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Clinicopathological Analysis Of Meningiomas In A Tertiary Care Centre – A 5 Year Study

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Abstract

Introduction - Meningiomas are derived from meningiothelial cells of the arachnoid layer and are categorized into 3 grades according to the WHO 2016 Classification. All the WHO grades of meningiomas have been included in our study. The aim of our study was to study the relevance of immunohistochemistry, the relation with age, sex & regional distribution.

Material & Methods: Total 217 cases in 5 years were included. The specimens were received and processed as per the standard protocols stained with H & E & appropriate IHC guidelines.

Result : Out of total 217 cases of meningiomas WHO Grade I were 127, Grade II were 77 out of which 71 cases were of Atypical meningiomas with high MIB -1 activity, 2 cases were of Clear Cell meningiomas and 3 cases were of Chordoid meningiomas. 1 case was of Lymphoplasmocytic rich meningioma with brain invasion and marginally increased MIB-1.

Total WHO Grade III were 13 cases (Anaplastic- 6, Papillary- 2, Rhabdoid-5). In our study overall female gender, middle age & cerebral convexity had higher predilection for all grades of meningiomas. Second most common site for WHO Grade I was spinal, Grade II was skull base and Grade III it was parasagittal. 1 case of Meningiothelial, 1 case of Atypical meningioma and 1 case of clear cell meningioma were situated at foramen magnum. 1 case of Anaplastic meningioma was situated at optic nerve sheath.

Conclusion: The treatment and follow up is affected by the grade, therefore it is important to classify meningiomas according to their grades & careful inspection of the sections is advised.

Keywords: atypical meningiomas, chordoid, clear cell, MIB-1 labelling index, papillary, rhabdoid. **Introduction**

Meningiomas are derived from meningiothelial cells of arachnoid layer comprising 36% of primary intracranial neoplasms ^[1].Meningiomas are categorized into 3 grades according to WHO 2016 classification. WHO Grade I meningiomas are noninvasive, benign and have low recurrence rate. Aggressive meningiomas includes WHO Grade II and III .The peak incidence is in middle aged ,more common in females, a female: male ratio of 3:1 and increasing to 9:1 for spinal lesions with the exception of higher grades that have a predilection for males and patients of younger age group^{.[2]}

Histological grading has a significant impact on prognosis, risk of recurrence and need for adjuvant radiation or chemotherapy.

Aggressive meningiomas grow at a faster rate than benign meningiomas and are often characterized by increased MIB1 LI, brain invasion & necrosis.

Material And Methods -

It is a 5 year retrospective study conducted from year 2018 to 2022. Total 217 cases of meningiomas have been included in our study and diagnosed according to 2016 WHO classification. The specimens received were fixed in 10% buffer formalin. Multiple serial sections of 4-5 microns thickness were taken, stained with H &E and appropriate IHCs were applied.

Results And Discussion-

In this study, 217 cases reported as meningiomas were included. The tumors were diagnosed and classified as per WHO 2016 CNS classification on H&E and then were analysed on CNS IHC panel.

Overall WHO Grade I meningiomas 127 cases (58.3%) were more common than WHO Grade II (35.4%) and WHO Grade III (5.99%) similar to studies by Perry A et al^[1], Lakshmi S et al^[2], Ishita pant et al^[3]

Total WHO Grade II cases were 77(35.4%) similar to study by Perry A et al ^[1] out of which 71 cases (32.71%) were of atypical meningiomas with high MIB -1 activity on IHC which was slightly higher to study by Wilson Taylor et al^{.[4]}

In our study, 2 cases were of clear cell meningiomas (0.92%) and 3 cases (1.38%) were of chordoid meningiomas similar to study by Nasrin Samadi et al ^[5] in which it was 0.8% for clear cell meningioma and 1.3% for chordoid meningioma.

In our study 1 (0.46%) case of lymphoplasmocytic rich meningioma with brain invasion and marginally increased MIB-1 was seen which can be classified as WHO grade II similar to study by Arie Perry^[6]

Total WHO Grade III cases were 13 (5.99%) which were similar in incidence in a study by Perry A et al^[1] out of which 5 cases were Rhabdoid (2.3%) which was slightly higher in study by Shri Lakshmi S et al ^[2] where it was 0.78% ,6 were Anaplastic (2.7%) similar to study by Cao et al ^[7] and 2 cases were Papillary (0.92%) similar to study by Shri Lakshmi et al ^[2] on HPE.

In our study, incidence of Meningiomas occurrence ranged from 12 years to 85 years with mean age of presentation 49 years . The most common decade of presentation for all grades was 5^{th} decade which was similar to study by Babu S et al^[8] and Raza AKM et al^{.[9]}

In our study most common site for meningiomas of all grades was intracranial (81.97%), followed by intraspinal (18.03%). Among intracranial most common location being Cerebral convexity (28.69%) similar to study by Smita Shah et al ^[10], Nasrin Samadi et al ^[5], Raza AKMM et al ^[9]

In our study 3 cases were located at foramen magnum which is a rare site similar to study by Shri lakshmi et al. ^[2] which accounted for 0.3% to 3.2% of meningiomas.

In our study most common location for WHO Grade I was cerebral convexity similar to study by Smita Shah et al ^[10] and Ishita P et al ^[3]

In our study most common location for WHO Grade II was cerebral convexity similar to study by Zaher et al ^[11],Komotar A et al ^{[12],}Anne Ressel et al ^[13]. In our study WHO Grade III was most commonly located at cerebral convexity similar to study by D Pasquier et al. ^[14] Ishita P et al^[3]

In our study 1 case of Clear cell meningioma (WHO Grade II) was seen in a 12 year old female at foramen magnum similar to study by D Jain et al ^[15] where it was seen between 10-65 years with female preponderance. Most common location being CP angle.

In our study overall meningiomas were more common in females (66.39%) than males (33.61%). In our study WHO Grade I meningiomas were more common in females than males similar to study by Smita Shah et al ^[10]

In our study WHO Grade II also were more common in females similar to study by Smita Shah et al ^[10] contradictory to study by Stephen T. Magill et al ^[16]. Kausya et al ^[17] and Babu S et al ^[18] where it was more common in males .

However, in our study WHO Grade III were more common in males than females similar to study by A Mahmood et al ^[19], Ari J kane et al ^[20] and Patel J P et al^{.[21]}

In our study we used IHC like SSTR-2, EMA, Vimentin and MIB-1 for diagnosing and grading of meningiomas..

Molecular Immunology Borsrel-1 is a marker for cellular proliferation and used for prognosis and grading, chances of recurrence and survival of patient^[22]. In our study all WHO Grade I

meningiomas had MIB-1 <7% on IHC. ,WHO Grade II had MIB-1 \geq 7-20% and WHO Grade III had MIB-1 \geq 20% .It showed correlation with proliferative activity in higher grade cases which was similar to the study done by Devprasath et al ^[23] which confirmed that WHO Grade II and WHO Grade III had a higher MIB-1 LI than benign tumors, and MIB-1 LI has highest validity at 7% in the diagnosis of histological atypia in meningioma and has a good correlation with individual WHO histological features of atypia.

immunohistochemical Histopathological and examination helped in reaching the diagnosis of lymphoplasmocytic rich meningioma with brain invasion which was graded as WHO Grade II . On microscopy sections studied show polygonal or spindle shaped tumour cells in whirlpool arrangement infiltrated by lymphocytes, plasma cells and sheets of macrophages and showed brain invasion thus proving the importance of examining all sections. On IHC it was CD 3 & CD45 Positive with marginally increased MIB-1 L1 similar to study by Manveen Kaur et al ^[24] where the massive infiltration of lymphocytes and plasma cells caused brain oedema. EMA and Vimentin were positive in meningiothelial component.

In our study lymphoplasmocytic rich meningioma was located at cerebral convexity similar to study by Zhu HD et al^{.[25]}

In our study lymphoplamocytic rich meningioma was seen in 3rd decade similar to study by Hosler MR et al ^[26] and Bruno MC et al ^[27] which found it to be more common in younger patients.

In our study, EMA and Vimentin was positive. SSTR-2 was applied on diagnostically tough cases, to differentiate meningiomas from other tumors, and it was strongly positive in meningiomas, proving to be a helpful diagnostic marker for meningiomas.

In our study we used SSTR-2 a family of Transmembrane G- protein couple receptors and are widely expressed in meningioma tissues as compared with normal tissue .It was found to be more sensitive and specific diagnostic marker for meningioma than epithelial membrane antigen in diagnostically challenged cases^[28] In 1 case we used SSTR-2 for differentiating the meningioma case from its mimic (ependymoma – SSTR-2 was negative).

In our study IHC was done for chordoid meningioma S100 was done to differentiate chordoid meningiomas from chondrosarcoma where S100 was positive in chondrosarcoma and for cytokeratin to differentiate from metastatic carcinomas and chordoma where cytokeratin was negative in chordoid meningioma and positive in metastatic carcinoma and chordoma. S100 is expressed in glial cells as well as non-glial cells like myoepithelial cells, chondrocytes and adipocytes.^[29]

EMA helps in distinguishing meningioma from Schwannoma the earlier show as EMA Vimentin is cytoplasmic immunopositivity. intermediate filament protein shows immunopositivity in cells of mesenchymal origin. Meningioma shows immunopositivity for Vimentin.

Conclusion– In this 5 year retrospective study it was concluded that majority of meningiomas were WHO grade I followed by WHO Grade II and III (aggressive meningiomas). Overall the peak incidence of meningiomas was in 5th decade with WHO Grade I and WHO Grade II showing female preponderance whereas WHO Grade Ш meningiomas were more common in males. Overall most common location of meningiomas was supratentorial more than infratentorial. Overall most common location of all grades of meningiomas was cerebral convexity (non - skull base). 1 case of meningiothelial meningioma,1 case of atypical meningioma and 1 case of clear cell meningioma was foramen magnum.MIB-1 located at showed correlation with proliferative activity in higher grades with MIB-1 <7 in WHO Grade I, MIB-1 > to 7-20 in WHO Grade II and MIB-1>20 in WHO Grade III.

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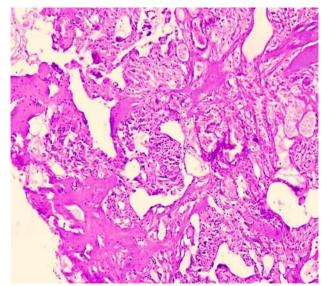
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FIGURE 1 H & E Metaplastic Meningioma

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FIGURE 2 H&E Angiomatous Meningioma



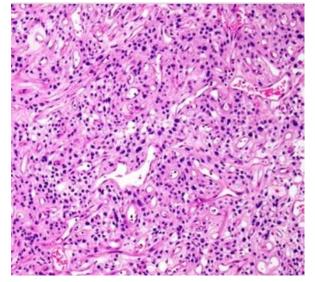


FIGURE 3 H&E Atypical Meningioma

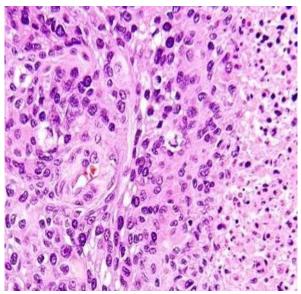


FIGURE 4 H&E Lymphoplasmacyte rich meningioma with brain invasion

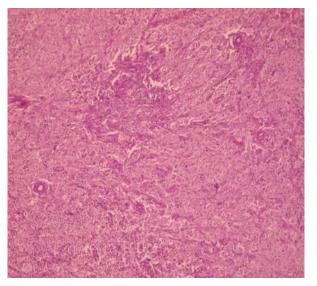


FIGURE 5 Meningiothelial meningioma with brain invasion – Atypical meningioma [WHO grade II] EMA +++

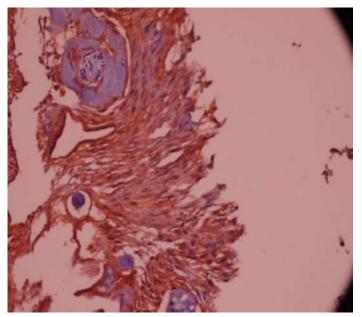
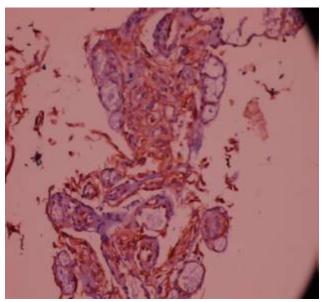


FIGURE-6 Meningiothelial meningioma with brain invasion – Atypical meningioma [WHO grade II] Vimentin +++



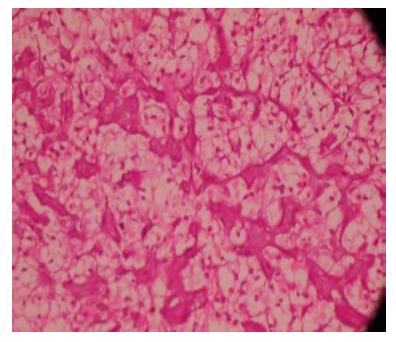
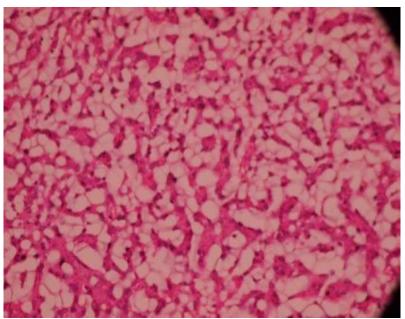


FIGURE- 7 H&E Clear cell meningioma [WHO grade II]

FIGURE-8 H &E - Chordoid meningioma [WHO grade II]



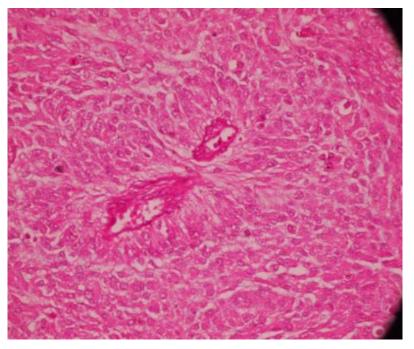


FIGURE-9 H&E Papillary meningioma (WHO grade III)

FIGURE -10 Anaplastic meningioma MIB-1 LI =20-25%

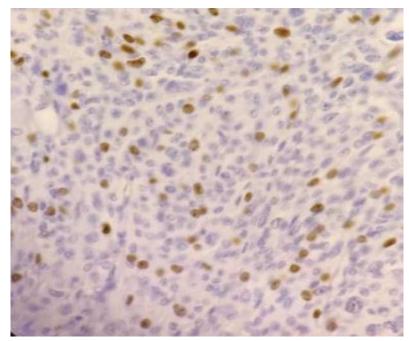


TABLE 1: DISTRIBUTING MENINGIOMAS ACCORDING TO ITS TYPES.

TYPE OF MENINGIOMA	NUMBER	PERCENTAGE
Meningiothelial meningioma	95	43.77
Fibrous meningioma	13	5.99
Transitional meningioma	9	4.14

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Angiomatous meningioma	4	1.84
Microcystic meningioma	2	0.92
Metaplastic meningioma	3	1.38
Psammomatous meningioma	1	0.46
Atypical meningioma	71	32.71
Clear cell meningioma	2	0.92
Chordoid meningioma	3	1.38
Lymphoplasmocytic rich meningioma	1	0.46
Anaplastic meningioma	6	2.76
Rhabdoid meningioma	5	2.30
Papillary meningioma	2	0.92
TOTAL	217	100

TABLE 2: TOTAL NO. OF MENINGIOMAS ACCORDING TO WHO GRADES.

WHO GRADE	NUMBER	PERCENTAGE
WHO GRADE 1	127	58.52
WHO GRADE 2	77	35.48
WHO GRADE 3	13	5.99
Total	217	100

TABLE 3: NUMBER OF STUDY SUBJECTS ACCORDING TO AGE GROUPS

AGE (YEARS)	NUMBER	PERCENTAGE
0-10 years	0	0
11-20 years	2	0.92
21-30 years	21	9.67
31-40 years	33	15.20
41-50 years	62	28.57
51-60 years	43	19.81
61-70 years	41	18.89
71-80 years	13	5.99
81-90 years	2	0.92
TOTAL	217	100

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MEAN	49.9

GENDER	NUMBER	PERCENTAGE				
Female	151	66.58				
Male	66	30.41				
Total	217	100				

TABLE 4: GENDER DISTRIBUTION OF STUDY SUBJECTS

TABLE 5: MENINGIOMAS IN RELATION TO GENDER

ТҮРЕ	FEMALES		MA	LES
	NUMBER	%	NUMBER	%
Meningiothelial meningioma	74	49.00	21	31.81
Transitional meningioma	7	4.63	2	3.03
Fibrous meningioma	12	7.94	1	1.51
Angiomatous meningioma	3	1.98	1	1.51
Metaplastic meningioma	1	0.66	2	3.03
Psammomatous meningioma	1	0.66	0	0.00
Microcystic meningioma	1	0.66	1	1.51
Atypical meningioma	45	29.80	26	39.39
Chordoid meningioma	1	0.66	2	3.03
Clear cell meningioma	2	1.32	0	0.00
Lymphoplasmocytic rich meningioma	0	0.00	1	1.51
Rhabdoid meningioma	2	1.32	3	4.54
Papillary meningioma	0	0.00	2	3.03
Anaplastic meningioma	2	1.32	4	6.06
Total	151	100	66	100

TABLE 6: GENDERWISE GRADING OF MENINGIOMAS

WHO GRADE	FEM	FEMALE		MALE	
	NUMBER	%	NUMBER	%	
WHO GRADE 1	99	65.56	28	18.54	
WHO GRADE 2	48	31.78	29	19.20	
WHO GRADE 3	4	2.64	9	5.96	

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Total	151	100	66	100

TABLE 7: DISTRIBUTION ACCORDING TO LOCATION OF MENINGIOMA

LOCATION	NUMBER	PERCENTAGE
Anterior cranial fossa	14	6.45
Posterior cranial fossa	10	4.60
Cerebral convexity	62	28.57
CP Angle	12	5.52
Falx¶falcine	4	1.84
Intraventricular	4	1.84
Parasagittal	20	9.21
Skull base	23	10.59
Sphenoid	22	10.13
Tentorial	10	4.60
Foramen Magnum	3	1.38
Brainstem	4	1.84
Spinal	29	13.36
Total	217	100

TABLE 8: WHO GRADE OF MENINGIOMAS IN RELATION TO LOCATION

LOCATION	Grade I Grade II		CATION Grade I Grade II G		Grade	Grade III	
	NUMBER	%	NUMBER	%	NUMBER	%	
Anterior cranial fossa	7	5.51	4	5.19	3	23.07	
Posterior cranial fossa	8	6.29	2	2.59	0	0	
Cerebral convexity	33	25.98	25	32.46	4	30.76	
Cerebello Pontine angle	6	4.72	6	7.79	0	0	
Falx¶falcine	3	2.36	1	1.29	0	0	
Intraventricular	3	2.36	1	1.29	0	0	
Parasagittal	14	11.02	3	3.89	3	23.07	
Skull base	12	9.44	11	14.28	0	0	
Sphenoid	12	9.44	9	11.68	1	0	
Tentorial	8	6.29	2	2.59	0	0	
Foramen Magmum	1	0.78	2	2.59	0	0	

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Brainstem	3	2.36	1	1.29	0	0
Spinal	17	13.38	10	12.98	2	15.38
Total	127	100	77	100	13	100
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TABLE 9: DISTRIBUTION OF STUDY SUBJECTS ACCORDING TO MIB-1

MIB-1	NUMBER	PERCENTAGE		
1-7%	127	80.33		
7-20%	77	15.57		
>20%	13	4.10		
TOTAL	217	100		

TABLE 10: MIB-1 IN RELATION TO WHO GRADE

MIB-1	GRADE I		GRADE II		GRADE III	
	No.	%	No.	%	No.	%
MIB-1 <7	127	100	0	0	0	0
MIB-1 > = 7 - 20	0	0	77	100	0	20
MIB-1 > 20	0	0	0	0	13	100
Total	127	100	77	100	13	100