

A 3 Year Retrospective Study of Meningiomas in a Tertiarycare Hospital with an Emphasis on Atypical Meningiomas

Dr.D.Gowri Manohari¹ · Prof.K.Rama²

¹(Pg Student ,Institute Of Pathology, Madras Medical College)

²(Profesor Of Pathology ,Institute Of Neuropathology, Madras Medical College)

Corresponding author: Dr.D.Gowri Manohari

Abstract: Background: Meningiomas are tumours that arise from a layer of tissue (the meninges) that covers the brain and spine. Most are considered “benign” because they are slow-growing with low potential to spread.

Methods: This is a retrospective study conducted at Department of neuropathology, Institute of neurosurgery MMC/RGGGH from January 2015 to December 2017. A total of 230 cases of meningiomas were reviewed and classified into grade I, II and III based upon WHO 2016 classification of tumors of CNS. IHC markers were done in deserving cases. Atypical and recurrent meningiomas were analysed and evaluated with proliferation markers and their biologic behaviour studied.

Results: In our Institute out of the 1130 cranial and spinal tumors, the incidence of meningioma is 20.35%. Among 132 paediatric tumor cases 2.2% were meningiomas. Out of the 230 meningiomas operated at this Institute, 92.60% were grade I, 6.08 % were grade II and 1.30% were grade III. The incidence of atypical meningiomas was 4.34 % applying the latest classification. The peak incidence of meningiomas are fourth and fifth decade The recurrence rate was 2.17% .

Conclusion : Meningiomas exhibit a broad range of histologic patterns and cellular features In our study we have emphasised that an accurate histopathological interpretation and use of proliferative markers are essential for predicting the prognosis , aggressiveness and recurrence . Further improvements in interobserver concordance will require clarification of subjective morphologic criteria, and identification of objective molecular biomarkers that more accurately predict tumour biology.

Key Words: Meningioma, WHO grade, atypical, skull base, non skull base, EMA, ki 67

Date of Submission: 30-07-2018

Date of acceptance: 17-08-2018

I. Introduction

In 1922, Harvey Cushing coined the term Meningioma for tumours arising from the meninges¹. Meningiomas are a diverse group of neoplasm arising from the meningotheial cells of leptomeninges. They comprise one third of all CNS tumours. They are mostly solitary and slow growing, affecting females more than the males. Age group commonly affected are between 40-60 years. Meningiomas are mostly benign, localized in intracranial, intraspinal or orbital locations. Uncommon locations are intraventricular, epidural and very rarely extramural. Since they are slow growing, they produce symptoms due to compression of adjacent structures, the common symptoms being headache and seizures.

Grading: The 2016 WHO classification classifies into grade I, II and III. Grade I tumours are mostly benign, less aggressive and have low recurrence rate, whereas grade II and III have features such as mitotic figures, macro nucleoli and necrosis. They are more aggressive and have more recurrence rate. Benign meningiomas have recurrence rate of about 7-25% whereas atypical have recurrence of 29-52% and anaplastic have 50 – 94% recurrence rates.

Atypical meningiomas: Atypical meningiomas belongs to WHO Grade II. In 2016 classification brain invasion joins a mitotic count of 4 or more as a histologic criterion that can alone suffice for diagnosing an atypical meningioma. They can also be diagnosed based on at least three of the following features.

- Increase cellularity
- Small cells with high nuclear to cytoplasmic ratio
- Prominent Nucleoli
- Sheetting Pattern
- Foci of spontaneous necrosis.

Recurrence: Male sex, non skull base locations and prior surgery are considered as risk factors. Brain invasion is characterized by irregular, tongue shaped and sheet like growth without intervening layer of leptomeninges. Similarly bone invasion is also associated with increased recurrence rate.

Immunohistochemistry: Majority of meningiomas are EMA and vimentin positive Ki 67 is used as a proliferation marker. Ki 67 index > 4% are associated with increased recurrence rates.

Aim of study: Our aim of the study was to assess the age wise incidence, various histomorphological variants and recurrence rate in our institute and compare it with national and international literature.

II. Materials And Methods

It is a retrospective study for a duration of three years from January 2015 to December 2017 received in our department of neuropathology, Institute of neurosurgery Madras Medical College.

Inclusion criteria: Of all CNS tumours, only cases of meningiomas during the period 2015 – 2017 were included. Meningiomas in all age groups, sites and both the sexes were included.

Exclusion criteria: Other CNS tumours were excluded.

Sample size: 230 cases of meningiomas

Methodology: Based on Histological and IHC features, grading of meningiomas was done as per the WHO 2016 classification. various parameters were studied and compared with national and international data on meningiomas.

Specimens were received from the Institute of neurosurgery, fixed in 10% formalin and processed as per specified guidelines. The clinical features, imaging and per operative findings were analysed. Histological subtyping were done as per WHO classification 2016. All the cases reported as atypical meningiomas and recurrent meningiomas were reviewed. Ki67 proliferative marker study was done to analyse the aggressive behaviour and recurrence potential.

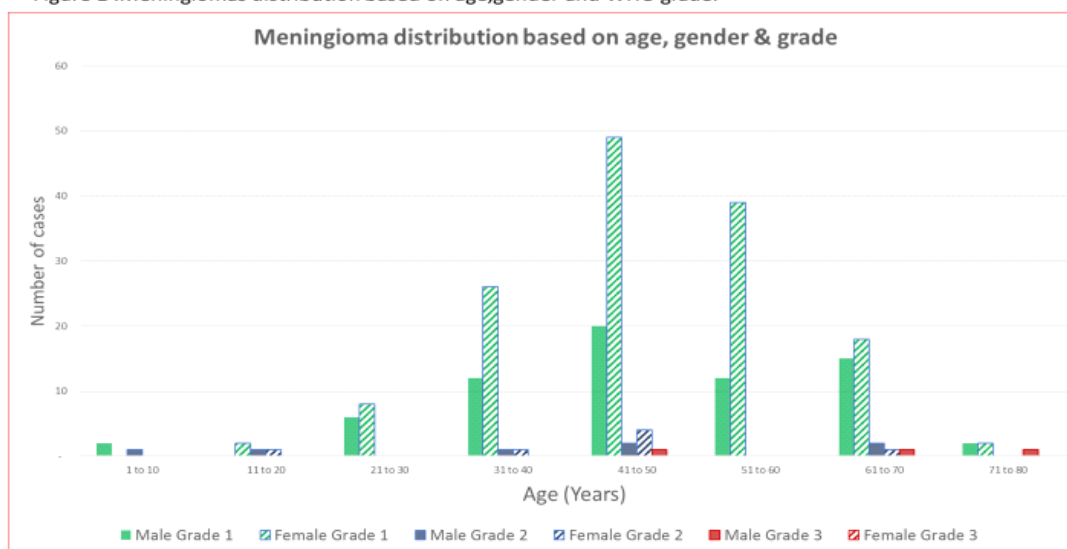
III. Results

Overall incidence: In our Institute out of the 1130 cranial and spinal tumours, the incidence of meningioma is 20.35%(230).

Distribution based on age ,sex, tumour grade and recurrence:

The peak incidence of meningiomas were between 4th and 5th decade , whereas atypical meningioma was in 6th decade.

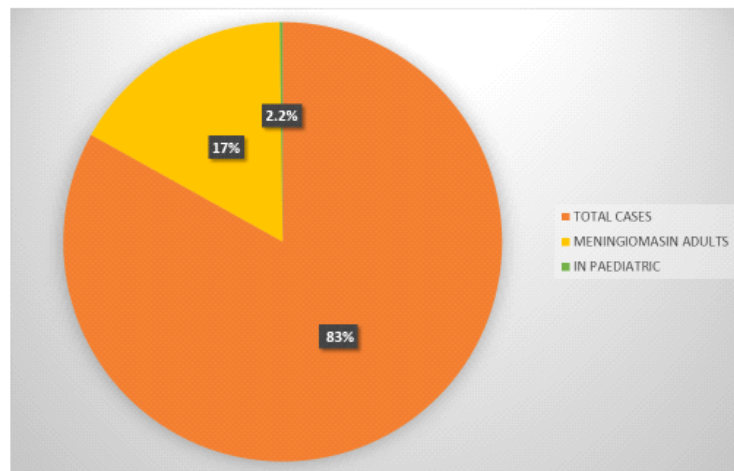
Figure 1 :Meningiomas distribution based on age,gender and WHO grade.



The male to female ratio was nearly 1:3 ,(66.22% in females and 33.77% in males).Tabular column 1 depicts the incidence of meningiomas in males and females based on WHO grade.

Out of the 230 cases histologically proven meningiomas, 213(92.60%) were WHO grade 1, 14 cases (6.08 %) were grade II and 3 cases (1.30%) were grade III. Of these 10 cases (4.34 %) were atypical meningiomas. The recurrence rate was 2.17%(5)

Figure 1 shows the incidence of meningiomas in adults and paediatric age group



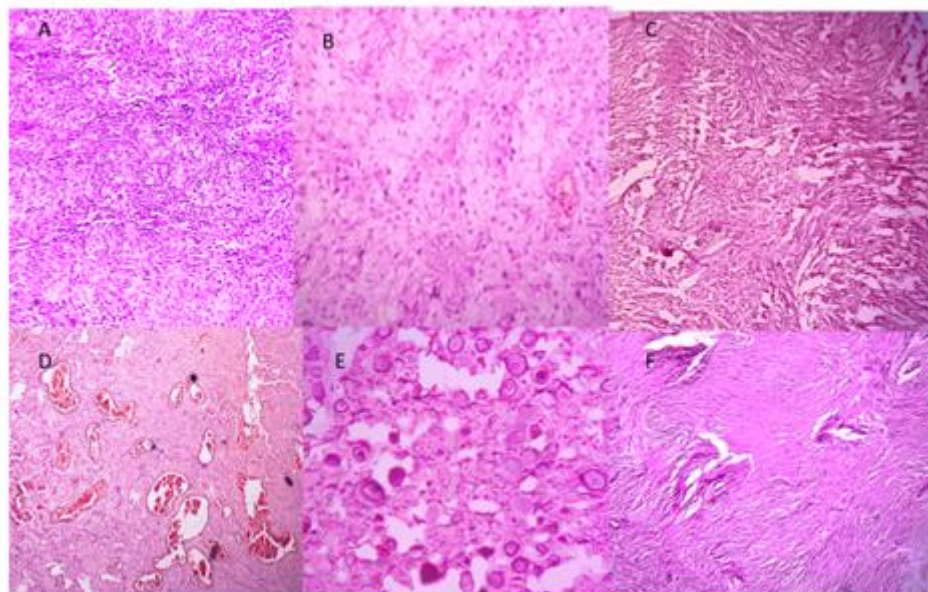
Distribution in paediatric age group Among 132 paediatric tumour cases 2.2% (3 cases) were meningiomas. Figure 1 shows the incidence of meningiomas in adult and paediatric age group among the total cranial and spinal tumours.

Distribution based on histologic subtypes: Of the grade I meningiomas , meningothelial meningiomas were the commonest accounting for 57.82% (133) followed by transitional 13.9% (32) , fibrous 11.3%(26),psammomatous 6.9%(16),microcystic 1.3% (3)and angiomatous 1.3%(3). Figure 2 depicts the histological pictures of WHO grade 1 meningiomas in the present study.

Among the grade II meningiomas atypical were 5.70% (10) clear cell were 0.8%(2) chordoid 0.8%(2). Figure 3 depicts the histological features of atypical meningioma and also other variants of grade II meningiomas.

Among the grade III variants papillary constitutes 0.4%(1) and anaplastic 0.8%(2). Figure 4 depicts grade III meningiomas presented during the study period.

Figure 2:Histological pictures of grade I meningiomas in H&E staining A) 10 X-Meningothelial B) 40 X microcystic C) 10 X transitional D) 10 X angiomatous E) 10 X- psammomatous F) 10 X-fibrous .



meningiomas.

Figure 3: H&E staining A) 4 X -atypical meningioma showing brain invasion B) 40 X- increased nuclear cytoplasmic ratio C)10 X-sheeting appearance D) 10 X-chordoid meningioma E) 40 X-clear cell meningioma F) 40 X-atypical meningioma shows rhabdoid features

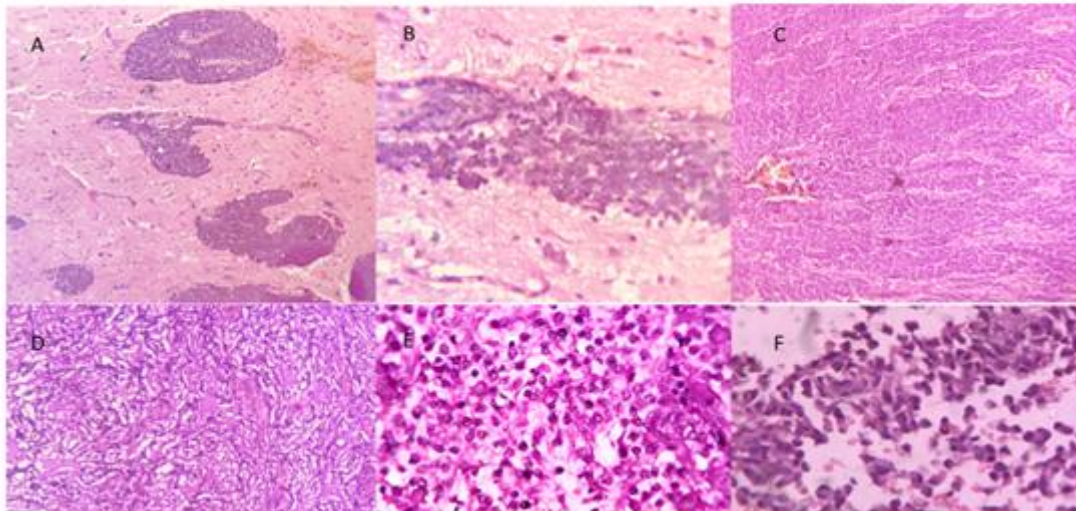
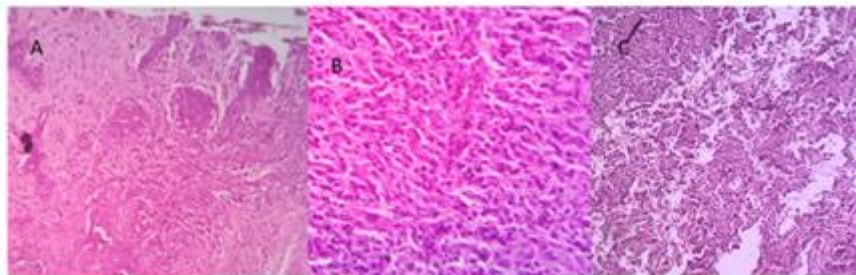


Figure 4 WHO grade III meningiomas in H&E staining A)4x- anaplastic meningioma showing brain invasion B)40 x -nuclear atypia in anaplastic meningioma c)10 x papillary meningioma.



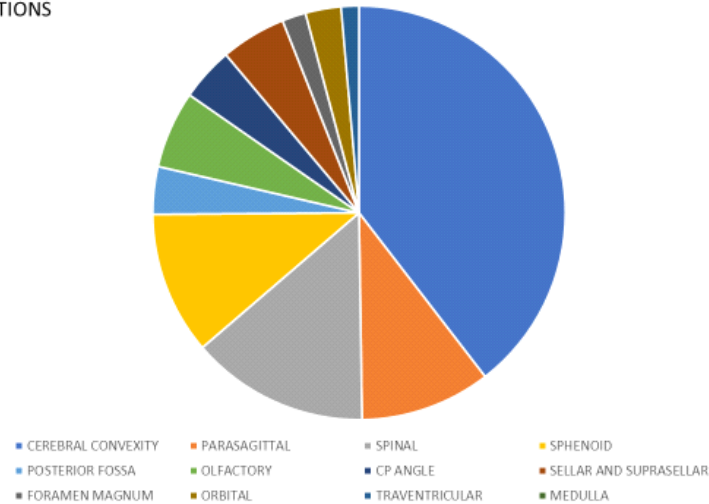
Tabular column 2 :Incidence of meningiomas based upon WHO grade.

S.NO	TYPE	WHO GRADE	NO.OF CASES	PERCENTAGE
1.	MENINGOTHELIAL	I	133	57.8%
2.	TRANSITIONAL	I	32	13.9%
3.	FIBROUS	I	26	11.3%
4.	PSAMMOMATOUS	I	16	6.9%
5.	ANGIOMATOUS	I	3	1.3%
6.	MICROCYSTIC	I	3	1.3%
7.	ATYPICAL	II	10	4.34%
8.	CLEAR CELL	II	2	0.8%
9.	CHORDOID	II	2	0.8%
10.	PAPILLARY	III	1	0.4%
11.	ANAPLASTIC	III	2	0.8%

Tabular column 2 shows the number of meningiomas according to their grading.

Distribution based on location: Of the 230 cases, 64.7% (149) were located in the non skull base areas and 35.3% (81) were located in the skull base areas. Among the non skull base areas 85 cases were located in the cerebral convexities followed by 30 cases in the spinal region .The next common location is parasagittal areas were 22 cases were located. Among the skull base meningiomas 24 were located in the sphenoid region followed by 13 cases in the olfactory region. Among the 30 spinal ,76%(23) were located in the thoracic level and 24%(7) were located in the cervical

FIGURE 5-PIE CHART TO SHOW THE DISTRIBUTION BASED OF MENINGIOMAS BASED ON LOCATIONS



region. Figure 5 shows the distribution of meningiomas based on their locations in our study group. Tabular column 3 and 4 shows the distribution of meningiomas located on the non skull base and skull base areas.

LOCATION	MALE	FEMALE	TOTAL CASES
CEREBRAL CONVEXITY	31	54	85
PARASAGITTAL AREA	6	16	22
INTRAVENTRICULAR	3	0	3
SPINAL	9	21	30
MEDULLA	0	1	1
POSTERIOR FOSSA	2	6	8
TOTAL	51	98	149

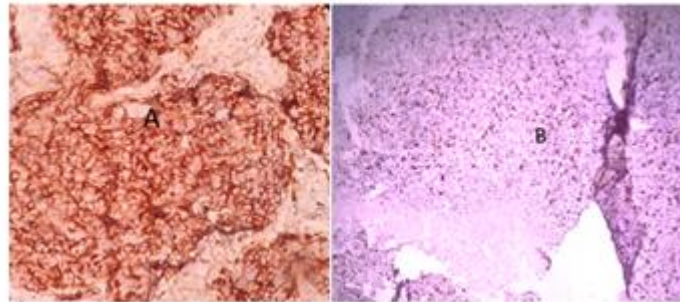
TABULAR COLUMN 4 TO SHOW THE DISTRIBUTION OF MENINGIOMAS IN MALES ANDFEMALES BASED ON LOCATION IN SKULL BASE AREAS

LOCATION	MALE	FEMALE	TOTAL CASES
SPHENOID REGION	10	14	24
FALCINE AND PARAFALCINE	2	6	8
OLFACTORY GROOVE	5	8	13
ORBITAL	2	4	6
CP ANGLE	0	9	9
CLIVAL	2	4	6
SELLAR AND SUPRASELLAR	1	10	11
FORAMEN MAGNUM	1	3	4
TOTAL	23	58	81

IV. Immunohisto chemistry:

Meningiomas show diffuse positivity for EMA,S 100 and vimentin .The most reliable marker is EMA in which 50 – 100% of the cases are positive, however the staining pattern is weak and diffuse. EMA was mainly used to exclude other differential diagnosis, .ki 67 is used as a proliferation marker. Figure 6 shows EMA positivity and ki 67 proliferation index which was used to confirm a case of chordoid meningioma. Other markers used are prostaglandin D synthase, E-cadherin, claudin -1, desmosomal plaque components such as desmoplakinandconnexins.

Figure 6 Immunohistochemistry staining A) Figure showing EMA positivity in 40 X B) ki 67 showing 20% proliferation index in 10 X



Recurrence Rate: The recurrence rate of meningiomas in present study is 2.17% (5 cases). Grade I constitute 60%(3/5) and grade II constitutes 40% (2/5) of the total recurrence. Figure 7 shows the recurrence percentage in grade I and grade II meningiomas.

V. Discussion:

The term meningioma was first coined by Cushing .^[1] Meningiomas account for 36% of all CNS tumours and are the most common tumours arising from the meninges. The incidence of meningioma in India ranges from 9-15 per cent of all intracranial neoplasms according to a study by Dr. Vincent Thamburaj. In our present study ,230 meningiomas were analysed and the overall incidence of meningiomas among CNS tumors was found to be 20.35%.^[4]Paediatric incidence is 2.2 % which is in concordance with other studies. ^[7,8]The most common age group is 41-50 which is parallel with other studies .^[3,4] The male to female ratio is 1:3 which is parallel with CBTRUS statistical report ^[2] and other studies. ^[3,4,5] .The higher incidence of meningiomas is observed in females in the age group og 41-50 .^[6] The incidence of grade I,II and III also parallels with other studies. ^[2,3]

Tabular column 5 :comparison of present study with other studies

	THOMAS BACKER ET AL	REDDY ET AL	PRESENT STUDY
GRADE I	69.9%	89.6%	92.98%
GRADE II	29.1%	5.2%	5.70%
GRADE III	1%	5.2%	1.31%

Tabular column 5 shows the comparison of present study with Reddy et al and Thomas et al.

The most common meningioma is meningothelial and other grade I meningiomas, followed by grade II and grade III meningiomas.^[9]

Recurrence Rate

To predict the aggressiveness and recurrence of benign and malignant meningiomas tumour grading and extent of surgery are important factors .The recurrence rate of meningiomas in present study is 2.17% (5 cases). Grade I constitutes 60%(3/5) and grade II constitutes 40% (2/5) of the total recurrence . Among the 3

grade I cases, 2 cases had features such as foci of necrosis and mild nuclear pleomorphism which probably increased the aggressiveness of the tumour. Other factors contributing recurrence are male sex, non skull base meningiomas and prior surgery. In present study, out of 5 recurrent meningiomas, 4 were in male sex. Based on location 4 were in non skull base areas which is in concordance with 1. Interestingly we found the ki 67 proliferation index was more than 5% in a case of recurrent meningothelial meningioma. In another case of recurrent atypical meningioma, the proliferation index was 4%. This is in parallel with the WHO classification of tumors of central nervous system which say that meningiomas with an index of more than 4% have an increased risk of recurrence similar to that of atypical meningioma. Hence a meticulous histopathological analysis like mitotic count and proliferation markers are also mandatory. Also the nature of surgery plays an important role in recurrence. Subtotal resections are associated with greater recurrence rates.^[10] In present study, all the recurrent cases underwent sub total resection which is in parallel with other studies.^[10, 11, 12]

Atypical Meningioma: Prior WHO classifications had considered brain invasion a staging feature rather than a grading feature, in the 2016 classification brain invasion joins a mitotic count of 4 or more as a histological criterion that can alone suffice for diagnosing an atypical meningioma.^[9]

Atypical meningiomas constitutes 4.34% (10 cases).^[2] Out of 10 cases 6 were in non skull base areas, a tendency that has been observed by other studies also.^[14] In present study we have also found that females are more affected (6 out of 10 cases) and median age of presentation is 41- 50. As atypical meningiomas commonly occur in the fourth decade.^[13] 2 out of 10 cases had brain invasion, 7 cases had features such as prominent nucleoli, increased mitotic count and increased nuclear cytoplasmic ratio. 1 out of 10 cases had rhabdoid features. Hence differential diagnosis of metastatic carcinomatous deposits was considered. Different immunohistochemistry markers were used to confirm the diagnosis. The tissue was subjected to cytokeratin and ki67. Cytokeratin was negative which ruled out metastatic deposits and ki 67 was found to be 25%, hence atypical meningioma with rhabdoid features was given as final report.

Spinal Meningiomas:

In present study out of 230 cases, 30 (13.04%) were spinal meningiomas.^[17] Among them 76% (23) were at the level of thoracic region. The next commonest location is cervical. 24 cases were presented as intradural extramedullary^[13] and one case was intradural and intramedullary.

Immunohisto chemistry:

Immunohistochemistry is used mainly to confirm meningiomas from other differential diagnosis and to know the proliferation index. In our study, EMA was used to confirm a case of chordoid meningioma in a six year old male child who presented with space occupying lesion in the clival area.^[14] ki 67 was used as a proliferation index to predict the aggressiveness of meningiomas.^[15] Meningiomas with proliferation index of more than 4% have an increased risk of recurrence. And index of more than 20% are associated with very bad prognosis.

VI. Conclusion:

Meningiomas are slow growing tumours arising from the meningothelial cells accounting for 20.17% of all CNS neoplasms with a wide variety of histological patterns. Our study shows that these tumours are common in women and Grade I tumours are predominant. Our study also suggest that WHO grading based on the histopathological features alone has certain limitations. Hence, the use of immunohistochemical markers aids in determining the aggressive nature of the tumour and its recurrence potential. Recurrence of tumour depends on tumour grade and extent of surgery. Further improvements in interobserver concordance will require clarification of subjective morphologic criteria, and identification of objective molecular biomarkers that more accurately predict tumour biology.

Dr.D.Gowri Manohari " A 3 Year Retrospective Study of Meningiomas in a Tertiarycare Hospital with an Emphasis on Atypical Meningiomas."IOSR Journal of Dental and Medical Sciences (IOSR-JDMS), vol. 17, no. 8, 2018, pp 77-83.