

Study of Clinico-Pathological Spectrum of Meningioma with WHO Grading

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ABSTRACT

Introduction: Meningiomas are the most frequent non glial primary Central Nervous System (CNS) tumour. Several histopathological patterns of meningiomas are classified and graded. A standard classification system aims at providing a tool for estimating the recurrence and overall survival of meningioma patients.

Aim: The aim was to study clinical, radiological and pathological presentation of Meningioma and to grade meningiomas according to 2016 WHO classification in a tertiary care centre.

Materials and Methods: It is an observational study of 51 cases of meningioma conducted in the department of Pathology, SDM college of Medical sciences and Hospital, Dharwad from June 2011 to June 2021. The demographic details, clinical features, radiological findings, histopathological findings and grading of meningioma according to 2016 WHO classification were analysed.

Results: A total of 51 meningioma cases were studied in which age ranged between 16 and 79 years. Among 51 cases, 33 (64.70 %) were females and 18 (35.29 %) were males. The most common symptom was headache seen in 39 patients (76.47%) followed by vomiting in 11 patients (21.56%). Radiologically, commonest lobe involved was frontal lobe in 22 cases (43.13%). The most common histological subtype was meningothelial meningioma in 18 (35.29%) cases followed by psammomatous meningioma in 13 (25.49%), transitional meningioma in 12 (23.52%), fibroblastic meningioma in 4 (7.84%), atypical meningioma in 2 (3.92%), secretory meningioma 1 (1.96%) and microcystic meningioma in 1 (1.96%) case. A total of 49 (96.07%) cases of meningiomas were of Grade-I & 2 (3.92 %) were of Grade-II with none in Grade-III.

Conclusion: Meningiomas occur more commonly in females than in males with multiple clinical presentation. Histopathological examination helps to type the meningioma and grade them accordingly.

Keywords: Histopathological Grading, Meningioma, WHO classification

INTRODUCTION

Meningiomas are the most common non-glial primary dural based intracranial tumours arising from the leptomeninges and they account for 15-30% of the primary brain neoplasms [1,2]. Meningioma arises from the arachnoid cap cells of the arachnoid villi in the meninges. The environmental risk factors implicated in the development of meningioma are ionising radiation and the risk is higher if exposed in childhood than as adults. They can occur at any age with an increasing risk with a higher age and with a female to male ratio of approximately 2:1 [3].

Meningiomas are typically slow growing with an insidious onset, many of which are identified as an incidental finding on imaging studies. They can arise from the intracranial, spinal and very rarely from the intraventricular region.

The clinical features of meningiomas like any other CNS tumour depend on the location of the tumour. The clinical features of meningiomas are vague and are due to local compression and increased intracranial tension. Meningioma patients can present with headache, generalised or partial seizures (caused by a local mass effect). Personality changes, confusion, altered consciousness may be a feature which may get initially misdiagnosed as depression or dementia. The differentials of a patient with such symptoms should include gliomas or metastatic tumours [4].

Magnetic Resonance Imaging (MRI) is the gold standard modality for the diagnosis of meningiomas. MRI typically shows a dural based, homogeneously enhancing well circumscribed lesion. Benign meningiomas classically show thickened, contrast enhancing 'Dural tail'. On CT, calcifications, bony changes such as hyperostosis and a 'beaten brass' appearance of the remodelled skull can be well appreciated in the tumours located near the convexity [5].

Histologically, meningiomas are heterogeneous group of tumours categorised into 14 distinct subgroups with three grades of

malignancy. The current WHO grading system incorporates various histological features to classify and grade the meningiomas. These features have been found to be of prognostic importance by several clinicopathological studies [6,7]. However, the assessment of grading is subjective. This makes practical application of the grading rather difficult. Based on histology {mitosis, criteria of 3 of 5 histological features: spontaneous necrosis, sheeting (loss of whorling or fascicular architecture), prominent nucleoli, high cellularity and small cells} and clinical behaviour (brain invasion), WHO 2016 classification categorises meningiomas into three grades: Grade-I (benign), Grade-II (atypical) and Grade-III (anaplastic/malignant) [8].

The known risk factors for recurrence include histological grade, specific subtypes, subtotal resection, young age of occurrence, brain infiltration and a high proliferation rate [9].

The present study was undertaken to evaluate the demographic details, clinical presentation, radiological and histopathological findings in meningioma patients and to classify the meningioma into three grades according to WHO 2016 grading system.

MATERIALS AND METHODS

The present study is an ambispective (retrospective and prospective) study carried out for a period of 10 years. Retrospective from 1st June 2011 to 31st May 2020 and prospective from 1st June 2020 to 31st May 2021. All excisional biopsies of meningioma received from department of Neuro surgery to the department of Pathology, SDM college of Medical sciences were included in the study. Inadequate and non representative samples were excluded. Institutional ethical clearance was taken (SDMCDS IEC.No.2021/ Medical/ Pathology/ PG/ 04).

Detailed clinico-radiological history was obtained from the hospital medical record section and laboratory information system. Recorded

clinical data included age, sex, presenting complaints, significant past history, site of lesion and radiological examination findings.

The specimens were processed as per the standard protocol of the histopathology laboratory. The specimens were fixed in 10% buffered formalin for 24 hours, after detailed gross examination the tissues were processed in a tissue processor. The processed tissues were paraffin embedded and sections were cut at 4-5 microns thick and stained with Haematoxylin and Eosin (H&E) stain and thoroughly examined. Routine H&E stained paraffin sections of retrospective cases were reviewed without knowledge of prior grading. New sections were cut if lost or when staining had faded. The histopathological diagnosis and grading was done as per 2016 WHO Grading system [Table/Fig-1] [8].

Grade-I	Grade-II	Grade-III
Recognised by their histologic subtype and lack of anaplastic features	Defined by one or more of the following four criteria	Defined by rhabdoid or papillary subtypes, a histological picture of frank sarcomatous or carcinomatous histology
1. Mitotic count <4/10 HPF	1. Atypical chordoid or clear cell histologic subtype	1. Mitotic count of 20 or more/ 10 HPF
2. Absence of brain invasion	2. 4 to 19 mitosis/10 HPF	2. Specific histological patterns: rhabdoid or papillary meningioma
3. Histologic subtypes: Meningothelial, fibrous, transitional, psammomatous, microcystic, angiomatous, secretory, lymphoplasmacytic rich.	3. Brain infiltration	
	4. Three or more of the following: a) Small cell change; b) increased cellularity; c) prominent nucleoli; d) sheet like growth; e) necrosis	

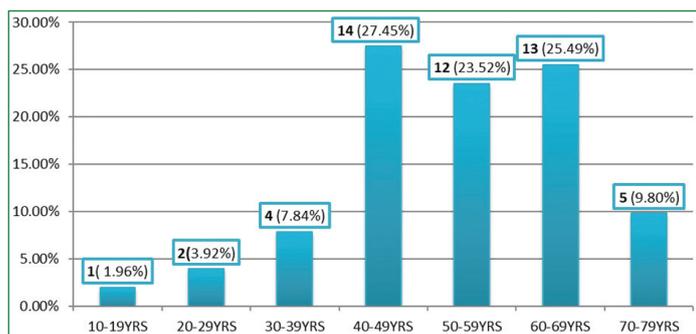
[Table/Fig-1]: WHO grades of meningioma [8].

STATISTICAL ANALYSIS

Statistical analysis was carried out by using Microsoft Excel. Total numbers and percentages of age wise distribution, sex distribution, tumour location on radiology, histopathological type and grading were calculated and comparison with other studies was carried out.

RESULTS

A total of 51 cases of meningioma were studied and analysed, of which 33 (64.70%) were female and 18 (35.29%) were male patients. The female: male ratio being 1.83. The age wise distribution graph showed, the most common age group of meningioma were between 40-49 years consisting of 14 cases (27.45%), followed by 60-69 years with 13 cases (25.49%), 50-59 years with 12 cases (23.52%), 70-79 years with five cases (9.80%), 30-39 years with four cases (7.84%), 20-29 years with two cases (3.92%) and 10-19 years with one case (1.96%) [Table/Fig-2].



[Table/Fig-2]: Age wise distribution.

Meningioma patients presented with multiple clinical symptoms. The most common being headache seen in 39 cases (76.47%) [Table/Fig-3]. Majority of patients had combination of symptoms.

Sl no	Clinical symptoms	Number of patients	Percentage
1	Headache	39	76.47%
2	Vomiting	11	21.56%
3	Diminution of vision	9	17.64%
4	Backache	3	5.88%
5	Tingling and numbness	2	3.92%
6	Blurring of Vision	1	1.96%
7	Neck pain	1	1.96%
8	Loss of consciousness	1	1.96%
9	Lower limb pain	1	1.96%

[Table/Fig-3]: Clinical presentation of 51 meningioma cases.

Radiologically, the location of meningiomas in decreasing order were supratentorial 45 (88.23%) >spinal 4 (7.84%) >infratentorial 2 (3.92%). Frontal region was the most common with 22 (43.13%) cases [Table/Fig-4].

Location	Exact site	Number of cases	Percentage
Supratentorial	Vestibular	1	(1.96%)
	Frontal	22	(43.13%)
	Temporal	2	(3.92%)
	Supra and parasellar	1	(1.96%)
	Sub occipital	1	(1.96%)
	Sphenoid	3	(5.88%)
	Parietal	3	(5.88%)
	Parieto-occipital	1	(1.96%)
	Para-sagittal	4	(7.84%)
	Olfactory groove	1	(1.96%)
	Occipital	1	(1.96%)
	Lateral ventricle	1	(1.96%)
	Fronto-parietal	4	(7.84%)
Infratentorial	Basal dura	1	(1.96%)
	C-P angle	1	(1.96%)
Spinal	Dorsal spine	3	(5.88%)
	Cervical spine	1	(1.96%)

[Table/Fig-4]: Site wise distribution of meningioma on radiology.

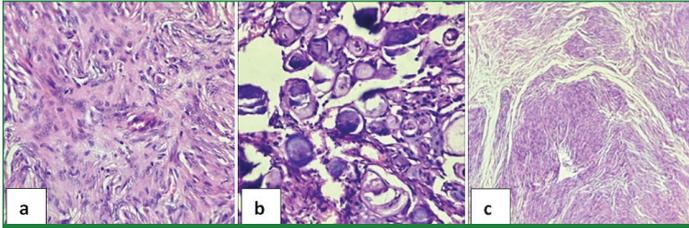
Histopathological examination of 51 cases of meningioma was carried out. The frequently encountered meningioma was meningothelial type of meningioma 18 (35.29%), followed by psammomatous meningioma 13 (25.49%), transitional meningioma 12 (23.52%), fibroblastic meningioma four (7.84%), atypical meningioma two (3.92%), secretory and microcystic meningioma one each (1.96% each) [Table/Fig-5-7].

Sl no	Histopathological type of meningioma	Number (%)
1	Meningothelial meningioma	18 (35.29%)
2	Psammomatous meningioma	13 (25.49%)
3	Transitional meningioma	12 (23.52%)
4	Fibroblastic meningioma	4 (7.84%)
5	Atypical meningioma	2 (3.92%)
6	Secretory meningioma	1 (1.96%)
7	Microcystic Meningioma	1 (1.96%)

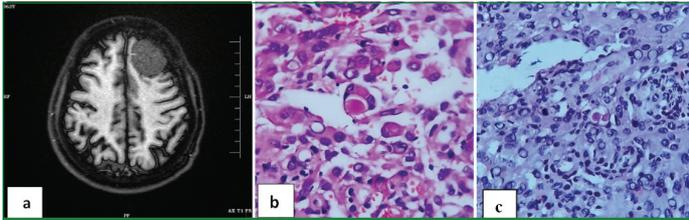
[Table/Fig-5]: Histopathological types of meningioma.

Comparison of clinical, radiology and histopathology diagnosis were tabulated [Table/Fig-8]. It was observed that 37 (72.5%) cases were clinically diagnosed as meningioma and 40 (78.4%) cases that were radiologically diagnosed as meningioma correlated with the histopathological diagnosis of meningioma. One case radiologically diagnosed as right fronto-temporal cystic lesion turned out to be microcystic meningioma on histopathology. One

case clinically diagnosed as hemangiopericytoma, radiologically as meningioma turned out to be atypical meningioma (Grade-II) on histopathology [Table/Fig-9].



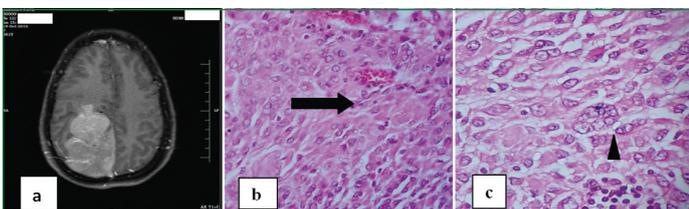
[Table/Fig-6]: a) Meningothelial meningioma showing large uniform epithelioid like cells forming lobules with oval nuclei with delicate chromatin & abundant eosinophilic cytoplasm (H&E: 40X); b) Psammomatous meningioma showing many psammoma bodies coalescing together (H&E: 40X); c) Transitional meningioma: Low power view showing both meningothelial & fibrous patterns (H&E:10X).



[Table/Fig-7]: a) Well defined homogeneously enhancing extra axial dural based soft tissue intensity in the left frontal region-meningioma; b) Secretory meningioma displaying secretory vacuoles intracellular lumina containing eosinophilic, granular, hyalinised secretions called "Pseudopsammoma bodies" (H&E: 40X); c) Periodic Acid Schiff stain showing positive intraluminal secretions in secretory meningioma (H&E:40X).

Sl no	Diagnosis	Clinical	Radiology	Histopathology
1	Meningioma	37	40	51
2	Space occupying lesion	10	8	0
3	Neurofibroma	0	1	0
4	Right Fronto-temporal cystic lesion	0	1	0
5	Gliotic changes	0	1	0
6	Pituitary microadenoma	1	0	0
7	Vestibular schwannoma	1	0	0
8	Left posterior communicating artery aneurysm	1	0	0
9	Hemangiopericytoma	1	0	0
	Total	51	51	51

[Table/Fig-8]: Comparison of clinical, radiology and histopathology diagnosis.



[Table/Fig-9]: a) Large well defined lobulated mildly enhancing extra axial soft tissue mass is seen in the right parietal region causing severe compression over the underlying brain parenchyma- suggestive of meningioma b&c) Atypical meningioma displaying increased cellularity, mitotic figures 6/10 hpf, prominent nucleoli, karyomegaly and multinucleation. Arrow shows mitotic figure. Arrow head shows multinucleation (H&E: 40X).

Grading of all the meningiomas were carried out according to WHO 2016 grading system. Among 51 cases of meningioma, studied 49 cases (96.07%) were Grade-I, 2 cases (3.92%) were of Grade-II and none of them were of Grade-III [Table/Fig-10].

Grade	Grade-I	Grade-II	Grade-III
No. of cases	49	2	0
%	96.07%	3.92%	0%

[Table/Fig-10]: Grades of meningioma.

DISCUSSION

Meningiomas display heterogenous histopathology, which allows for recurrent revision of the classification schemes. Molecular and genetic basis for meningioma tumorigenesis has been thoroughly researched and studied for the understanding of mechanism behind their pathogenesis [1, 10]. In clinical practice, however, the diagnosis is based on light microscopy of routinely stained H&E sections, which is the proven gold standard. The WHO classification scheme provides guidelines for tumour grading and subtypes. Reported recurrence rates of Grade-I, II, and III meningiomas are 7-25%, 29-52%, 50-94%, respectively [6].

In the present meningioma study, 33 (64.70%) cases were females and 18 (35.29%) were males which are comparable with study conducted by Niranjana J et al., Bhat AR et al., and Roser F et al., [Table/Fig-11] [3, 11, 12]. Literature search has also shown the female preponderance, which is attributed to the hormonal factor [Table/Fig-11] [2,3,9,11-17]. Meningiomas express progesterone, oestrogen and androgen receptors on their membranes [18]. Progesterone receptors can be found in up to 72% of the tumours. Studies have shown that they exhibit changes in size during pregnancy and the luteal phase of the menstrual cycle [18,19].

Majority of the study population was in the age group of 40-49 years which was in concordance with the study by Niranjana J et al., and ShriLakshmi S [3,20]. The next age group was 60-69 years followed by 50-59 years in the present study.

Frequencies of histopathological type of meningioma studied showed commonest type being meningothelial type of meningioma, which corresponded with the study of Niranjana J et al., and Khade S et al., [3,13]. The second most common type of meningioma was psammomatous followed by transitional meningioma which corresponded with the study of Niranjana J et al., and Khade S et al., [Table/Fig-12] [3,13]. Occurrence of several variants may be related to the progenitor cell's myriad functions. For example, meningothelial cap cells display varied morphological appearances and carry out a unique set of functions that overlap with both mesenchymal and epithelial cells, possible due to the complex ontogenesis of meninges that originate both from mesodermal cells and the neural crest [9]. The Arachnoidal cap cells display single fibroblast-like cell layer, or as epithelioid nests having several layers. With time, the arachnoidal cap cell clusters become increasingly prominent, forming whorls and psammoma bodies identical to those found in meningiomas. Cytologically and functionally arachnoidal cap cells resemble meningioma cells, hence it is favoured that arachnoidal cells are the most likely cell of origin.

The commonest grade of meningioma in the present study is Grade-I with 96.07% followed by grade with 3.92% which corresponded with the other studies [Table/Fig-13] [2,3,9,11,12,13,16,17], concluding that Grade-I meningioma is the most common type. Literature search has shown that 80% of meningiomas are benign (Grade-I) with broad biological spectrum and with few having difficult clinical course. Studies suggest that even benign meningiomas may spread peripherally through the dura, possibly in a discontinuous fashion in some cases. If microscopic nests are left behind, then recurrence is possible despite a relatively indolent biology [20].

The high grade meningiomas are very aggressive and (Grade-II and Grade-III) constitute approximately 20% of cases. These type of meningiomas are associated with increased mortality and morbidity [7,10]. On the contrary, atypical meningioma (WHO Grade-II) has significant increased risk of mortality when compared with age and gender matched controls. They carry approximately 8-fold increased risk or recurrence over benign tumours (WHO Grade-I). Anaplastic meningiomas (WHO Grade-III) are rare (1-2% of cases) but are associated with considerable risk of death from disease, with the average survival rate being less

Sex	Present study N=51	Khade S et al., [13] N=29, 2019, Mumbai	Patel JP et al., [2] N=30, 2019, Vadodara	Bhat AR et al., [11] N=729, 2014	Roser F et al., [12] N=580, 2004, Hannover, Germany	Grondahl TB et al., [9] N=196, 2012, Trondheim, Norway	Niranjan J et al., [3] N=57, 2019, Bangalore	Mubeen B et al., [14] N=254, 2019, Srinagar	Shri Lakshmi S [15] N=128, 2015, Vishakapatnam AP	Gupta PK et al., [16] N=44, 2019, Sawangi	Hussein AG et al., [17] N=57, 2021, Baghdad
Female	64.70%	68.96%	70%	64.60%	67.41%	79.3%	63.16%	66.92%	73.44%	56.81%	78.80%
Male	35.29%	31.03%	30%	35.39%	32.58%	20.7%	36.84%	33.07%	26.56%	43.18%	21.20%

[Table/Fig-11]: Comparison of sex distribution between present study and other studies [2,3,9,11,12,13,14,15,16,17].

Type of Meningioma	Present study N=51	Khade S et al., [13] N=29, 2019, Mumbai	Patel J.P et al., [2] N=30, 2019, Vadodara	Bhat AR et al., [11] N=729, 2014	Niranjan J et al., [3] N=57, 2019, Bangalore	Mubeen B et al., [14] N=254, 2019, Srinagar	Shri Lakshmi S [15] N=128, 2015, Vishakapatnam AP	Hussein A G et al., [17] N=57, 2021, Baghdad
Meningothelial	35.29%	34.48%	40.00%	57.75%	33.33%	41.30%	23.44%	72%
Fibroblastic	7.84%	3.45%	3.34%	11.11%	8.77%	9.44%	23.44%	5.30%
Transitional	23.52%	27.58%	0%	10.43%	28.07%	18.50%	15.63%	3.50%
Psammomatous	25.49%	17.25%	46.66%	3.84%	8.77%	11.81%	21.88%	7.00%
Secretory	1.96%	3.45%	3.34%	0%	0%	0.39%	2.34%	0%
Atypical	3.92%	3.45%	6.66%	16.87%	3.51%	5.90%	4.69%	3.5%
Angiomatous	0%	10.34%	0%	0%	10.53%	4.72%	2.34%	7.00%
Microcystic	1.96%	0%	0%	0%	3.51%	0%	0.78%	1.70%
Clear cell	0%	0%	0%	0%	0%	0.39%	2.34%	0%
Anaplastic	0%	0%	0%	0%	1.75%	2.36%	0.78%	0%
Rhabdoid	0%	0%	0%	0%	1.75%	0.78%	0.78%	0%

[Table/Fig-12]: Comparison of histopathological types of meningioma between Present study and other studies.

Grades of meningioma	Present study, N=51	Khade S et al., [13] N=29, 2019, Mumbai	Patel J.P et al., [2] N=30, 2019, Vadodara	Bhat AR et al., [11] N=729, 2014	Roser F et al., [12] N=600, 2004, Hannover, Germany	Grondahl TB et al., [9] N=196, 2012, Trondheim, Norway	Niranjan J et al., [3] N=57, 2019, Bangalore	Gupta PK et al., [16] N=44, 2019, Sawangi	Hussein A G et al., [17] N=57, 2021, Baghdad
Grade-I	96.07%	96.55%	93.33%	89.30%	91%	80.1%	92.98%	95.45%	96.50%
Grade-II	3.92%	3.45%	6.66%	5.90%	7%	17.9%	3.51%	4.55%	3.50%
Grade-III	0%	0%	0%	4.8%	2%	2%	3.51%	0%	0%

[Table/Fig-13]: Grades of meningioma of present study and other studies [2,3,9,11,12,13,16,17].

than two years in published study [10,21]. Hence, atypical and anaplastic meningioma needs more aggressive treatment along with radiotherapy to the tumour bed. Eventually, Grade-II and Grade-III tumours will recur and often exhaust both surgical and radiation therapy options [10,22].

Limitation(s)

As it a single institutional based study the sample size was restricted. Hence, we opine that the same needs comparison with future articles with good sample size and cohorts.

CONCLUSION(S)

Majority of meningiomas are benign neoplasms of the CNS with female preponderance with varied clinic-radiological presentation. Histopathological examination is an invaluable tool for confirmatory diagnosis due to the diverse histological variants. Also, the prognosis of the disease depends on histopathological grading of the lesion. A standard WHO classification of grading system aims at providing a tool for the management, treatment, prognosis, estimating the recurrence and overall survival of meningioma patients.

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