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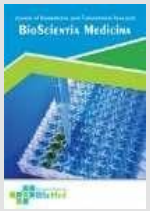

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Recurrent Giant Parasagittal Meningioma WHO Grade I: A Case Report Highlighting the Challenges of Management and the Role of Molecular Markers

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A B S T R A C T

Background: Meningiomas are common intracranial tumors, but their recurrence, especially in giant parasagittal locations, presents significant management challenges. This case report underscores these challenges and emphasizes the potential role of molecular markers in improving prognostication and treatment strategies. **Case presentation:** A 31-year-old female presented with recurrent giant parasagittal meningioma WHO Grade I. She underwent multiple surgeries and embolizations due to persistent tumor regrowth despite histologically benign features. The tumor's location, size, and involvement of critical structures posed surgical difficulties, highlighting the limitations of current management approaches. **Conclusion:** This case emphasizes the need for a more nuanced understanding of meningioma recurrence beyond histological grading. Molecular markers may offer valuable insights into tumor behavior and guide personalized treatment decisions, potentially improving outcomes for patients with recurrent meningiomas.

1. Introduction

Meningiomas, arising from the arachnoid cap cells nestled within the meninges, stand as one of the most prevalent primary intracranial tumors, accounting for approximately 30% of all such neoplasms. While the majority exhibit benign behavior, classified as World Health Organization (WHO) Grade I, a subset demonstrates a propensity for recurrence, posing a significant challenge in neurosurgical management. This recurrence phenomenon is particularly pronounced in the context of giant parasagittal meningiomas, where the tumor's substantial size, intricate relationship with critical neurovascular structures, and potential for extensive dural attachment amplify the complexities of achieving complete surgical resection. The current gold standard for classifying meningiomas rests upon the WHO grading system, which primarily hinges on histopathological characteristics. While this system offers valuable insights into tumor behavior and prognosis, it may not fully encapsulate the intricate molecular underpinnings driving recurrence, especially in cases where tumors recur despite exhibiting benign histological features. This limitation underscores the pressing need for a more nuanced understanding of meningioma biology, one that transcends traditional histopathological assessment and delves into the realm of molecular markers and genetic alterations.[1-4]

Giant parasagittal meningiomas, typically defined as those exceeding 6 cm in diameter, present a unique set of challenges that extend beyond their sheer size.

Their strategic location along the superior sagittal sinus (SSS), a major dural venous sinus responsible for cerebral venous drainage, renders complete surgical extirpation a formidable task. The intimate association of these tumors with the SSS, often involving invasion of the sinus wall or even occlusion of its lumen, necessitates meticulous surgical techniques to preserve vital venous outflow and prevent devastating neurological sequelae. Furthermore, the propensity of giant parasagittal meningiomas to infiltrate the dura mater, the outermost meningeal layer, adds another layer of complexity to their surgical management. This dural attachment can be extensive, requiring meticulous dissection to minimize the risk of residual tumor and subsequent recurrence. The challenges inherent in achieving complete resection in these cases contribute significantly to the higher recurrence rates observed in giant parasagittal meningiomas compared to their smaller counterparts.[5-7]

Recent strides in molecular biology have illuminated a multitude of genetic alterations implicated in meningioma pathogenesis, recurrence, and aggressive behavior. These alterations encompass mutations in genes orchestrating critical cellular processes, including cell cycle regulation, tumor suppression, and differentiation. The identification of these molecular markers has opened new avenues for prognostication, potentially enabling clinicians to identify patients at a higher risk of recurrence and tailor treatment strategies accordingly. Among the molecular markers under investigation, Ki-67, a nuclear protein expressed during active phases of the cell cycle, has garnered considerable attention. Its expression level, often quantified as the Ki-67 labeling index (LI), has been correlated with tumor proliferation and aggressiveness in various malignancies, including meningiomas. However, its role in predicting recurrence, particularly in WHO Grade I meningiomas, remains a subject of ongoing debate.[8-10]

In addition to molecular markers, advancements in neuroimaging have also contributed to our understanding of meningioma behavior. Diffusion-weighted imaging (DWI), a magnetic resonance imaging (MRI) technique sensitive to the random motion of water molecules within tissues, has emerged as a potential tool for predicting meningioma recurrence. The apparent diffusion coefficient (ADC), a quantitative measure derived from DWI, reflects the degree of water diffusion restriction within a tumor. Lower ADC values have been associated with increased cellularity, higher tumor grade, and a greater likelihood of recurrence. The management of recurrent giant parasagittal meningiomas necessitates a multidisciplinary approach that integrates the expertise of neurosurgeons, neuro-oncologists, radiation oncologists, and other specialists. While surgery remains the cornerstone of treatment, its success hinges on achieving the most extensive resection possible while preserving critical neurovascular structures. Preoperative embolization of tumor-feeding vessels can aid in reducing intraoperative blood loss and facilitating resection.[11-13]

In cases where complete resection is not feasible or carries an unacceptable risk of neurological morbidity, adjuvant radiotherapy may be considered. Stereotactic radiosurgery (SRS), a highly precise form of radiation therapy, has shown promise in controlling residual or recurrent meningiomas, particularly those located in eloquent brain regions. However, the optimal timing and role of radiotherapy in the management of WHO Grade I meningiomas remain areas of active investigation.[14,15] The present case report chronicles the clinical journey of a 31-year-old female grappling with the challenges of recurrent giant parasagittal meningioma WHO Grade I. Despite multiple surgeries and embolizations, her tumor exhibited relentless regrowth, underscoring the limitations of current management paradigms. The persistent recurrence, despite histologically benign features and low Ki-67 expression, highlights the need for a more comprehensive understanding of meningioma biology that incorporates molecular markers and advanced imaging techniques.

2. Case Presentation

A 31-year-old female presented to our Emergency Department with a constellation of neurological symptoms, including severe headaches and left-sided weakness. These complaints had been escalating in severity over the preceding three months, accompanied by a concerning decline in visual acuity affecting both eyes. Her medical history was notable for a backdrop of intermittent chronic headaches that had persisted since 2017, suggesting a protracted underlying pathology. In light of her clinical presentation, magnetic resonance imaging (MRI) was performed, unveiling a significant intracranial lesion. The MRI scans depicted a large, isointense mass occupying the bilateral parasagittal region. This mass exhibited homogenous enhancement following the administration of contrast, indicative of increased vascularity within the lesion. Furthermore, the presence of peritumoral edema, representing fluid accumulation in the surrounding brain tissue, underscored the mass effect exerted by the tumor. The mass was observed to be intimately attached to the cerebral falx, a dural fold separating the cerebral hemispheres, raising concerns about potential dural invasion (Figure 1).

In March 2017, the patient underwent a preoperative embolization procedure aimed at reducing tumor vascularity and facilitating subsequent surgical resection. Digital subtraction angiography (DSA) during embolization revealed the right middle meningeal artery as the principal arterial feeder to the tumor (Figure 2). Additionally, the imaging demonstrated some degree of invasion into the superior sagittal sinus (SSS), a major dural venous sinus coursing along the midline of the brain. Following embolization, the patient underwent a craniectomy, a surgical procedure involving the removal of a portion of the skull to access the intracranial space. The tumor, exposed and meticulously dissected, was characterized as a large, white-greyish, rubbery mass measuring 10x5x4 cm. It exhibited a propensity for bleeding, reflecting its rich vascular supply (Figure 3). The tumor was found to be firmly attached to the SSS and had infiltrated the falx cerebri, extending across the midline to the contralateral side. A portion of the tumor intimately adhered to the sinus wall was deliberately preserved to mitigate the risk of damaging this critical venous structure. The tumor had also infiltrated the adjacent bony structures of the skull vault, necessitating careful removal to ensure adequate tumor clearance. Following surgical resection, the excised tumor underwent histopathological examination. The findings were consistent with a meningothelial meningioma, classified as WHO Grade I, signifying its benign nature. Immunohistochemical staining for Ki-67, a marker of cellular proliferation, revealed a labeling index of less than 3%, further supporting the low-grade diagnosis.

In the immediate postoperative period, the patient was hospitalized for seven days. During this time, she exhibited mild left-sided hemiparesis, a neurological deficit attributable to the tumor's mass effect on the adjacent motor cortex. Following discharge, she continued to experience this mild hemiparesis. Approximately one year later, in March 2018, the patient presented once again with severe headaches and a worrisome exacerbation of her left-sided weakness. Repeat contrast-enhanced MRI revealed a disheartening finding: the tumor had recurred, attaining a size comparable to its original preoperative dimensions. Moreover, the imaging demonstrated evidence of tumor invasion into the contralateral side, suggesting aggressive biological behavior despite its histologically benign classification (Figure 4).

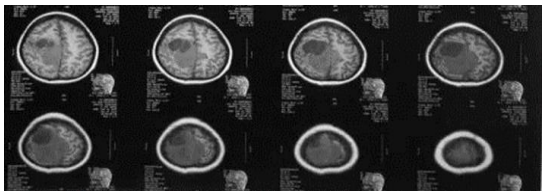
In light of the tumor recurrence, the patient underwent a second craniotomy for tumor removal. The surgical approach aimed to achieve maximal resection while safeguarding critical neurovascular structures. However, the portion of the tumor-infiltrating the SSS was once again left undisturbed to avoid compromising venous drainage. Histopathological analysis of the resected tumor mirrored the findings of the initial surgery, confirming a meningothelial meningioma WHO Grade I with a Ki-67 labeling index of less than 3%. The patient's

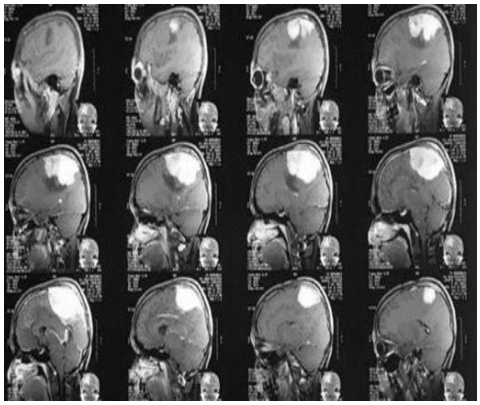
postoperative course was uneventful, and she was discharged after ten days of hospitalization.

Five years elapsed before the patient's next presentation in April 2023. She reported a resurgence of severe headaches, accompanied by persistent mild left-sided weakness. The latest MRI scan painted a grim picture, revealing a further increase in tumor size at the original site. Additionally, the ADC value, a measure of water diffusion restriction within the tumor, was found to be 0.75 x 10^-3 mm^2/second, a value suggestive of increased cellularity and a higher risk of recurrence. Given the tumor's relentless growth and its impact on the patient's quality of life, a multidisciplinary team convened to discuss further management options. The decision was made to pursue DSA and tumor embolization as a prelude to a third surgical resection. Angiography during embolization identified multiple feeding arteries, including the right superficial temporal artery, left middle meningeal artery, and branches of the bilateral anterior cerebral arteries. Following embolization, the patient reported a significant reduction in headache severity, with her VAS score improving from 6/10 to 3/10.

Emboldened by the success of embolization, the patient underwent a third craniotomy for tumor removal. The surgical team, armed with the knowledge gleaned from prior interventions and preoperative imaging, embarked on a meticulous resection, striving to achieve the most extensive tumor removal possible while preserving vital neurovascular structures. Histopathological evaluation of the resected specimen, once again, yielded a diagnosis of meningothelial meningioma WHO Grade I, with a Ki-67 labeling index of less than 3%. This persistent histological benignity in the face of multiple recurrences underscored the limitations of relying solely on histopathological grading for prognostication and treatment decisions.

Following her third surgery, the patient experienced a notable improvement in her neurological symptoms. Her headaches subsided, and her left-sided weakness showed signs of amelioration. She was discharged after ten days of hospitalization and enrolled in a rigorous follow-up program, including regular imaging surveillance to monitor for any signs of recurrence. The patient's case serves as a stark reminder of the challenges inherent in managing recurrent giant parasagittal meningiomas, even those classified as WHO Grade I. The relentless tumor regrowth, despite multiple surgeries and embolizations, highlights the limitations of current treatment paradigms and underscores the pressing need for innovative approaches that incorporate molecular markers and advanced imaging techniques to enhance prognostication and guide personalized treatment decisions.





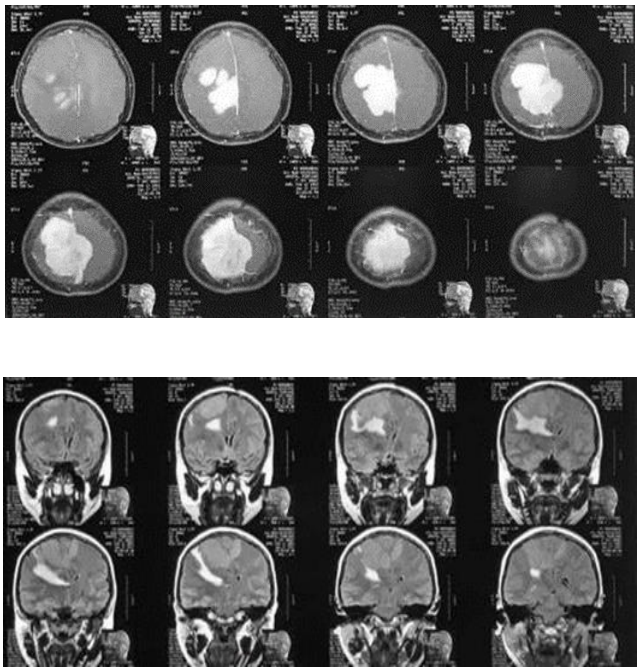


Figure 1. MRI showed intracranial mixintensity mass which enhanced homogenously with contrast administration at the bilateral parasagittal with some peritumoral oedema attached to cerebral falx.

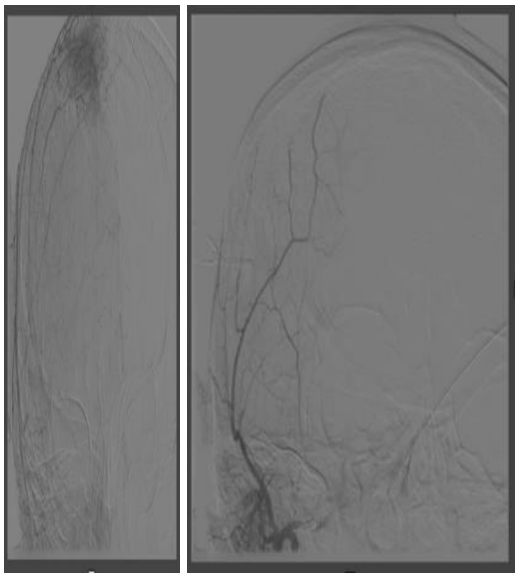


Figure 2. The angiography revealed a tumor blush from the right middle meningeal artery.

Figure 3. Craniotomy tumor removal for the 1st time.

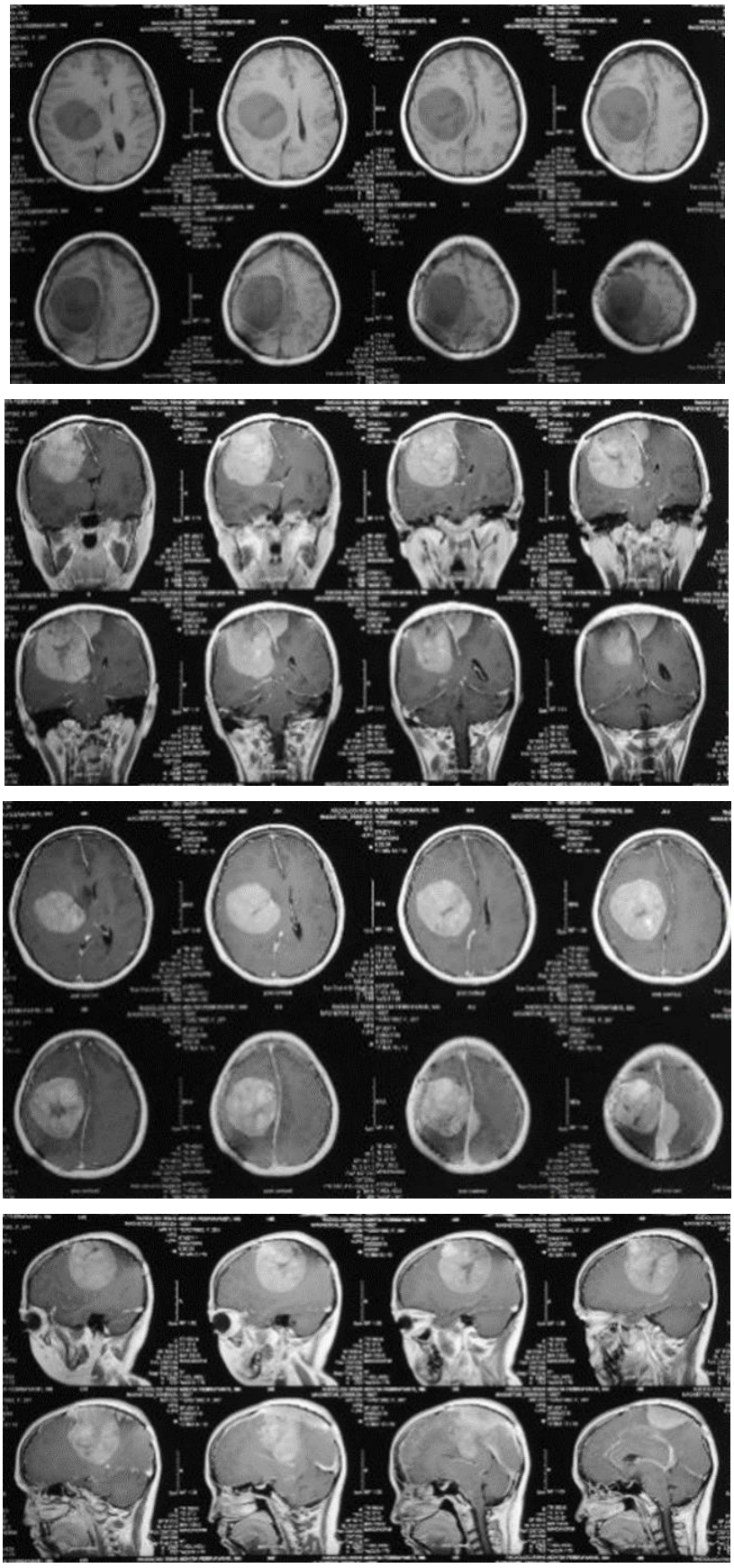


Figure 4. MRI 1 year after the first surgery showed a massive intracranial mass at the site of the previous tumor.

3. Discussion

The persistent recurrence of meningiomas classified as WHO Grade I, as exemplified by the patient in this case report, challenges the conventional understanding of tumor behavior and underscores the limitations of relying solely on histopathological features for prognostication. This phenomenon, often referred to as the "enigma of recurrence," highlights the intricate and multifaceted nature of meningioma biology, where factors beyond histological grade play a crucial role in determining tumor aggressiveness and recurrence potential. The World Health Organization (WHO) grading system, based primarily on histopathological characteristics such as mitotic activity, nuclear atypia, and brain invasion, has long served as the cornerstone for classifying meningiomas and predicting their clinical behavior. While this system provides valuable insights into tumor prognosis and guides treatment decisions, it may not fully capture the complex molecular and genetic landscape underlying meningioma recurrence, particularly in cases where tumors recur despite exhibiting benign histological features. The patient in this case report exemplifies this discrepancy. Despite consistently demonstrating WHO Grade I histology and a low Ki-67 labeling index, indicative of low proliferative activity, her tumor exhibited relentless regrowth, defying conventional expectations. This observation suggests that factors beyond those readily discernible under the microscope contribute to tumor recurrence, necessitating a deeper exploration of the molecular and genetic underpinnings of meningioma biology. Tumor location and size emerge as critical determinants of recurrence risk, particularly in the context of giant parasagittal meningiomas. The parasagittal region, characterized by its proximity to the superior sagittal sinus (SSS) and intricate network of dural venous sinuses, poses unique challenges for surgical resection. The intimate association of these tumors with the SSS often involves invasion of the sinus wall or even occlusion of its lumen, necessitating meticulous surgical technique to preserve vital venous outflow and prevent devastating neurological complications. The surgeon's decision to preserve portions of the tumor adherent to the SSS, while judicious in minimizing the risk of venous sinus injury, may inadvertently leave behind microscopic nests of tumor cells capable of seeding recurrence. Furthermore, the sheer size of giant meningiomas, exceeding 6 cm in diameter, amplifies the surgical complexities. These tumors exert significant mass effect on surrounding brain structures, potentially leading to neurological deficits and complicating surgical access. The extensive dural attachment often observed in giant meningiomas necessitates meticulous dissection, increasing the risk of incomplete resection and residual tumor. Even with the most advanced surgical techniques and meticulous attention to detail, achieving complete resection in these cases can be challenging, contributing to the higher recurrence rates observed in giant parasagittal meningiomas. Recent advances in molecular biology have illuminated a multitude of genetic alterations implicated in meningioma pathogenesis, recurrence, and aggressive behavior. These alterations encompass mutations in genes orchestrating critical cellular processes, including cell cycle regulation, tumor suppression, and differentiation. The identification and characterization of these molecular markers have opened new avenues for prognostication and personalized treatment, potentially enabling clinicians to identify patients at a higher risk of recurrence and tailor therapeutic strategies accordingly. Among the molecular markers under investigation, Ki-67, a nuclear protein expressed during active phases of the cell cycle, has garnered considerable attention. Its expression level, often quantified as the Ki-67 labeling index (LI), has been correlated with tumor proliferation, aggressiveness, and recurrence risk in various malignancies, including meningiomas. However, the prognostic significance of Ki-67 in WHO Grade I meningiomas remains a subject of ongoing debate, with conflicting results reported in the literature. In the present case, the Ki-67 LI remained consistently low (<3%) throughout the patient's clinical course,

despite multiple recurrences. This observation challenges the notion that Ki-67 alone can reliably predict recurrence risk in all meningiomas, particularly those classified as WHO Grade I. It suggests that other molecular factors, beyond Ki-67, may be driving tumor behavior in this particular case and underscores the need for a more comprehensive understanding of the molecular landscape underlying meningioma recurrence. Beyond Ki-67, several other molecular markers have been implicated in meningioma recurrence and aggressive behavior. These include mutations in genes involved in cell cycle regulation, such as CDKN2A, CDKN2B, and NF2 tumor suppression, such as TP53 and PTEN and cell differentiation, such as SMO and AKT1. The identification and characterization of these molecular alterations may offer valuable insights into tumor biology and provide a more nuanced understanding of recurrence risk, potentially guiding personalized treatment decisions. The enigma of recurrence in WHO Grade I meningiomas, as exemplified by the patient in this case report, highlights the limitations of relying solely on histopathological grading for prognostication and treatment planning. This observation calls for a paradigm shift in meningioma management, one that embraces a more comprehensive approach incorporating molecular markers, advanced imaging techniques, and novel therapeutic strategies. The integration of molecular markers into routine clinical practice may enable clinicians to identify patients at a higher risk of recurrence, even in the absence of overt histological atypia. This, in turn, may facilitate earlier and more aggressive intervention, potentially improving long-term outcomes. Advancements in neuroimaging, such as DWI and functional MRI, hold promise in refining our ability to predict tumor behavior and guide surgical planning, further enhancing the precision and efficacy of treatment. The development of novel therapeutic approaches, including molecularly targeted therapies and immunotherapies, offers new hope for patients with recurrent meningiomas, particularly those refractory to conventional treatment modalities. By targeting specific molecular alterations driving tumor growth and recurrence, these therapies may offer a more personalized and effective approach to treatment, potentially improving outcomes and quality of life for patients facing the daunting challenges of recurrent meningiomas.[16-20]

The case presented in this report, where a patient experienced multiple recurrences of a histologically benign meningioma despite low Ki-67 expression, underscores a critical limitation in the current approach to meningioma management. It highlights the pressing need to move beyond traditional histopathological assessment and incorporate molecular markers into the diagnostic and therapeutic armamentarium. Such an integrated approach could potentially revolutionize our understanding of meningioma behavior, enabling more precise prognostication, personalized treatment strategies, and ultimately, improved patient outcomes. Ki-67, a nuclear protein expressed during active phases of the cell cycle, has long been investigated as a prognostic marker in various cancers, including meningiomas. Its expression level, often quantified as the Ki-67 labeling index (LI), serves as a surrogate for tumor cell proliferation. In general, higher Ki-67 LI values correlate with increased mitotic activity, aggressive tumor behavior, and a greater likelihood of recurrence. However, the prognostic significance of Ki-67 in WHO Grade I meningiomas, which are histologically benign, remains a subject of ongoing debate. While some studies have reported an association between elevated Ki-67 LI and increased recurrence risk even in low-grade tumors, others have failed to demonstrate such a correlation. This discrepancy may be attributed to several factors, including variability in Ki-67 assessment methods, heterogeneity in tumor biology, and the influence of other molecular and genetic factors on tumor behavior. In the present case, the patient's tumor consistently exhibited a low Ki-67 LI (<3%) despite multiple recurrences. This observation challenges the notion that Ki-67 alone can reliably predict recurrence risk in all meningiomas, particularly those classified as WHO Grade I. It

suggests that other molecular factors, beyond Ki-67, may be driving tumor behavior in this particular case and underscores the need for a more comprehensive approach to molecular profiling in meningiomas. Recent advances in molecular biology have unveiled a multitude of genetic alterations associated with meningioma recurrence and aggressive behavior. Mutations in genes such as CDKN2A, CDKN2B, and NF2 can disrupt the cell cycle checkpoints, leading to uncontrolled cell growth and proliferation. CDKN2A and CDKN2B encode proteins that inhibit cyclin-dependent kinases, key regulators of cell cycle progression. NF2, encoding the protein Merlin, acts as a tumor suppressor by inhibiting mitogenic signaling pathways. Loss of function mutations in these genes can unleash cell growth and contribute to tumor recurrence. Mutations in tumor suppressor genes, such as TP53 and PTEN, can impair the cell's ability to detect and repair DNA damage, leading to genomic instability and increased susceptibility to malignant transformation. TP53 encodes the p53 protein, a critical regulator of cell cycle arrest and apoptosis in response to DNA damage. PTEN encodes a phosphatase that antagonizes the PI3K/AKT signaling pathway, a key driver of cell growth and survival. Loss of function mutations in these genes can promote tumorigenesis and contribute to aggressive tumor behavior. Mutations in genes involved in cell differentiation, such as SMO and AKT1, can disrupt normal cellular development and contribute to tumorigenesis. SMO encodes a protein involved in the Hedgehog signaling pathway, which plays a crucial role in embryonic development and tissue homeostasis. AKT1 encodes a serine/threonine kinase involved in various cellular processes, including cell growth, proliferation, and survival. Activating mutations in these genes can promote uncontrolled cell growth and contribute to tumor recurrence. The identification and characterization of these molecular markers have the potential to revolutionize meningioma management. Molecular profiling may allow for more accurate prediction of recurrence risk, even in histologically benign tumors. This information can guide treatment decisions and surveillance strategies, potentially leading to earlier detection and intervention in cases of recurrence. The identification of specific molecular alterations driving tumor growth and recurrence may pave the way for targeted therapies that exploit these vulnerabilities. This personalized approach to treatment holds the promise of improved efficacy and reduced toxicity compared to conventional therapies. Molecular markers may serve as valuable tools for monitoring treatment response and detecting minimal residual disease, potentially guiding further therapeutic interventions and improving long-term outcomes. The incorporation of molecular markers into routine clinical practice represents a paradigm shift in meningioma management. However, several challenges must be addressed before this vision can be fully realized. The lack of standardized protocols for assessing molecular markers, such as Ki-67, can lead to variability in results and hinder their clinical utility. The development and validation of standardized assessment methods are essential for ensuring reproducibility and comparability of results across different laboratories and studies. The cost of molecular profiling can be a barrier to its widespread implementation in clinical practice. The development of more cost-effective technologies and strategies for identifying high-risk patients may be necessary to facilitate the integration of molecular markers into routine care. While numerous studies have investigated the prognostic significance of various molecular markers in meningiomas, further clinical validation is needed to establish their definitive role in predicting recurrence and guiding treatment decisions. Large-scale prospective studies are warranted to assess the impact of molecular profiling on patient outcomes and to identify the most clinically relevant markers. Despite these challenges, the potential benefits of incorporating molecular markers into meningioma management are undeniable. By providing a more nuanced understanding of tumor biology, these markers may enable clinicians to refine prognostication, personalize treatment, and

ultimately, improve outcomes for patients with meningiomas. The case presented in this report serves as a powerful reminder of the limitations of relying solely on histopathological assessment and underscores the pressing need for a more comprehensive approach that embraces the power of molecular diagnostics.[21-23]

The case presented in this report highlights the limitations of relying solely on histopathological features and conventional imaging modalities for predicting meningioma recurrence. Despite exhibiting benign histological characteristics and low Ki-67 expression, the patient's tumor demonstrated aggressive behavior with multiple recurrences. This underscores the need for more sophisticated tools to assess tumor biology and predict its clinical course. Advanced imaging techniques, such as diffusion-weighted MRI (DWI), offer a promising avenue for refining our ability to prognosticate and personalize treatment strategies for meningioma patients. DWI, a specialized MRI technique, provides a unique window into the microstructure of tissues by measuring the random motion of water molecules. In biological tissues, water diffusion is influenced by various factors, including cellular density, membrane permeability, and the presence of macromolecules. By quantifying the degree of water diffusion restriction, DWI can provide valuable insights into tissue composition and cellularity, which can be indicative of tumor aggressiveness and recurrence potential. The apparent diffusion coefficient (ADC), a quantitative parameter derived from DWI, reflects the average diffusivity of water molecules within a region of interest. In general, lower ADC values correspond to greater diffusion restriction, suggesting increased cellular density, higher nuclear-to-cytoplasmic ratio, and potentially more aggressive tumor behavior. In the context of meningiomas, several studies have demonstrated a correlation between low ADC values and increased recurrence risk, even in histologically benign tumors. In the present case, the ADC value of 0.75 x 10^-3 mm^2/second observed on the latest MRI scan aligns with these findings. This low ADC value, indicative of increased cellularity and restricted diffusion, may have served as an early warning sign of impending recurrence, even in the absence of overt histological atypia or elevated Ki-67 expression. This observation underscores the potential value of DWI in supplementing traditional imaging modalities and refining prognostication in meningioma patients. While ADC remains the most widely used DWI metric in meningioma research, other parameters derived from DWI data may offer additional insights into tumor biology and recurrence risk. FA (Fractional Anisotropy) measures the degree of directional preference in water diffusion. Higher FA values indicate greater diffusion anisotropy, suggesting the presence of organized tissue structures, such as white matter tracts. In meningiomas, lower FA values have been associated with increased cellularity and higher tumor grade. MD (Mean Diffusivity) represents the average diffusion coefficient in all directions, providing a measure of overall water mobility within a tissue. Lower MD values, indicative of restricted diffusion, have been linked to increased tumor cellularity and aggressiveness. DKI (Diffusion Kurtosis Imaging) is a more advanced DWI technique that quantifies the non-Gaussian behavior of water diffusion, providing additional information about tissue microstructure beyond what is captured by conventional DWI. DKI-derived parameters, such as mean kurtosis (MK), have shown promise in differentiating between different grades of meningiomas and predicting recurrence risk. The exploration of these and other DWI-derived metrics may further enhance our ability to characterize meningioma biology and predict its clinical course. By integrating multiple DWI parameters, we may be able to develop more sophisticated prognostic models that can guide personalized treatment decisions and improve patient outcomes. The promise of advanced imaging in meningioma management extends beyond DWI. The integration of multiple imaging modalities, such as perfusion MRI, magnetic resonance spectroscopy (MRS), and positron emission tomography (PET), can provide a more comprehensive assessment of tumor

biology and its microenvironment. Perfusion MRI, for instance, can measure blood flow and permeability within the tumor, providing insights into its vascularity and metabolic activity. MRS can detect and quantify various metabolites within the tumor, offering clues about its metabolic profile and potential for aggressive behavior. PET, using radiolabeled tracers, can visualize specific molecular targets and pathways, enabling the assessment of tumor receptor status and the identification of potential therapeutic targets. The combination of these advanced imaging techniques, along with molecular markers and histopathological assessment, may usher in a new era of multiparametric imaging in meningioma diagnostics. This integrated approach has the potential to revolutionize our understanding of tumor biology, enabling more precise prognostication, personalized treatment strategies, and ultimately, improved patient outcomes. While the potential of advanced imaging in meningioma management is undeniable, several challenges must be addressed before these techniques can be fully integrated into routine clinical practice. The lack of standardized protocols for acquiring and analyzing advanced imaging data can lead to variability in results and hinder their clinical utility. The development and validation of standardized protocols are essential for ensuring reproducibility and comparability of results across different institutions and studies. The cost of advanced imaging techniques can be a barrier to their widespread implementation in clinical practice. The development of more cost-effective technologies and strategies for identifying high-risk patients may be necessary to facilitate the integration of these techniques into routine care. While numerous studies have investigated the prognostic value of advanced imaging in meningiomas, further clinical validation is needed to establish their definitive role in predicting recurrence and guiding treatment decisions. Large-scale prospective studies are warranted to assess the impact of advanced imaging on patient outcomes and to identify the most clinically relevant imaging biomarkers. Despite these challenges, the promise of advanced imaging in meningioma management is undeniable. By providing a non-invasive window into tumor biology and its microenvironment, these techniques have the potential to revolutionize our understanding of this complex disease and pave the way for more personalized and effective treatment strategies.[24-27]

The management of recurrent giant parasagittal meningiomas necessitates a multifaceted and nuanced approach that extends beyond the conventional reliance on histopathological grading and standard treatment algorithms. The complexities inherent in these tumors, as exemplified by the patient in this case report, demand a multidisciplinary collaboration that integrates the expertise of neurosurgeons, neuro-oncologists, radiation oncologists, and other specialists. The therapeutic landscape for these patients is continually evolving, with advancements in surgical techniques, imaging modalities, and molecularly targeted therapies offering new hope for improved outcomes. Surgical resection remains the cornerstone of treatment for recurrent giant parasagittal meningiomas. The primary goal is to achieve the most extensive resection possible while preserving critical neurovascular structures and minimizing the risk of neurological morbidity. The surgeon's expertise and experience play a pivotal role in navigating the intricate anatomy of the parasagittal region, where the tumor often intimately adheres to the superior sagittal sinus (SSS) and other vital structures. Advancements in surgical techniques, such as the use of intraoperative neurophysiological monitoring and neuronavigation systems, have enhanced the safety and precision of resection. These tools enable real-time assessment of neurological function and accurate localization of tumor margins, facilitating maximal resection while minimizing the risk of iatrogenic injury. However, complete resection in recurrent giant parasagittal meningiomas can be challenging, particularly when the tumor invades the SSS or other critical structures. In such cases, the surgeon must carefully weigh the benefits of aggressive resection against the potential risks of

neurological complications. The decision to preserve portions of the tumor adherent to vital structures, while prudent in minimizing immediate morbidity, may inadvertently leave behind microscopic foci of tumor cells capable of seeding recurrence. This delicate balance between achieving maximal resection and preserving neurological function underscores the complexities inherent in the surgical management of these tumors. Preoperative embolization, as employed in the present case, can serve as a valuable adjunct to surgical resection. This minimally invasive procedure involves the selective occlusion of tumor-feeding vessels using embolic agents, thereby reducing tumor vascularity and intraoperative blood loss. By facilitating tumor dissection and potentially improving the extent of resection, embolization can enhance the safety and efficacy of surgery. Several studies have investigated the impact of preoperative embolization on outcomes in meningioma surgery. While the evidence remains somewhat mixed, some studies have reported reduced blood loss, shorter operative times, and improved resection rates in patients undergoing embolization. However, the long-term impact of embolization on recurrence rates remains a subject of investigation. Further research is needed to elucidate the optimal timing and role of embolization in the management of recurrent giant parasagittal meningiomas. In cases where complete resection is not feasible or carries an unacceptable risk of neurological compromise, adjuvant radiotherapy may be considered. Stereotactic radiosurgery (SRS), a highly precise form of radiation therapy, has demonstrated efficacy in controlling residual or recurrent meningiomas, particularly those located in eloquent brain regions. By delivering high doses of radiation to the tumor while sparing surrounding healthy tissue, SRS can achieve local tumor control and potentially delay or prevent recurrence. However, the optimal timing and role of radiotherapy in the management of WHO Grade I meningiomas, especially those with low Ki-67 expression, remain areas of active debate. While some studies have suggested the benefit of adjuvant radiotherapy in reducing recurrence risk, others have failed to demonstrate a significant impact on long-term outcomes. The potential risks of radiation-induced complications, such as brain necrosis, edema, and cognitive decline, must also be carefully weighed against the potential benefits of treatment. The decision to pursue adjuvant radiotherapy in recurrent giant parasagittal meningiomas should be individualized based on a careful assessment of the patient's clinical status, tumor characteristics, and the extent of resection achieved. Factors such as tumor size, location, histological grade, Ki-67 expression, and the presence of residual tumor following surgery should all be considered in the decision-making process. The advent of molecularly targeted therapies and immunotherapies has opened new frontiers in the treatment of meningiomas. These novel approaches, which aim to exploit specific molecular alterations driving tumor growth and recurrence, hold the promise of more personalized and effective treatment strategies. Several molecularly targeted therapies are currently under investigation for the treatment of meningiomas. These drugs target specific receptor tyrosine kinases, such as the vascular endothelial growth factor receptor (VEGFR) and the platelet-derived growth factor receptor (PDGFR), which are often overexpressed in meningiomas. By inhibiting these receptors, these drugs can disrupt tumor angiogenesis and growth signaling pathways. The mTOR pathway plays a crucial role in cell growth and proliferation. mTOR inhibitors, such as everolimus and sirolimus, have shown promising results in clinical trials for the treatment of recurrent and progressive meningiomas. Immunotherapies, such as immune checkpoint inhibitors and vaccines, aim to harness the power of the immune system to recognize and destroy tumor cells. While still in their early stages of development, these approaches have shown encouraging results in select patient populations. The identification of specific molecular alterations driving tumor growth and recurrence in individual patients may pave the way for personalized treatment strategies that target these vulnerabilities. This

precision medicine approach holds the potential to improve outcomes and reduce toxicity compared to conventional therapies.[28-30]

4. Conclusion

This case report underscores the intricate challenges associated with recurrent giant parasagittal meningiomas, even those classified as WHO Grade I. The patient's clinical journey highlights the limitations of relying solely on histopathological grading and emphasizes the need for a more nuanced understanding of tumor behavior, incorporating molecular markers and advanced imaging techniques. By integrating these emerging tools into clinical practice, we can strive to improve prognostication, personalize treatment strategies, and ultimately, enhance outcomes for patients facing the daunting challenges of recurrent meningiomas.

5. References

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