, fractionated radiotherapy (50−55 Gy in 1.8−2.0 Gy fractions) is recommended. SRS often involves a single dose of 14-16 Gy for small meningiomas. Posttherapy, annual MRI follow-ups are suggested for five years, followed by a transition to biannual follow-ups thereafter [70].

4.2. WHO Grade II Meningiomas

Surgery is the primary treatment for WHO Grade II meningiomas, aiming for Simpson Grade I resection. Given the higher recurrence rates (up to 50% at five years) associated with these tumors, more frequent monitoring is necessary [71]. In cases of incomplete resection, adjuvant radiotherapy (54–60 Gy in 1.8−2.0 Gy fractions) is recommended. If the tumor progresses, radiotherapy should be administered, with or without additional surgical intervention. Fractionated radiotherapy is preferred over stereotactic radiosurgery for WHO Grade II meningiomas [2,72].

4.3. WHO Grade III Meningiomas

Anaplastic (WHO Grade III) meningiomas exhibit more irregular morphology and greater relative cerebral blood volume than lower-grade tumors [73]. These aggressive tumors have a high propensity for recurrence (72–78% at five years post-GTR) and may metastasize systemically. Following surgical resection, fractionated radiotherapy with doses of at least 54 Gy in 1.8−2.0 Gy fractions is essential. Continuous follow-up every 3–6 months is crucial due to the high recurrence risk associated with these tumors [68].

5. Conclusion

The management of meningiomas has undergone significant advancements through innovations in diagnostic imaging, surgical techniques, and radiation therapy. Surgical resection remains the cornerstone for treating resectable meningiomas, with newer techniques enhancing safety and efficacy. Stereotactic radiosurgery and fractionated radiotherapy have emerged as critical alternatives, particularly for inoperable or highrisk tumors. Despite these advancements, challenges persist in achieving optimal outcomes, particularly for atypical and anaplastic meningiomas, which exhibit higher recurrence rates. Future directions should focus on refining diagnostic methods, improving surgical and radiotherapeutic techniques, and exploring novel treatment avenues, including targeted therapies and hormonal treatments. Addressing healthcare disparities and ensuring equitable access to advanced treatments are essential for improving overall patient care. Continued research and clinical trials are vital to further enhance the understanding and management of meningiomas, ultimately leading to better prognostic outcomes and quality of life for patients.

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