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Is progesteron receptor status really a prognostic factor for intracranial meningiomas?

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ABSTRACT

Objective: Presence of steroid hormone receptors in meningiomas is well-known, but their correlation with tumour behaviour is unclear. The purpose of this study was to assess the relation between steroid hormone receptor expression and tumour behaviour.
Methods: We retrospectively reviewed 48 patients undergoing surgery for intracranial meningioma between January 2002 and December 2004. We included World Health Organization (WHO) Grade I meningiomas in Group 1 and WHO Grades II and III in Group 2. Tumour grade, progesterone receptor (PR), oestrogen receptor (ER) expressions, MIB-1 Index and Mitotic Index were assessed. We sought the correlation between tumour grade and MIB-1, Mitotic Indices, and also PR expression. Furthermore, the correlation between PR expression and MIB-1 and Mitotic Indices was assessed in Group 1 and Group 2, separately.
Results: 26 patients were in Group 1 and 22 patients in Group 2. PR expression was determined in 56% of the tumours while there was no ER expression. PR expression was found to be higher in Group 1 compared to Group 2. The Mean MIB-1 Index and the Mean Mitotic Index were significantly higher in Group 2 compared to Group 1. However, when Groups 1 and 2 were assessed separately, PR expression does not appear to be correlated with MIB-1 and Mitotic Indices in benign and also in non-benign meningioma groups.
Conclusion: Our findings suggest that tumour grade, but not PR expression, is correlated with meningioma behaviour.

1. Introduction

Meningiomas are common intracranial tumours and they constitute nearly 20% of all intracranial tumours. Although they are usually benign, up to 15% of these tumours have aggressive behaviour with atypical or malignant histological features [1,2]. Higher incidence of meningioma in woman, reports on rapid growth of meningioma during pregnancy and the association between meningioma and breast cancer suggested that sex steroids can play an important role in the growth of meningioma. Therefore, many studies have been performed to evaluate progesterone receptor (PR) and oestrogen receptor (ER) in these tumours [3–8], however these studies have failed to give constant results. In the literature, PR expression has been found in 50–85% of the meningiomas, although ER levels were usually found to be undetectable.

Studies evaluating the prognostic value of PR expression in meningiomas have been widely studied in the literature. Some researchers have found negative PR expression to be correlated with High Mitotic Index, high tumour grades, High Cellular Proliferative Index, and tumour recurrence, although the same correlation was not found by others [3–12]. However, the problem with assessing the correlation of PR expression with MIB-1, Mitotic Index and tumour grade is that benign and non-benign meningiomas are evaluated together for statistical analysis. This may cause a misevaluation. Although negative PR expression has been proposed to be a poor prognostic factor, PR expression is not correlated with MIB-1 and Mitotic Indices, when this is sought in benign meningiomas and non-benign meningioma groups separately.

The purpose of this study was to assess the association between PR expression and meningioma behaviour. For this purpose, the correlations between PR expression and MIB-1 Index and also

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Mitotic Index were sought in benign and non-benign meningioma groups, separately.

2. Materials and methods

2.1. Patient population

Patients undergoing surgery for intracranial meningioma at Okmeydani Training and Research Hospital between January 2002 and December 2004 were retrospectively reviewed. Patients were divided into two groups; Group 1: patients with benign meningioma (World Health Organization (WHO) Grade I) and Group 2: patients with non-benign meningioma (WHO Grades II and III). Ethics committee of Okmeydani Hospital approved the study.

2.2. Histopathology

Tumour specimens were fixed in 4.5% formalin solution for 24 h and were embedded in paraffin blocks. Embedded tissue sections measuring 3 μm in thickness were used for staining. Hematoxylin and Eosin staining was performed for histological diagnosis. Histological subtypes and grades were classified according to the WHO classification by single pathologist. The Mitotic Index was determined by counting the number of cells with mitotic figures found in 10 high-power field.

2.3. Immunohistochemical analysis

Assessment of PR, ER and MIB-1 (Ki-67) proliferation markers was performed using the manufacturers, neomarkers instructions for primary antibodies [ER(SP1)RB-9101-R for ER, PR(SP2)RM-9102-R1 for PR and Ki-67(SP6)RM-9106R1 for Ki-67 proliferation marker]. Strong nuclear staining was accepted as "positive" for Ki-67 and the Scale of Positivity was evaluated according to the percentage of positive cells. For ER and PR evaluation, any nuclear staining was accepted as positive. A breast cancer specimen was used as a positive control for PR and ER immunostaining.

Table 1
Summary of the patients and tumour characteristics.

Characteristic	Value
No. of cases (F/M)	48 (30/18)
The mean age in years	55.7 ± 12.6
Histological grade, no. of cases	
Grade I	26 (54%)
Grade II	16 (33%)
Grade III	6 (13%)
Progesterone receptor (PR), no. of cases	
Overall patients	27 (56%)
Group 1 (Benign meningioma)	19 (73%)
Group 2 (Non-benign meningioma)	8 (36%)
The mean MIB-1 (%)	
Overall patients	8.60 ± 12.86
Group 1	3.34 ± 3.27
Group 2	14.82 ± 16.82
PR (+) patients	5.72 ± 9.32
PR (−) patients	12.31 ± 15.8
The Mean Mitotic Index	
Overall patients	4.62 ± 9.83
Group 1	0.73 ± 1.37
Group 2	9.22 ± 13.15
PR (+) patients	2.62 ± 7.7
PR (−) patients	7.19 ± 11.7
Group 1	
The mean MIB-1 (%) (PR+/PR−)	3.10 ± 2.62/4.00 ± 4.8
The Mean Mitotic Index (PR+/PR−)	0.57 ± 1.1/1.14 ± 1.86
Group 2	
The mean MIB-1 (%) (PR+/PR−)	11.9 ± 15.5/16.47 ± 17.8
The Mean Mitotic Index (PR+/PR−)	7.5 ± 13.3/10.21 ± 13.4

2.4. Statistical analysis

Correlation of the tumour grade with PR expression, Mitotic Index, and MIB-1 Index was assessed. Also, correlation between PR expression and MIB-1 Index and also Mitotic Index were sought in benign and non-benign meningiomas, separately. Student's *t*-test, Mann–Whitney *U* test and chi-square tests were used for comparison of the 2 groups. Statistical analyses were performed with the software Statistical Package for the Social Sciences (SPSS) version 15.0. A p value of ≤ 0.05 was considered statistically significant.

3. Results

3.1. Patient population

Study included 48 patients (30 females and 18 males), and the mean age was 55.7 ± 12.6. The patients' characteristics were presented in Table 1. Histological examination revealed WHO Grade I benign meningioma in 26 patients, atypical Grade II meningioma in 16 and malignant Grade III meningioma in six. Twenty-six patients with Grade I meningioma were included in benign meningioma group (Group 1) and 22 patients with Grades II and III meningiomas were included in non-benign meingioma group (Group 2).

3.2. Progesterone receptor status

Nuclear immunostaining for PR was positive in 56% of the patients whereas no ER expression was detected. 73% of the tumours in Group 1 and 36% of the tumours in Group 2 showed PR expression. PR expression was found to be significantly higher in benign meningioma group (Group 1) compared to non-benign meningioma group (Group 2) ($p = 0.01$) (Table 2).

3.3. Immunohistochemical analysis

Immunostaining with MIB-1 antibody yielded interpretable results in all 48 specimens. Overall, the Mean MIB-1 Index was 8.60% ± 12.86% (mean ± SD). The Mean MIB-1 Index was 3.34% ± 3.27% in Group 1 and 14.82% ± 16.82% in Group 2. The Mean MIB-1 Index was significantly higher in non-benign meningioma group compared to benign meningioma group ($p = 0.001$). The Mean Mitotic Index was 4.62 ± 9.83 for all patients. The Mean Mitotic Indices in Group 1 and Group 2 were 0.73 ± 1.37 and 9.22 ± 13.15, respectively. The Mean Mitotic Index was higher

Table 2
The comparison between benign meningiomas and non-benign meningiomas in terms of their progesterone receptor expression, MIB-1 Index and Mitotic Index.

		Group		
		Benign (26) Mean ± SD	Non-benign (22) Mean ± SD	p
MIB-1 Index (%)		3.34 ± 3.27	14.82 ± 16.82	0,001*
Mitotic Index		0.73 ± 1.37	9.22 ± 13.15	0,001*
		No. of cases (%)	No. of cases (%)	p
Progesterone receptor	Positive	19 (73)	8 (36)	0.01*
	Negative	7 (26)	14 (64)	

* There is significant difference in MIB-1 Index, Mitotic Index and Progesterone receptor expression between benign and non-benign meningioma groups.