



## STUDY OF PROGNOSTIC SIGNIFICANCE OF ESTROGEN RECEPTOR AND PROGESTERONE RECEPTOR STATUS IN PATIENTS OF MENINGIOMA

### Pathology

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### ABSTRACT

Meningiomas are important benign tumors of the central nervous system and usually originates from the dura and arise from the meningotheial cells of the arachnoid matter. This study was mainly undertaken to evaluate the progesterone receptor and estrogen receptor status in meningiomas and their histopathological and immunohistochemistry correlation. A retrospective study was undertaken among 52 cases of meningioma admitted to department of neurosurgery at RIMS, Ranchi. About 30.8% of the patients in this study belonged to less than 30 years in this study. About 59.6% of the patients in this study were females. Meningothelial meningioma was the commonest meningioma in 50% of the cases followed by Psammomatous meningioma in 21.2%. The progesterone receptor was positive in 11.5% of the cases in this study. All the cases with progesterone receptor were females in this study. About 50% of the cases with meningothelial meningioma and Psammomatous meningioma had progesterone receptors. All the cases with progesterone receptors had no first year recurrence. The estrogen receptor was positive in 5.8% of the cases in this study. About 66.7% of the cases with estrogen receptors were females and 33.3% were males. There was first year recurrence in 9.6% of the cases in this study.

### KEYWORDS

meningioma, estrogen receptor, progesterone receptor, immunohistochemistry, tumour.

### INTRODUCTION

Meningiomas are predominantly benign tumours of adults, usually attached to the dura; that arise from the meningotheial cells of the arachnoid matter. The meningiomas are diverse set of tumours arising from the meninges, the membranous layers surrounding the central nervous system. Meningiomas account for about one third of all primary brain and central nervous system tumors. It is most common central nervous system tumour that occur with a frequency 19% at intracranial and 25% at spinal localization. They are derived from arachnoid cells of meninges. The incidence of meningioma increases progressively with age, with most cases occurring in older individuals. Meningiomas are rare in children. A number of factors have been incriminated in the etiology of meningiomas for a possible relationship to the development of meningiomas and other brain tumors. The common factors include ionizing radiation, radiation therapy for malignancy and incidental medical imaging are common risk factors. Some genetic and hormonal factors are also incriminated in the etiology. Meningiomas are most often slow growing tumors and symptoms at presentation are rarely precipitous, but more often insidious in nature. New onset and slowly evolving headache is common and usually unassociated with other symptoms suggestive of raised intracranial pressure, reflecting the slow growth of these tumours. The meningioma harbour different quantities of progesterone, estrogen, glucocorticoids, androgen, prostaglandin, dopamine, prolactin and growth factor receptors. The presence of hormonal receptors would help for hormonal manipulation of tumors in patients with tumor recurrence, incomplete surgical resection and in inaccessible tumors. Given this widespread role for estrogen in human physiology, it is not surprising that estrogen is also implicated in the development or progression of numerous disease, which include but are not limited to various types of cancer (breast, ovarian, colorectal, prostate, endometrial), osteoporosis, neurodegenerative diseases, cardiovascular disease, insulin resistance and others. Several investigators have detected progesterone receptors in high percentage of meningioma specimens and have noted progesterone receptors to be more common than estrogen receptors. The expression of estrogen and progesterone receptors may relate to tumour grade and recurrence. This study was mainly undertaken to evaluate the progesterone receptor and estrogen receptor status in meningiomas and their histopathological and immunohistochemistry correlation.

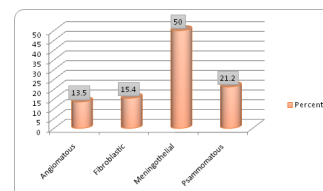
### MATERIAL AND METHODS

A retrospective study was undertaken among 52 cases of meningioma admitted to department of neurosurgery at RIMS, Ranchi. This study was conducted in the Department of Pathology, Rajendra Institute of Medical Sciences, Ranchi, Jharkhand. Clearance from institutional ethics committee was obtained before the study was started. An

informed, written and bilingual consent was obtained before including the study subjects in to the study. The records were examined for details of macroscopic examination of those specimens included in the study and the following details were noted. Study was conducted in Department of Pathology, Rajendra Institute of Medical Sciences, Ranchi. Cases comprised of patients admitted and operated in RIMS, and tissue sent for histopathology in Department of pathology. During the study period, 52 cases which were clinically, cytologically diagnosed as malignant were operated in Neurosurgery Department and its histopathology was done in Department of Pathology, Rajendra Institute of Medical Sciences, Ranchi. All these cases which were initially diagnosed by Hematoxylin and Eosin (H&E) stained tissue sections, immunohistochemistry using monoclonal antibody to estrogen receptor (ER) and Progesterone Receptor (PR) performed on two separate sections for each individual case. Tissue for histopathological study was obtained in the form of post-operative material and processed after proper grossing through steps of fixation, dehydration, clearing and impregnation until finally to block preparation and section cutting. The respective sections from all 52 cases were studied by selecting the areas showing good cellularity. A minimum of 200 cells per sections were counted for ER positivity and result expressed as positive or negative based on Allred scoring. Percentage of cells showing distinctive brown staining of the nuclei along with intensity of staining was taken into account. The results of both histopathology and immunohistochemistry were correlated with further prognosis of tumour. The mean follow up time of studied cases was 18 months. The data thus obtained was collected in a predesigned and pretested proforma. All the relevant data so collected were entered in the master chart and analysed using Statistical Package for Social Services (SPSS vs 20). Descriptive statistical evaluation was done by mean and median values and statistical significance was evaluated by T-test/ chi-square test as applicable. Values were presented as charts, bar etc. Results were discussed and correlated with the analysed literature and conclusions were drawn keeping in mind about the limitation of the study.

### OBSERVATIONS AND RESULTS

**Chart 1. Distribution of the study group according to histological type**

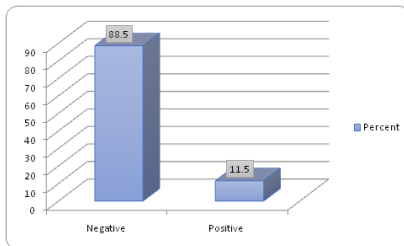


Meningothelial meningioma was the commonest meningioma in 50% of the cases followed by Psammomatous meningioma in 21.2%, Fibroblastic meningioma in 15.4% and Angiomatous meningioma in 13.5% of the cases.

**Table 1. Distribution of the study group according to Progesterone receptor**

PR	Frequency	Percent
Negative	46	88.5
Positive	6	11.5
Total	52	100

**Chart 2. Distribution of the study group according to Progesterone receptor**

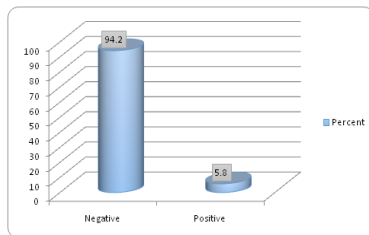


The progesterone receptor was positive in 11.5% of the cases in this study.

**Table 2. Distribution of the study group according to Estrogen receptor**

ER	Frequency	Percent
Negative	49	94.2
Positive	3	5.8
Total	52	100

**Chart 3. Distribution of the study group according to Estrogen receptor**



The estrogen receptor was positive in 5.8% of the cases in this study.

**Table 3. Distribution of the study group according to first year recurrence**

First year recurrence	Frequency	Percent
Negative	47	90.4
Positive	5	9.6
Total	52	100

**Table 4. Distribution of the study group according to Progesterone receptor with Sex**

Sex	Negative n (%)	Positive n (%)
Male	20 (40.8)	0
Female	29 (59.2)	6 (100)
Total	46 (100)	6 (100)

$\chi^2$  value=4.59 df=1 p value=0.032, Sig

All the cases with progesterone receptor were females in this study. This difference in presence of progesterone receptors was statistically significant between the two sexes.

**Table 5. Distribution of the study group according to estrogen receptor with sex**

Sex	Negative n (%)	Positive n (%)
Male	20 (40.8)	1 (33.3)
Female	29 (59.2)	2 (66.7)
Total	49 (100)	3 (100)

$\chi^2$  value=0.066 df=1 p value=0.798, NS

About 66.7% of the cases with estrogen receptors were females and 33.3% were males. This difference in estrogen receptors and sex was not statistically significant.

**DISCUSSION**

The progesterone receptor was positive in 11.5% of the cases in this study. About 33.3% of the cases with progesterone receptors were aged between 31 – 40 years and 51 – 60 years. About 16.7% of the cases belonged to less than 30 years of age and more than 60 years of age. All the cases with progesterone receptor were females in this study. About 50% of the cases with meningothelial meningioma and Psammomatous meningioma had progesterone receptors. All the cases with progesterone receptors had no first year recurrence. Milenkoiv et al had shown that, 57% of the patients had progesterone receptors. PR were positive in 47.5% tumours in females and 69.23% tumours in males. Age tumour localization and histological subtype did not correlate with PR status. In a study by Hilbig et al, 58.3% were positive for PR and 48.2% were positive among non typical. Patient's age, gender and histological subtypes have not correlated with PR status. Among non typical tumours, the recurrence was higher when meningioma was negative than when it was positive for PR but not statistically significant. In a study by Taghipour et al, 68.6% had negative progesterone receptors. The frequency of positive receptors in patients with benign tumours was significantly more in benign tumours than the anaplastic and atypical groups. The correlation between the positive progesterone receptor and sex was statistically significant with sex.

**The Estrogen receptor**

The estrogen receptor was positive in 5.8% of the cases in this study. About 33.3% were aged between 31 – 40 years, 41 – 50 years and 51 – 60 years of age had estrogen receptors in this study. About 66.7% of the cases with estrogen receptors were females and 33.3% were males. About 33.3% of the cases with estrogen receptors had angiomatous, fibromatous and meningothelial meningiomas in this study. All the cases with estrogen receptors had no first year recurrence in this study. In a study by Milenkovic et al, all the tissues were negative for ER status. In a study by Hilbig et al, the estrogen receptors were negative in all the specimens tested.

**First year recurrence**

There was first year recurrence in 9.6% of the cases in this study. In a study by Hilbig et al, the rate of recurrence was 13% among all the cases, including 3.78% of the typical, 42.5% of the atypical and 45.5% of anaplastic.

**CONCLUSION**

This study was mainly undertaken to find the ER and PR and their association with the meningiomas. Age above 40 years and female sex were found to be associated with the meningiomas. Meningothelial meningioma was common meningioma in this study. The recurrence was less in this study in order to establish the association of ER and PR with the meningioma. This study is not without limitations. This was a retrospective study which has weakness by the methodology itself and the sample size was not calculated and sampling method was not followed. Hence further study with a sound methodology, scientific calculation of the sample size and a good sampling method can bring out more facts about the association of ER and PR with prognosis.

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