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Original Research Article

Association of progesterone receptor status with histopathological grading in patients with intracranial meningioma

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ABSTRACT

Background: Intracranial meningioma is a common primary brain tumor. Although most are benign, recurrence and variable behavior remain concerns. While World Health Organization (WHO) histopathological grading is an established prognostic tool, it does not always accurately predict tumor behavior. Progesterone receptor (PR) expression may serve as an additional prognostic marker. Objective of the study was to assess the association between progesterone receptor status and histopathological grading in patients with intracranial meningioma.
Methods: This cross-sectional observational study was conducted in the Department of Neurosurgery, Bangladesh Medical University, Dhaka, Bangladesh from June 2018 to March 2020. A total of 35 patients with histologically confirmed intracranial meningioma were included. Clinical and radiological data were collected using a structured data sheet. Tumors were graded according to WHO classification. Progesterone receptor status was evaluated by immunohistochemistry and categorized based on percentage of nuclear positivity. Data were analyzed using statistical package for the social sciences (SPSS) version 22, and associations were tested using Fisher's exact test. A p value <0.05 was considered statistically significant.
Results: Among 35 patients, 88.57% had WHO grade I and 11.43% had grade II meningioma. A significant association was found between PR status and histopathological grade (p=0.013). Lower PR expression was more common in grade II tumors. No significant association was observed between PR status and tumor size.
Conclusions: Progesterone receptor status is significantly associated with histopathological grading and may serve as an additional prognostic marker in intracranial meningioma.

Keywords: Intracranial meningioma, Progesterone receptor, WHO grading, Histopathology, Immunohistochemistry

INTRODUCTION

Meningioma is one of the most common primary intracranial tumors, arising from the arachnoid cap cells of the meninges. The term "meningioma" was first introduced by Harvey Cushing in 1922. These tumors account for approximately 35–40% of symptomatic primary brain tumors in adults and represent the second most frequent intracranial neoplasm after glioma.[1] The incidence increases with advancing age, peaking after the fifth decade of life, and shows a marked female predominance with a female-to-male ratio of nearly 2:1. Annual incidence rates range from 2–7 per 100,000 population in females and 1–5 per 100,000 in males.[2] Although predominantly intracranial, less than 2% of meningiomas arise extracranially, most commonly in the head and neck region.[3]

According to the World Health Organization (WHO) classification of tumors of the central nervous system (2016), meningiomas are categorized into three grades based on histopathological criteria. WHO grade I tumors are benign and slow-growing, constituting nearly 80–90% of cases. Grade II (atypical) tumors account for approximately 15–20% and exhibit increased mitotic activity and higher recurrence risk, while grade III (anaplastic/malignant) tumors represent 1–3% and are associated with aggressive behavior and poor prognosis.[4,5]

Histological features such as increased cellularity, high mitotic index, necrosis, nuclear pleomorphism, loss of architectural pattern, and brain invasion are indicators of aggressive biological behavior.[6]

Surgical excision remains the mainstay of treatment, and prognosis is largely determined by the extent of resection as described by Simpson's grading system, along with the WHO histopathological grade.[7] Despite gross total resection, recurrence occurs in 7–32% of benign meningiomas and up to 40% in atypical cases within five years.[5] Recurrence prediction remains challenging in clinical practice, as tumors that appear histologically benign may still demonstrate aggressive or recurrent behavior. Therefore, reliance solely on histopathological grading may be insufficient for predicting tumor biology and clinical outcomes.

The observed female predominance and reports of tumor enlargement during pregnancy or the luteal phase of the menstrual cycle have led to the hypothesis that meningiomas are hormone-sensitive tumors.[8] Epidemiological associations between meningioma and breast cancer further support a possible hormonal influence. In some cases, regression of meningioma following termination of pregnancy has been documented.[9] These findings have prompted extensive research into steroid hormone receptor expression in meningiomas, particularly progesterone receptor (PR) and estrogen receptor (ER).

Earlier studies using radiolabeled steroid binding assays demonstrated high levels of PR expression in meningioma tissue, whereas ER expression was either absent or present at very low levels. The development of monoclonal antibodies has enabled reliable immunohistochemical detection of PR and ER directly in tumor specimens.[10] Most studies agree that the majority of meningiomas express progesterone receptors, while estrogen receptor expression is rare.[11]

Progesterone receptor expression has been proposed as a potential prognostic biomarker in meningioma. Several reports suggest that higher PR expression is associated with lower tumor grade and delayed recurrence, whereas reduced or absent PR expression may correlate with higher-grade tumors and increased proliferative activity. Progesterone is also known to possess proapoptotic properties, and loss of PR expression may reflect increased cellular turnover and aggressive tumor behavior.[8,12] However, findings across studies remain inconsistent, and the exact relationship between PR status and histopathological grading requires further clarification.

Given the limitations of histological grading alone in predicting recurrence and biological behavior, assessment of progesterone receptor status may provide additional prognostic information. Understanding the association between PR expression and WHO histopathological grade could help identify tumors with higher malignant potential and guide postoperative surveillance strategies. Therefore, this study aims to evaluate the association of progesterone receptor status with histopathological grading in patients with intracranial meningioma, contributing to improved prognostic stratification and therapeutic decision-making.

Objectives

The main objective was to assess the association between progesterone receptor status and histopathological grading in patients with intracranial meningioma.

METHODS

The prospective randomized comparative interventional study was conducted in the Department of Neurosurgery, Bangladesh Medical University, Dhaka, Bangladesh. The study was carried out over nineteen months from June 2018 to March 2020.

A total of 35 histologically confirmed cases of intracranial meningioma were included in this study. Patients were selected consecutively during the study period according to predefined inclusion and exclusion criteria.

Patients were included if they had a radiological diagnosis of intracranial meningioma based on contrast-enhanced magnetic resonance imaging (MRI) of the brain and if the diagnosis was confirmed by histopathological examination following surgical excision or biopsy. Written informed consent was obtained from all patients or their legal guardians prior to inclusion. Patients whose histopathology reports were not consistent with meningioma and those who declined to participate were excluded from the study.

After admission, a detailed history was taken and thorough general and neurological examinations were performed. MRI diagnosis was established based on characteristic imaging features such as homogeneous enhancement of the mass, dural tail sign, and cerebrospinal fluid (CSF) cleft sign. Tumor size was calculated from imaging findings and categorized as small, medium, or large. Resected tumor specimens were fixed in formalin, processed routinely, and examined histopathologically. Tumors were graded according to the World Health Organization (WHO) classification of central nervous system tumors into grade I, grade II, and grade III based on established histological criteria. Progesterone receptor (PR) status was determined by immunohistochemical staining of tumor tissue, and nuclear staining was assessed and recorded as positive or negative according to standard laboratory reporting criteria.

Statistical analysis

Data were entered and analyzed using statistical package for the social sciences (SPSS) version 22. Results were expressed as frequencies and percentages, and the association between progesterone receptor status and

histopathological grading was evaluated using the Chi-square test. A p value of less than 0.05 was considered statistically significant. Ethical principles were maintained throughout the study, and confidentiality of patient information was strictly ensured.

RESULTS

Table 1 shows the baseline characteristics of 35 patients. The mean age was 59.65±16.03 years (range 17–82 years), with most patients (31.4%) in the 51–60 years age group. Females were predominant (57.1%). Most tumors were medium-sized (62.9%), and the commonest location was parasagittal (28.6%), followed by convexity (25.7%).

Table 1: Baseline characteristics of the study subjects (n=35).

Variables	Frequency (N)	Percentage (%)
Age (years)		
≤30	6	17.1
31–40	7	20
41–50	4	11.4
51–60	11	31.4
61–70	5	14.3
>70	2	5.7
Mean±SD	59.65±16.03	
Range	17–82 years	
Sex		
Male	15	42.9
Female	20	57.1
Tumor size		
Small	7	20
Medium	22	62.9
Large	6	17.1
Tumor location		
Parasagittal	10	28.6
Convexity	9	25.7
Sphenoidal ridge	6	17.1
Tuberculum sellae	3	8.6
CP angle	3	8.6
Falcine	2	5.7
Tentorial	1	2.9
Petroclival	1	2.9

Table 2 demonstrates that the majority of tumors were WHO grade I (88.6%), while 11.4% were grade II. No grade III tumors were found.

Table 3 shows a significant association between progesterone receptor status and histopathological grade (p=0.013). Lower PR expression (<10%) was more common in WHO grade II tumors, whereas higher PR expression was seen mostly in WHO grade I tumors.

Table 4 indicates no significant association between progesterone receptor status and tumor size (p=0.099).

Table 2: Distribution of histopathological grading of meningioma (n=35).

WHO grade	Frequency (n)	Percentage (%)
Grade I	31	88.6
Grade II	4	11.4
Grade III	0	0
Total	35	100

Table 3: Association between progesterone receptor status and histopathological grade (primary outcome table).

Progesterone receptor status (%)	WHO grade I (n=31), N (%)	WHO grade II (n=4), N (%)	WHO grade III (n=0)	P value
<10	3 (9.7)	3 (75.0)	0	0.013
10–50	19 (61.3)	1 (25.0)	0	
51–80	9 (29.0)	0 (0.0)	0	
>80	0	0	0	

Statistical test: Fisher's exact test. Interpretation: a statistically significant association was observed between progesterone receptor status and histopathological grading (p=0.013)

Table 4: Association between progesterone receptor status and tumor size.

Progesterone receptor status (%)	Small (n=7)	Medium (n=22)	Large (n=6)	P value
<10	0	6	0	0.099
10–50	4	10	6	
51–80	3	6	0	
>80	0	0	0	

Statistical test: Fisher's exact test. Interpretation: no statistically significant association was found between progesterone receptor status and tumor size (p>0.05)

DISCUSSION

Intracranial meningioma has traditionally been considered a benign, encapsulated, and surgically curable tumor; however, recurrence remains a significant clinical concern. Reported recurrence rates range from 10–32% even after complete surgical excision.[2] Although the extent of resection, as described by Simpson's grading system, and the WHO histopathological grading are recognized as strong prognostic indicators, they do not always reliably predict tumor behavior. Recurrence rates of 7%, 40%, and 80% have been reported for WHO grade I, II, and III meningiomas, respectively.[13] Furthermore, late recurrences may occur even after 20 years in completely resected grade I tumors.[14] These observations suggest that additional biological markers, such as hormonal receptor status, may improve prognostic stratification. Hormonal influence in meningioma has been widely investigated since the first description of sex hormone receptors in these tumors by Donnell et al in 1979.[15] Earlier studies using

receptor-binding assays yielded variable results due to technical limitations.[10] The introduction of immunohistochemistry using monoclonal antibodies significantly improved the reliability of detecting PR expression in tumor tissue.[16,17] PR expression is now considered a potentially important biological and prognostic marker in meningioma. In the present study, a significant association was found between progesterone receptor status and histopathological grading (p=0.013). Lower PR expression (<10%) was predominantly observed in WHO grade II tumors, whereas higher PR expression (10–50% and 51–80%) was mainly seen in WHO grade I tumors. These findings suggest that reduced PR expression is associated with higher-grade tumors and possibly more aggressive biological behavior. Our findings are consistent with those of Roser et al, who reported significantly higher PR expression in benign meningiomas compared with atypical and anaplastic tumors.[18] Similarly, Cahill et al and Brandis et al observed decreased progesterone receptor expression in higher-grade meningiomas.[19,20] Maiuri et al also demonstrated that PR negativity was predictive of recurrence in benign meningiomas.[21] Shayanfar et al reported a reverse correlation between PR positivity and WHO grade, supporting the concept that PR expression decreases with increasing tumor grade.[22] The present study therefore reinforces the hypothesis that progesterone receptor status may serve as an additional prognostic indicator beyond conventional histopathological grading. In contrast, no significant association was observed between progesterone receptor status and tumor size (p=0.099) in this study. This finding aligns with reports by Fewings et al, who found no correlation between PR expression and tumor size, age, sex, or tumor location.[23] These observations indicate that PR status may reflect intrinsic tumor biology rather than tumor burden. With regard to demographic characteristics, the mean age in our study was 59.65±16.03 years, with most patients in the 51–60-year age group. A female predominance (57.1%) was observed, consistent with previous reports.[9,24] The higher PR expression observed among female patients in our study further supports the role of hormonal influence in meningioma pathogenesis. However, some investigators have reported no significant correlation between PR status and sex, suggesting that additional factors may modulate receptor expression.[23] The majority of tumors in this study were WHO grade I (88.57%), while 11.43% were grade II, and no grade III tumors were identified. These findings are comparable to previous large series, where approximately 80% of meningiomas were grade I and 15–20% were grade II.[5,24] The absence of grade III tumors in our study may be attributed to the relatively small sample size and short study duration. Clinically, headache was the most common presenting symptom (91.4%), followed by visual disturbances and seizures, findings that are comparable to reports by Moradi et al and Magill et al.[24,25] Parasagittal and convexity regions were the most frequent tumor locations, consistent with previously published data.[14,24] Overall, the present study demonstrates a statistically significant association between progesterone receptor status and histopathological grading in intracranial meningioma. Reduced PR expression was more common in higher-grade tumors, suggesting that progesterone receptor status may serve as a useful adjunct prognostic marker. Incorporating hormonal receptor evaluation into routine histopathological assessment may improve prediction of tumor behavior and help guide postoperative follow-up and management strategies.

Limitations

The study had a small sample size and was conducted in a single center, which may limit generalizability. No WHO grade III tumors were included, restricting comparison across all grades. The cross-sectional design and absence of long-term follow-up data prevented evaluation of recurrence and survival outcomes. Additionally, progesterone receptor assessment was based only on immunohistochemistry without advanced molecular analysis.

CONCLUSION

This study demonstrates a statistically significant association between PR status and histopathological grading in intracranial meningioma. Lower PR expression was more frequently observed in higher-grade tumors, suggesting that decreased progesterone receptor positivity may be associated with more aggressive tumor behavior.

Although most tumors in this study were WHO grade I, the findings support the potential role of progesterone receptor status as an additional prognostic marker alongside conventional histopathological grading. Larger studies with long-term follow-up are recommended to further establish its clinical significance.

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