

A Clinicopathological Study of Meningioma with Special Reference on Variants and Grading in a Tertiary Care Centre

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ABSTRACT

Introduction: Meningioma are histologically diverse group of tumors derived from meningotheial cells. In the present study incidence, clinical features, anatomical location, histopathological spectrum of Meningioma were studied in a tertiary care hospital.

Materials and Methods: The study included 500 CNS tumors operated over one year duration. All the cases of meningioma were studied by histopathological examination using H and E staining. Immunohistochemistry was done as and when required.

Results: In our study, meningiomas accounted for 17.6 % (88 cases) of the CNS tumors. The most common age group was 40-59 years (59%). Female predominance (69.31%) was noted . Intracranial meningiomas (90.90%) were common than spinal meningiomas. The most common histopathological type was meningotheiomatous meningioma (50%). 94.3% of the meningioma was WHO grade I tumor. Brain invasion and mitosis were statistically significant histological features for determining Meningioma Grade.

Conclusion: Meningiomas display a wide diversity of histopathological appearances. Majority are benign hence

curable by surgical resection. Few histological features and variants are associated with aggressive behaviour and high risk of recurrence. Thus accurate histopathological diagnosis and grading of these tumours is essential.

Key words: Central nervous system tumors, Histopathology, Meningioma ,WHO grade.

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INTRODUCTION

In 1922 Cushing termed tumor originating from the meninges as Meningioma.¹ They originate from the arachnoidal cap cell, a meningotheial cell in the arachnoidal membrane.² Meningiomas account for 15% of all intracranial tumors and usually occur in fourth to sixth decades of life .They occur more often in females than males.³

Meningiomas display a wide diversity of histopathological appearances. They are classified into benign, atypical or malignant. Although most are benign, some of histological features and variants are associated with aggressive behaviour and high risk of recurrence even after complete resection. The WHO classification aims to better predict the clinical behaviour with the histological grading system.⁴

MATERIAL AND METHODS

This was Hospital based descriptive type of observational study conducted at a tertiary care state hospital. The study included 500 CNS tumors who underwent surgical resection from January 2014 to Dec 2014. Meningiomas were studied in detail by histopathological examination using H and E staining. Parameters studied were prevalence, age and sex distribution, anatomical location of tumor, clinical features, histological subtype, histopathological features and WHO Grade of tumor. Immunohistochemistry was done as and when required. Mitotic figures were assessed in the areas of high mitotic activity by

taking average in ten consecutive non overlapping hpf. Irregular tongue like protrusion of tumor cells infiltrating the brain parenchyma without intervening layer of leptomeninges was noted as either present or absent for evaluating Brain invasion.

Statistical analysis: Chi-square was used to calculate the relation between histological factors with WHO grade and variants. P-values less than 0.05 were regarded as statistically significant.

OBSERVATIONS & RESULTS

A total of 88 cases diagnosed as meningioma by histopathological examination were studied. Out of total 500 cases of CNS tumors studied , tumors of Neuroepithelial tissue (51.6%) were the most common entity followed by the tumors of meninges (17.6%).Other tumor were of the sellar region (13.6%), tumors of peripheral nerves (12.2%), metastatic tumors (3.3%), hemolymphoid neoplasm(0.8%) and germ cell tumor (0.4%).

In present study the age group ranged from 15 years to 76 years (average 45yrs). Female predominance (69.3%) was noted. Female to male ratio was 2.1:1 for intracranial and 7:1 for spinal meningiomas. Most of them were intracranial (90.9%) as opposed to spinal (Fig1). Majority of cases presented with complaint of headache (62%) and vomiting (22.22%) and seizures (13.33%). Others presented with decreased vision (7.77%), decreased hearing (3.33%), limb numbness (7.77%), weakness (7.77%) and loss of consciousness (6.66%).

Table 1: Histological features observed in different WHO grades of Meningioma

Histological Characteristics	WHO grade I (n=83)		WHO grade II (n=3)		WHO grade III (n=2)		Total	P value
	n	%	n	%	n	%		
Pseudoinclusions	56	67.46	3	100	0	0	59	0.06 (NS)
Homogenisation of nucleus	61	73.49	3	100	1	50	65	0.43
Psammoma bodies	32	38.55	0	0	0	0	32	0.66
Lymphocytes	34	40.96	2	66.66	0	0	36	0.66
Foamy macrophages	4	4.81	1	33.33	0	0	5	0.1
Collagenisation	27	32.53	1	33.33	1	50	29	0.99
Brain invasion	0	0	3	100	0	0	3	0.001 (S)
Necrosis	8	9.63	1	33.33	1	50	10	0.09
Hyalinised blood vessels	13	15.66	0	0	0	0	13	0.63
Calcification of vasculature	4	4.81	0	0	0	0	4	0.88
Prominent vasculature	25	30.12	2	66.66	1	50	28	0.35
Whorls	67	80.72	2	66.66	0	0	69	0.02 (S)
Areas of hemorrhage	28	33.73	0	0	0	0	28	0.29

Table 2: Histological features observed in different variants of Meningioma

Histological Characteristics	Meningothelial (n=46)		Transitional (n=15)		Fibroblastic (n=10)		Psammomatous (n=5)		Microcystic (n=5)		Angiomatous (n=3)		Metaplastic (n=1)		Atypical (n=1)		Papillary (n=2)	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
Pseudoinclusions	36	78.2	11	73.3	3	30	4	80	3	60	1	33.3	0	0	1	100	0	0
Homogenisation of nucleus	41	89	12	80	4	40	4	80	1	20	1	33.3	0	0	1	100	1	50
Psammoma bodies	19	41.3	6	40	2	20	5	100	0	0	0	0	0	0	0	0	0	0
Lymphocytes	18	39.1	11	73.3	3	30	0	0	2	40	2	66.6	0	0	0	0	0	0
Foamy macrophages	1	2.1	3	20	0	0	0	0	0	0	0	0	0	0	1	100	0	0
Collagenisation	15	32.6	3	20	5	50	2	40	1	20	1	33.3	1	100	0	0	1	50
Brain invasion	2	4.3	0	0	0	0	0	0	0	0	0	0	0	0	1	100	0	0
Necrosis	6	13.0	1	6.66	0	0	1	20	0	0	0	0	0	0	1	100	1	50
Hyalinised blood vessels	5	10.8	1	6.66	0	0	0	0	3	60	3	100	1	100	0	0	0	0
Calcification of vasculature	2	4.34	1	6.66	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Prominent vasculature	16	34.7	2	13.3	1	10	1	20	4	80	3	100	0	0	0	0	1	50
Whorls	44	95.6	13	86.6	6	60	4	80	1	20	0	0	0	0	1	100	0	0
Areas of hemorrhage	19	41.3	6	40	2	20	0	0	1	20	0	0	0	0	0	0	0	0
P value	0.02 (S)		0.001 (S)		0.02 (S)		0.11		0.14		0.23		0.32		0.44		0.35	

TABLE 3. WHO GRADE of meningiomas and the number of mitoses/10high power feild(hpf)

WHO GRADE	NO OF MITOSIS/10HPF			P value
	<4	4-19	>19	
WHO GRADE I	83	0	0	0.001 (S)
WHO GRADE II	1	2	0	
WHO GRADE III	1	1	0	

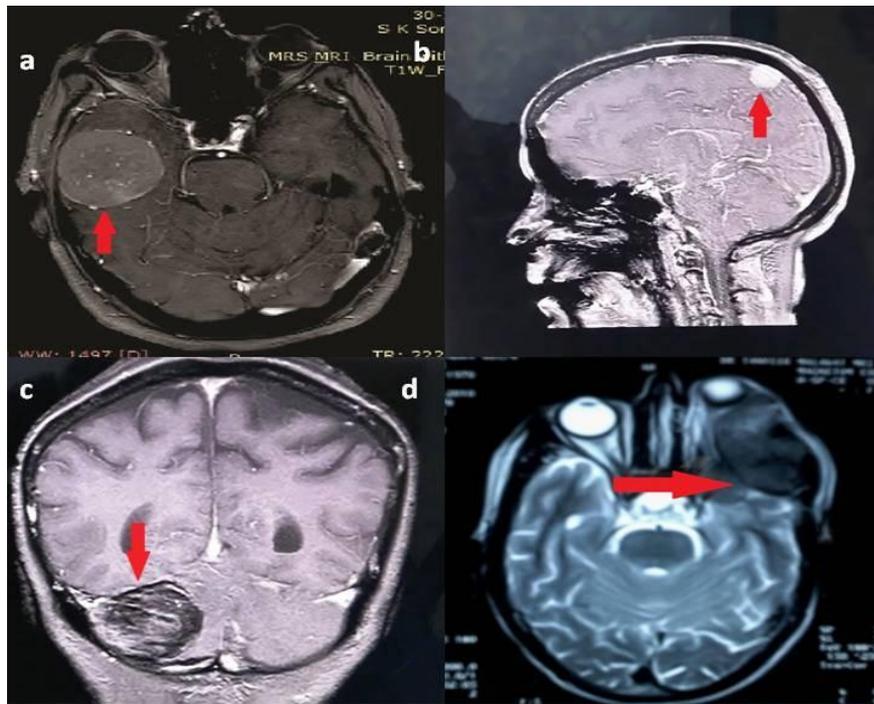


Figure 1: MRI brain showing extraaxial contrast enhancing lesion at a) frontal convexity, b) parasagittal and c) cerebellar location. d) Shows Atypical Meningioma in sphenoid wing extending to orbit

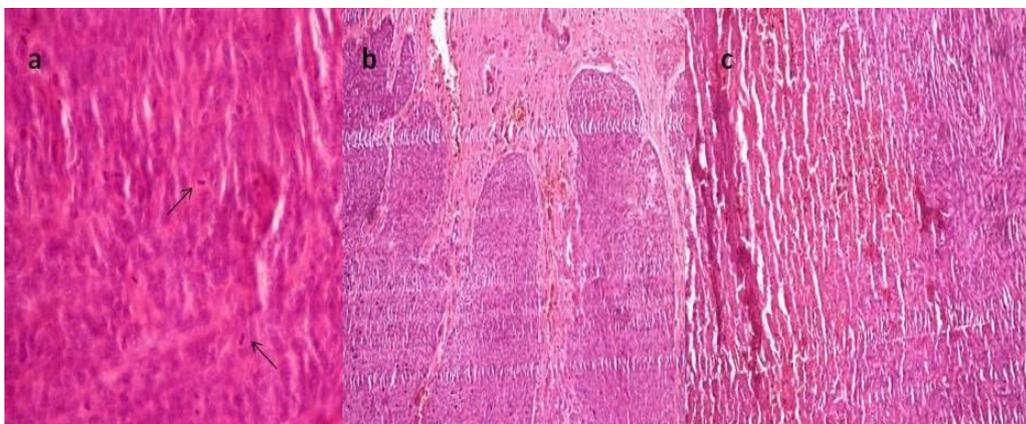


Figure 2: Atypical Histopathological features observed in meningioma .a) increased mitotic count, b) brain invasion and c) necrosis

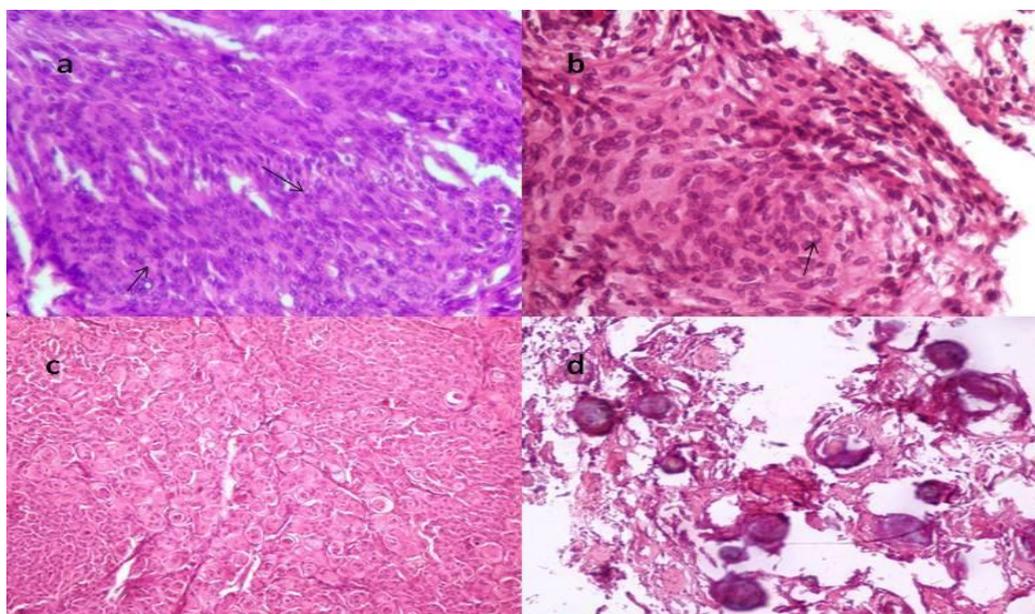


Figure 3: Photomicrograph showing a) nuclear homogenisation, b) nuclear inclusions, c) whorls and d) psammoma bodies

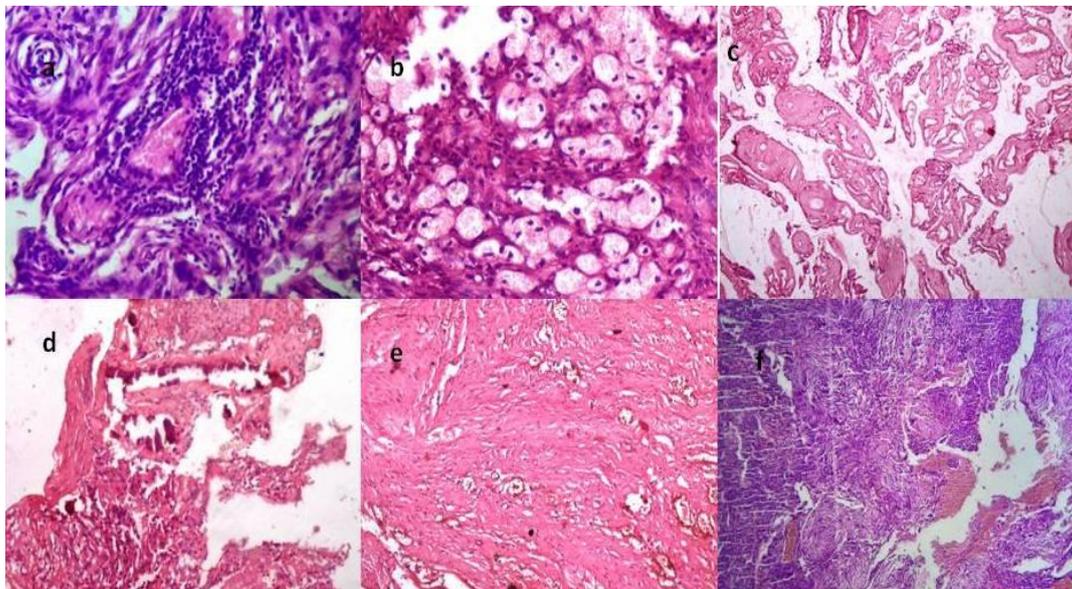


Figure 4: Photomicrograph showing histopathological features a) lymphocytic infiltrate, b) macrophages, c) hyalinised blood vessels, d) calcified vasculature ,e) collagen deposition and f) intratumoral hemorrhage.

Histologically Meningothelial Meningioma was found to be most common subtype (44 cases, 50%) followed by Transitional (15 cases,17.04%), Fibroblastic (10 cases ,11.36 %), Psammomatous (5 cases,5.68%), Microcystic (5 cases,5.68%), Angiomatous (3 cases,3.40%) and Metaplastic (1 cases,1.14%). Three cases of Atypical Meningioma and two cases of Papillary Meningioma were observed.

The meningiomas were graded according to WHO grading system (2007). In present study WHO Grade I tumour were 94.31% (83 cases), WHO Grade II tumour were 3.40% (3 cases) and WHO Grade III tumour were 2.27% (2 cases).

Fourteen histopathological features were studied. The frequency and statistical association between these features in different grades and variants of meningioma was evaluated (Table 1, 2, 3). Out of fourteen features, mitosis and Brain invasion were statistically significant features associated with higher grades (Fig 2.a & 2.b). Necrosis was frequent in grade III meningioma (Fig 2.c). Homogenisation of nucleus and whorls were statistically significant among Meningothelial, transitional and fibroblastic meningioma.(Fig 3.a & 3.c)

DISCUSSION

Meningioma was the second most common CNS tumor in studies by G Aryal (14%), Liang Chen et al (36%), N Chawala et al (18.18%) and Nibhoria et al (34.8%).⁵⁻⁸ In our study it constituted 17.6% which is comparable with the above studies.

In our study meningiomas were common in fourth decade. The results were similar to studies done by Haradhan et al, Shah et al and Shrilakshmi et al.⁹⁻¹¹ In the present study , 60.24% of grade I tumours were observed in fourth and fifth decade. 66.66 % of grade II were observed in age group of 50-59 years while all WHO grade III meningiomas occurred in third decade. Older age of grade I patients may be from the slow growing character of grade I meningiomas leading to delayed tumor diagnosis as noted by Wang Dai-jun et al.¹²

A female preponderance (69.3%) was noted in the present study which was comparable to studies done by Shah et al (67%), Joseph Wanjeri et al (69.2%), Thomas Backer et al (75%), Srilakshmi (73.4%) and Haradanlal et al (52%)^{9-11,13,14}. In the

present study Grade I (2.3:1) and Grade II meningiomas (2:1) have female predominance while Grade III meningiomas had equal female to male sex ratio (1:1). WHO grade I (2.57) had a significantly higher female to male ratio than that of grade II (1.03) or grade III meningiomas (0.76) was observed by Wang Dai-jun et al.¹² In our study most common location of tumor was intracranial (90.9%) and were frequently at convexity of brain. The above results were similar to studies done by Shah et al, Haradhan et al and Shrilakshmi, WANG Dai-jun et al.⁹⁻¹²

In present study, most common clinical feature was headache (62%) followed by vomiting (22.22%) and seizures (13.33%). This was in concordance with Shah et al, Haradhan et al and Shrilakshmi studies.⁹⁻¹¹

Meningothelial meningioma were most common variant in Shah et al, Haradhan et al, Srilakshmi accounting for 37%, 32% and 22% respectively.⁹⁻¹¹ Our results were comparable with the above studies. Transitional variant was commonest as noted by Joseph Wanjeri et al (25.4%) and Thomas backer et al (40%).^{13,14} In present study, WHO Grade I tumour were 94.31%, WHO Grade II tumour were 3.40% and WHO Grade III tumour were 2.27%. WHO grade was commonest grade in Shah et al (92%), Joseph Wanjeri et al (94.7%), Srilakshmi (90.63%), Haradan et al (92%) and Thomas backer et al (69%) studies.^{9-11,13,14}

In our study we observed that high mitotic count was a significant criteria for determining the meningioma grade. Differences due to Interobserver reproducibility were eliminated by single pathologist examination of all the cases. Brain invasion was also significant criteria associated with higher WHO grades. Nuclear pseudoinclusions and homogenisation characteristic of meningothelial cell were noted frequently in benign meningiomas.(Fig 3.a & 3.b). Presence of Psammoma bodies were protective prognostic factors for tumour recurrence.¹⁵ We observed that psammoma bodies occur more frequently in benign tumours.(Fig 3.d) The presence of lymphocytes, plasma cells and macrophages in the tumor tissue reflects various immune responses against the tumour.^{16,17}(Fig 4.a & 4.b) Prominent vasculature, hyalinised and calcified vasculature were studied in meningiomas.(Fig 4.c & 4.d) It is proposed that VEGF (vascular endothelial growth factor) played an important role in the

neovascularization of meningiomas.¹⁸⁻²⁰ Increased fibrosis or collagen formation was commonly seen in meningiomas regardless of tumour grade possibly due to the proposed meningothelial cells functions.²¹(Fig 4.e). Growth factors and their receptors, such as EGFR (epidermal growth factor receptor) and VEGF are proposed for collagen deposition.^{22,23} Intratumoral hemorrhages are frequently noted have been associated with more aggressive and recurrent meningiomas.²⁴ In our study no association was noted with any atypical features.(Fig 4.f) Necrosis is associated with higher grades and increase risk of recurrence.^{25,26} In our study necrosis was more frequently seen in grade III tumors.

In conclusion Meningiomas are slow growing neoplasm that exhibits a remarkably wide range of clinical spectrum and histologic Appearances with female preponderance. They usually present with headache and vomiting and are frequently located intracranially. Majority are grade I meningioma with meningothelial meningioma as commonest variant and are curable by surgical resection. Few histological features and variants are associated with aggressive behaviour and high risk of recurrence. Due to histological diversity they may mimic other tumors. Thus, accurate histopathological diagnosis and grading of these tumours is essential.

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