Arşiv Kaynak Tarama Dergisi
Archives Medical Review Journal

DERLEME/REVIEW

Meningiomas: From Pathogenesis to Therapeutics-Current Perspectives and a Holistic Review

Menenjiyomlar: Patogenezden Tedaviye- Güncel Perspektifler ve Bütünsel Bir İnceleme

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ABSTRACT
Meningiomas are the most common primary central nervous system tumors. They are benign and slow-growing neoplasms. Although they are benign, they can cause symptoms and morbidity depending on their location. Molecular markers gained importance in the 2021 World Health Organization classification of central nervous system tumors, and specific molecular biomarkers have been suggested to support the grading of meningiomas. Surgery is the standard therapy, providing tissue for histopathological typing and grading. Radiotherapy is an alternative for meningiomas that cannot be operated on or completely resected. Radiotherapy is not recommended for completely resected grade-1 meningiomas, while adjuvant radiotherapy is recommended for patients with grade-2 or grade-3 meningiomas. In this review, we discuss the epidemiology, etiology, risk factors, treatment, and the role of radiotherapy in the treatment approach of meningiomas following the WHO 2021 classification updates.
Keywords: Radiotherapy, meningioma, stereotactic radiotherapy, radiosurgery, brain tumors

ÖZET
Menenjiyomlar, en sık görülen primer santral sinir sistemi tümörleridir. İyi huylu ve yavaş büyüyen neoplazmlardır. İyi huylu olmalarına rağmen, bulundukları yere bağlı olarak semptomlara ve morbiditeye neden olabilirler. Moleküler belirteçler, 2021 Dünya Sağlık Örgütü'nün MSS tümörleri sınıflandırmasında önem kazanmıştır ve menenjiyomların derecelendirilmesini desteklemek için spesifik moleküler biyobelirteçler önerilmiştir. Cerrahi, histopatolojik tiplendirme ve derecelendirme için doku sağlayan standart tedavidir. Radyoterapi, ameliyat edilemeyen veya tamamen çıkarılamayan menenjiyomlar için bir alternatiftir. Tamamen çıkarılmış grad 1 menenjiyomlar için radyoterapi önerilmezken, 2. veya 3. grad menenjiyomlu hastalar için adjuvan radyoterapi önerilir. Bu derlemede, WHO 2021 sınıflandırma güncellemelerini takiben menenjiyomların epidemiyolojisi, etiyolojisi, risk faktörleri, tedavisi ve radyoterapinin tedavi yaklaşımındaki rolünü inceledik.
Anahtar kelimeler: Radyoterapi, menenjiyom, stereotaktik radyoterapi, radyocerrahi, beyin tümörleri

Introduction

Meningiomas are the most common primary brain tumors in adults, accounting for 37.6% of all intracranial neoplasms and 53.3% of benign intracranial neoplasms[1]. They are generally slow-growing and benign neoplasms originating from meningothelial cells The median age of diagnosis is 65 years, and the incidence of meningiomas increases with age[1,2]. Meningioma is three times less common in men than in women, while spinal lesions have a significant female predominance, increasing to 9:1[2].

The most important known risk factor is exposure to ionizing radiation. Compared to sporadic meningiomas, the incidence of atypicality is increased in radiation-associated meningiomas. It has generally been observed to occur several decades after radiation exposure[3]. In a cohort study of more than 4,000 children exposed to cranial radiation during childhood, the cumulative risk of meningioma was 5.6% by age 40[3]. Risk factors identified in this study included radiotherapy (RT), exposure before the age of five, female

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2026;35(1):1-9
doi:10.17827/aktd.1534133
Geliş tarihi/ Received: 15.08.2024
Kabul tarihi/Accepted: 09.02.2026

gender, and radiation dose[3,4]. Another study reported that the cumulative incidence of meningioma was 12% 40 years after childhood cranial radiation exposure[5].

Exogenous hormone use is considered a risk factor because meningiomas express sexual hormone receptors. In one study, 88% of meningiomas were positive for progesterone, 40% for estrogen, and 39% for androgen receptors. Estrogen-positive tumors had a higher proliferation index than estrogen-negative tumors. However, no difference was observed in the expression of sex hormone receptors by gender or age group [5,6]. In another study, no relationship was found between hormone replacement therapy or oral contraceptive use and the incidence of meningioma[6]. A slight increase in the incidence of meningioma was also observed in patients with breast cancer; it is not known whether this is due to genetic predispositions or hormonal risk factors[7].

Neurofibromatosis type 2, caused by mutations in the NF2 gene, a tumor suppressor gene located on chromosome 22, is the most common genetic syndrome associated with meningioma. Approximately half of the patients with this syndrome develop meningiomas, and their tumors are typically multiple[8]. Furthermore, this type of meningioma tends to occur at a younger age and in a more aggressive form compared to sporadic cases [8]. While AKT1, SMO, PIK3CA, NF2, and TRAF7 mutations are present in approximately 80% of sporadic meningiomas, they have not been directly linked to tumor aggressiveness[9]. The loss of CDKN2A (usually at locus 9p) has been identified as a prognostic marker associated with the progression from grade-1 to grade-2 tumors[9]. Telomerase reverse transcriptase promoter (TERTp) mutations are associated with high-grade meningiomas and significantly lower overall survival[9,10].

Classification and Pathology of Meningiomas

The 2016 World Health Organization (WHO) classification for central nervous system tumors introduced molecular features for the first time in the classification of meningiomas. This classification identified 15 different meningioma subtypes distinguished by histopathological and molecular features, which can be categorized into three grading subgroups. Most subtypes fall under WHO grade-1, comprising nine different subtypes, with fibroblastic and meningothelial subtypes being the most common. WHO grade-2 meningiomas encompass chordoid, atypical, and clear cell subtypes. Lastly, grade-3 meningiomas include anaplastic, papillary, and rhabdoid meningiomas, characterized by a poor prognosis. The 2021 WHO classification of central nervous system tumors integrated molecular biomarkers into the algorithm, but histopathological criteria still form the foundation for grading and subtype classification of meningiomas[9,11,12]. According to the 2021 WHO classification for CNS tumors, the determination of subtypes is based on both the histopathological features of the tumors and the examination of their molecular mutations. Mutations are associated with both tumor progression and location. Convexity meningiomas typically exhibit transitional histology with fibrosis and frequently contain mutations in NF2, AKT1, KLF4, PIK3CA, TRAF7, SMO, and SMARCE1 genes[9]. Meningothelial, secretory, and microcystic histology are frequently observed in skull base meningiomas and are accompanied by mutations in AKT1, KLF4, TRAF7, SMO, PIK3CA, and RNA polymerase II subunit A (POLR2A) genes. KLF4/TRAF7 mutations are specifically associated with the secretory subtype [9]. Spinal cord-localized meningiomas often exhibit a different molecular profile and frequently contain SMARCE1 mutations, which are associated with the clear cell phenotype[13]. Grade-3 papillary and rhabdoid meningiomas have been found to have BAP1 mutations, and the loss of H3K27me3 nuclear expression is indicative of a poor prognosis[9,14]. Traditionally, if the subtype of a meningioma can be determined histopathologically, the diagnosis of molecular biomarkers is not required. However, in the new classification, the presence of homozygous CDKN2A deletion and/or TERT promoter mutation can lead to a diagnosis of anaplastic meningioma, even in the absence of anaplastic histopathological features[9,10,11,15].

In the 2021 WHO classification, the grading system and histopathological subtyping remain the same as in the 2016 classification, with the WHO grade remaining the primary prognostic factor. Grade-2 meningiomas have a 7-8 times higher risk of recurrence compared to grade-1 tumors[16]. Grade-3 meningiomas are significantly more aggressive, with a 5-year overall survival rate ranging between 32% to 64%[17]. Unlike some other CNS tumors, meningiomas do not have a grade-4 subgroup, and the terms atypical and anaplastic/malignant are used for grade-2 and grade-3 meningiomas, respectively[11,12].

Meningiomas are classified on a scale of 1 to 3 based on their histopathological features, including the mitotic index, histological subtypes, and molecular features[11]. The diagnosis of grade-1 meningiomas is established by excluding grade-2 and grade-3 subtypes[14]. For grade-2 meningiomas, the diagnosis is confirmed by the presence of an increased mitotic index (4-19 mitoses/10 HPF), clear cell or chordoid histopathology, and at least three of the following features: increased cell number, necrotic leaf-like growth, prominent nucleoli, and small cell appearances with a high nuclear/cytoplasmic ratio[9,14]. Grade-3 meningiomas are diagnosed based on the presence of homozygous deletion of CDKN2A/B, 20 or more mitoses, TERT promoter mutation, and a sarcoma, carcinoma, or melanoma-like appearance[9,10,14,15].

Clinical Symptoms and Imaging of Meningioma

Symptoms mostly depend on the location of the meningioma. Meningiomas have a tendency to spread throughout the dura and may extend to the skull base or skull foramen. Brain invasion is not observed, but peritumoral vasogenic edema may occur due to vasoactive substrates. Cranial nerve palsies can occur in skull base meningiomas. Epileptic seizures may be observed in meningiomas adjacent to the temporal bone or sphenoid wing. Headaches are a common symptom[18]. However, meningiomas are often diagnosed incidentally, and these cases typically involve small, slow-growing tumors[19].

Contrast-enhanced brain MRI is the primary imaging modality for diagnosis. For tumors located at the skull base, CT imaging may be used to differentiate them from hyperostosis and to diagnose cranial nerve involvement. Calcifications can also be visualized on CT scans.

On T1-weighted brain MRI sequences, meningiomas are typically isointense or hypointense, especially the fibrous and psammomatous subtypes. They may appear hyperintense on gadolinium contrast-enhanced imaging. While they are usually isointense on T2-weighted sequences, hypervascular meningiomas can be hyperintense at T2, particularly in secretory, microcystic, angiomatous, and chordoid subtypes. Less commonly, if they appear hypointense on T2, they are often fibrous and calcified meningiomas[20]. Severe adjacent edema is typically associated with aggressive meningiomas, but edema may also be disproportionately present in some histologically benign types, such as the secretory subtype (especially in larger tumors)[21].

Grade-2 and grade-3 tumors can restrict further diffusion. While MRI spectroscopy is not always used, its benefits are limited. In MRI spectroscopy, alanine peaks (1.3-1.5 ppm) can be observed, along with increased levels of glutamate/glutamine and choline. N-acetyl aspartate (NAA) and creatine (Cr) levels are significantly decreased[20].

Treatment

Surgery

Surgery is the standard treatment method for meningiomas, providing tissue for histological typing and grading. The extent of surgical resection is closely associated with the risk of tumor recurrence[22]. The extent of surgery is graded using Simpson's grading system, which ranges from I to V. Recurrence rates are significantly influenced by this grading system, with differences ranging from 9% to 44% between complete and partial excision[23]. The primary risk factors for recurrence following surgery include histopathological grade, the extent of resection, a history of previous recurrence, and the presence of peritumoral edema as observed on imaging[22,24,25].

Surgery is particularly suitable for convexity meningiomas, where resection is often feasible. However, the resection of meningiomas located at the base of the skull can be more challenging. Surgical procedures involving cavernous sinus-located meningiomas carry a higher risk of morbidity due to their proximity to critical neurovascular structures. In cases of optic nerve sheath meningiomas, surgical resection can potentially lead to further vision loss; therefore, radiation therapy is typically the preferred initial treatment option [22]. Additionally, given the slow growth nature of meningiomas, follow-up may be considered as an alternative for non-symptomatic and incidentally detected meningiomas.

Observation

The 30% of newly diagnosed intracranial meningiomas are incidental meningiomas. There is no consensus on their optimal management, in a meta-analysis observing incidentally diagnosed meningioma of 2130 patients, applied treatment options were surgery (27.3%, n = 560), SRS (22.0%, n = 450), and observation (50.7%, n = 1040). FSRT was not an option [27]. Only %25 of the patients undergoing active monitoring showed clinical and radiological progression that required intervention. Risk factors for progression were found as tumor size larger than 3 cm and the presence of peritumoral edema.

Observation is an important option due to the typically slow natural course of meningiomas, particularly when they have grade-1 histopathology. Various studies have explored criteria for determining which patients are suitable for observation. In a meta-analysis of nine studies, it was found that the growth rate of meningiomas is inversely proportional to calcification and directly proportional to MRI T2 signal intensity [28]. Gender, tumor location, and peritumoral edema were not found to be related to tumor growth.

In a study aiming to predict tumor growth in untreated meningiomas, Lee et al. analyzed tumor progression (>2 cm^3/year) using a logistic regression model. They found that the absence of calcification in the tumor (p=0.004), the presence of peritumoral edema (p=0.025), and isointense or hyperintense signal on MRI T2 (p=0.049) were prognostic factors. They suggested using the Asan Intracranial Meningioma Scoring System (AIMSS) to predict tumor growth[29]. Another study examining the benefit of AIMSS also demonstrated its ability to predict the risk of failure of active surveillance at the time of diagnosis [30]. In a study involving 441 patients to create a prognostic model, Islim et al. identified risk factors such as hyperintensity, peritumoral edema, proximity to critical neurovascular structures, male gender, and tumor size >3 cm [31]. It was also noted that patients with a Charlson comorbidity index ≥6 were 15 times more likely to die from causes other than meningioma, suggesting that short-term follow-up may not be necessary for this patient group in order to reduce healthcare costs.

Radiotherapy

Radiotherapy can be utilized for definitive or adjuvant purposes in meningiomas. An increasing number of studies have demonstrated the success of radiotherapy as an alternative to surgery or as an adjuvant treatment for newly diagnosed or recurrent meningiomas. However, when radiotherapy is used as an alternative to surgery, it becomes challenging to determine the prognosis through grading, proliferative index determination, or histopathological/molecular assessments, as obtaining tissue samples from the patient is not feasible[26,32].

Radiotherapy in WHO grade-1 Meningioma

Adjuvant radiotherapy is not recommended for grade-1 meningiomas that have undergone gross total resection (GTR). However, in cases of subtotal resections (STR), where randomized clinical studies are lacking, different clinical approaches may be considered. Adjuvant treatments such as conventionally fractionated external beam radiotherapy (EBRT), single-fraction stereotactic radiosurgery (SRS), and (hypo)fractionated stereotactic radiotherapy (FSRT) can be considered for subtotal resected grade-1 meningiomas. Additionally, follow-up without immediate adjuvant therapy is also an option for suitable patients.

In seven long-term follow-up studies assessing recurrence rates after STR alone, local progression rates were found to be 37%-47% at 5 years, 55%-63% at 10 years, and 70%-91% at 15 years[32]. Another study on patients with benign meningiomas reported a 15-year disease-specific survival of 51% with only STR, while it was 88% after GTR and 86% after STR followed by radiotherapy[33]. Therefore, the addition of radiotherapy increases tumor control rates in patients who cannot undergo GTR.

In a historic retrospective study examining the effect of adjuvant external beam radiotherapy after STR, 54 Gy of RT was administered to 140 meningioma patients, with 117 having benign tumors[23]. The 5-year progression-free survival rate (PFS) was 98% in patients for whom CT or MRI image-based RT treatment planning was used, compared to 77% in patients treated before these imaging techniques were available. A recent review of clinical and molecular prognostic features of meningiomas also reported that STR alone

was associated with worse PFS and overall survival[34]. Despite these findings, observation following STR alone remains a common approach.

Stereotactic radiosurgery is considered the most effective radiotherapy technique for patients with small meningiomas, typically those with tumor sizes less than 10 cc in volume or 3 cm in diameter and located at a sufficient distance from critical structures. High local control rates have been achieved for WHO grade-1 meningiomas with single-fraction doses ranging from 12 to 16 Gy[26,32]. In a study comparing single-fraction doses of 10 Gy and 12 Gy, local control failure and recurrence were observed at 10 Gy [35]. Another study involving 190 patients found that SRS doses below or above 16 Gy did not significantly affect local control [36]. Similarly, no improvement in local control was observed above 15 Gy compared to doses below 15 Gy, particularly at marginal doses[37]. This study also examined the effect of tumor size on local control, revealing that the best local control was achieved in patients with small tumors (<7.5 cc)[37]. In a separate study involving 162 patients, the 5-year PFS rate was 68% for tumors larger than 10 cc (equivalent diameter 2.7 cm) compared to 91.9% for smaller tumors. Furthermore, patients with large tumors experienced more side effects[38].

In a retrospective study by Pollock et al., surgery and SRS were compared in 188 patients with small to medium-sized (<35 mm in average diameter) benign meningiomas without symptomatic mass effect [39]. After a median follow-up of 64 months, the 7-year PFS was similar for patients who underwent Simpson grade-I resection or SRS (95% and 96%, respectively). Additionally, SRS demonstrated better PFS outcomes compared to Simpson grade-II and III resections. Complication rates were 10% in the SRS group versus 22% in the surgery group. These findings indicated that SRS can serve as a primary treatment option when Simpson grade-I resection is not feasible. In an updated analysis of primary SRS, Pollock reported a 10-year tumor local control rate of 99.4%[40]. The mean tumor margin dose for SRS treatments was 15.8 Gy. These results underscored the effectiveness of SRS as a primary treatment for meningiomas. However, long-term follow-up was recommended due to the occurrence of local progression in two patients more than 12 years after SRS.

Hypofractionated stereotactic radiotherapy (FSRT) is a suitable option for larger meningiomas (>4.9 cc). It has been demonstrated that side effects such as edema may occur less frequently with FSRT when compared to single-fraction SRS[41]. Post-treatment edema (PTE), which can lead to focal deficits, seizures, and intracranial hypertension, is a relatively common complication following treatment for meningiomas. However, in a retrospective study conducted by Conti et al., radiotherapy was administered in single-fraction, 2-5 fractions, and 6-15 fractions, and it was found that fractionation did not significantly affect the development of PTE[42]. Instead, factors such as tumor volume and the extent of tumor invasion into the brain were identified as independent predictive factors for PTE[25].

One of the purposes of fractionation is to spare normal tissues, particularly in cases of meningiomas located close to critical structures like optic organs. The most common FSRT regimen is 25 Gy delivered in 5 fractions. Equivalent outcomes have been achieved with FSRT compared to a single fraction[43]. In general, for small tumors (<3 cm or <4 cc) without adjacent critical organs, a single-fraction SRS with doses ranging from 12 to 16 Gy is used. For slightly larger tumors (>3-5 cm or >12-15 cc), where the proximity to critical structures may be a concern, 25-30 Gy delivered in 5 fractions of FSRT is often employed[26,44]. External beam radiotherapy is recommended for larger tumors with irregular borders, parenchymal invasion, and significant edema. In EBRT, the typical total dose is 54 Gy with conventional fractionation (1.8-2 Gy per day). If there is a critical organ adjacent to the tumor volume, the EBRT dose may be reduced to 50 Gy[44].

Radiotherapy in WHO Grade-2 Meningioma

The primary treatment for meningiomas is surgery. However, the indications for adjuvant therapy remain a subject of debate due to the higher likelihood of recurrence compared to grade-1 meningiomas. The practice of adjuvant RT varies widely among centers, with rates ranging from 13% to 74%[27,44]. Adjuvant RT is typically recommended following subtotal resection[45].

For grade-2 meningiomas, a higher dose of RT is typically recommended when compared to grade-1 tumors. In a retrospective study, it was observed that local control rates increased at doses of 53 Gy and above with

fractionated RT[23]. Hakim et al. reported a 4-year local control rate of 83% with a margin dose of 16 Gy using SRS for grade-2 meningiomas[46]. In another study involving 24 patients with pathologically proven atypical meningiomas treated between 1999 and 2008, the median marginal dose was 14 Gy (range 10.5-18 Gy) for SRS. Overall local control rates were 75%, 51%, and 44% at 1, 2, and 5 years, respectively[47]. In this study, where non-optimal local control rates were reported, doses above 14 Gy were found to be statistically significant in improving both local control and progression-free survival[47].

The use of adjuvant RT after GTR in atypical meningiomas remains a topic of debate. In one series involving 257 patients diagnosed with atypical meningioma following Simpson grade-I and II resection, 31% of patients received postoperative adjuvant RT. The recurrence rates in patients who received SRS or intensity-modulated radiotherapy were 25% (8/32) and 18% (7/39), respectively, which was not significantly different from the group without adjuvant RT[48].

In another study of 108 patients diagnosed with atypical meningioma who underwent Simpson grade-I resection, the 5-year recurrence rate was 41%. Eight of these patients (7%) received adjuvant external beam radiotherapy, and nonexperienced recurrence[49]. The RTOG-0539 phase II study examined treatment approaches in different prognostic groups based on grade, recurrence status, and surgical status[50]. In this study, adjuvant EBRT was administered as 54 Gy in 30 fractions for grade-2 and recurrent grade-1 meningiomas that underwent GTR in the intermediate-risk group, and 60 Gy in 30 fractions after STR for grade-3 and recurrent grade-2 meningiomas in the high-risk group. The latest evaluation reported a 3-year local control rate of 96%, progression-free survival of 94%, and overall survival of 96%. Side effects were limited to grade 1-2, with no grade 3 or higher side effects observed.

Promising results from the European study (EORTC 22042-26042) investigating adjuvant RT in atypical and malignant meningiomas have spurred further research. Among the 56 patients with WHO grade-2 (atypical meningioma) who underwent GTR in this study, the 3-year progression-free survival was 88.7%, and the overall survival was 98.2% after receiving 60 Gy in 30 fractions of RT[51]. These findings have led to the initiation of two separate phase III and randomized studies to investigate the role of adjuvant RT in patients with atypical meningiomas following GTR. The ROAM/EORTC 1308 study has already reached its targeted number of patients, and their follow-up is ongoing[52]. Meanwhile, the phase III NRG-BN-003 study is currently underway, assigning atypical meningioma patients who underwent GTR to either the observation arm or the adjuvant 59.4 Gy in 33 fractions RT arm. The results of these studies are eagerly awaited, as they will provide high-level evidence to answer questions about the role of adjuvant radiotherapy in patients with atypical meningiomas who have undergone GTR[53,54].

Radiotherapy in WHO Grade-3 Meningioma

WHO grade-3 meningiomas are highly aggressive tumors, with a 5-year recurrence rate ranging from 72% to 78% and a 5-year overall survival rate between 32% and 64%[16]. Adjuvant RT is considered the cornerstone of treatment following safe maximal resection[45]. A study conducted at the Cleveland Clinic demonstrated that adjuvant EBRT can significantly improve survival when compared to surgery alone in patients with grade-3 meningiomas[51]. In the publication by Dziuk et al., out of 38 patients, 19 received postoperative RT, resulting in a significant improvement in 5-year disease-free survival with rates of 80% versus 15% (p=.002)[55].

Similar to grade-2 meningiomas, there is a dose-dependent response observed in grade-3 meningiomas. DeVries et al. demonstrated that doses of 60 Gy and above were effective in both local control and overall survival [56]. Similarly, Boskos et al. reported that doses of 60 Gy and above improved overall survival in combined therapy involving both photon and proton radiation, with doses above 65 Gy also showing effectiveness in terms of survival[57]. However, it's essential to exercise caution regarding radiation doses to avoid radionecrosis. In summary, it is recommended to deliver 59.4-60 Gy in fractionated doses of 1.8-2 Gy to the gross tumor area, tumor bed, and a 2-3 cm margin if present[45].

In the phase II study RTOG-0539, patients were categorized into three groups, and those with anaplastic histology received 60 Gy in 30 fractions of adjuvant EBRT. In the published evaluation, the 3-year local control rate was 68.9%, progression-free survival was 58.8%, and overall survival was 78.6%. Notably,

grade-5 necrosis was observed in one patient[58]. In another phase II study, EORTC 22042-26042, even though a small number of grade-3 patients were included (n=9), the results provided further support for the use of adjuvant radiotherapy[51].

SRS Side Effects

The side effects of SRS primarily depend on the administered dose, as well as the size and location of the tumor[26]. Neuropathic injuries often result from nerve toxicity or edema compression due to radiation therapy. Sensory nerves, such as the optic nerve, are more sensitive to radiation than motor nerves. There is a 1-2% risk of optic neuropathy when doses equal to or less than 10 Gy are delivered to the optic structures. However, the risk increases significantly with doses exceeding 10 Gy[36].

In a Japanese study involving single-fraction SRS, a maximum point dose ranging from 2 to 18 Gy was administered to the optic structures, leading to the development of optic neuropathy in 3 out of 109 patients (5%). Notably, one of these patients had previously undergone RT, while the other two received doses of 15 Gy or higher to the optic structures[59]. Post-treatment edema is more commonly observed in SRS compared to fractionated RT[26]. The main risk factors for post-treatment edema include tumor diameter exceeding 4 cm, high radiation doses, and tumors located in periventricular and parasagittal regions[26,41].

Follow-up

In the follow-up of meningiomas, it is recommended to conduct contrast-enhanced brain MRI scans at specific intervals. Initially, MRIs are advised at 3, 6, and 12 months during the first year after diagnosis, followed by MRIs every 6 months for the first 5 years. Subsequently, annual MRI scans are recommended, provided there is no evidence of disease progression[45]. Meningiomas are typically slow-growing tumors, which also means they may exhibit a delayed response to radiation therapy. In a study involving 99 patients, only 58% of the tumors showed signs of shrinking within the first four years of follow-up, while 88% of the tumors demonstrated reduction at the 10-year mark[60]. Another study focusing on patients treated with fractionated stereotactic radiotherapy found that 70% of tumors remained unchanged during a median follow-up period of 5.7 years[61].

Conclusion

Meningiomas, the most common primary brain tumors in adults, exhibit a range of behaviors and require diverse treatment approaches. Recent advances in molecular biology and imaging technologies have significantly improved diagnosis and management. Understanding the genetic mutations and environmental factors contributing to meningioma development is crucial. The WHO grading system helps in classifying the tumors, which is vital for determining the appropriate treatment and predicting outcomes. Diagnosis primarily relies on MRI and CT scans to assess the tumor and plan treatment strategies. Surgical resection remains the primary treatment method, with adjuvant radiotherapy used depending on the tumor's grade and the extent of resection. Ongoing research aims to refine treatment approaches and deepen our understanding of tumor biology, highlighting the importance of a personalized, multidisciplinary approach for optimal patient care.

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