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"Histopathological study of meningiomas at a tertiary care hospital at Pune .

Running title: "**Meningioma- a histopathological study in tertiary care hospital."**

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ABSTRACT:

Introduction: Meningiomas are the most prevalent primary non-glial intracranial brain tumours to develop from the meninges, accounting for 15–30% of all primary cerebral tumours. Even though the majority of these tumours are benign, a very few number of them are malignant. Amongst the meningiomas more than 90% are solitary for unfamiliar reasons. Only risk factor known for meningioma are ionizing radiation. The WHO assigns these tumours grades I, II, and III. Surgery can treat benign meningiomas, however higher grade meningiomas need radiation following surgery because of their high recurrence rate and aggressive behaviour. Materials and methods: This case study was conducted retrospectively in the pathology department of a tertiary care hospital in Pune from the year 2020 to 2022. A total of 39 biopsies were received for histopathological examination and some as frozen samples during this period. Results: In our study 29 patients were females (74.35%) and 10 patients were males (25.65%). The age group between 41 and 50 is the most common (28.2%).Meningothelial meningioma was the most frequent histological form, occurring in 23 cases (58.9%), followed by transitional meningioma in 7 patients (17.9%). (17.9%), fibrous meningioma(7.6%). Conclusion: For WHO Grade I tumours and those who have had a complete surgical resection, the prognosis is favourable; however, for grade III tumours, it is less favourable. Because some histological subtypes with

higher WHO Grades have a greater risk of recurrence and a worse prognosis, accurate histological grading and typing are necessary.

Key words: Meningioma, intracranial tumors, benign.

Introduction-

The most frequent primary non-glial intracranial brain tumors emerging from the meninges are meningiomas. [1] Meningioma is the name Harvey Cushing gave to the most prevalent dural-based tumor, which accounts for 15–30% of all primary cerebral tumors. [2] The arachnoid cap cells of the arachnoid villi in the meninges give birth to meningiomas. Although most of these tumors are benign, a tiny fraction of them is malignant. Amongst the meningiomas more than 90% are solitary for unfamiliar reasons. Only risk factor known for meningioma are ionizing radiation and children who are exposed to it have a higher risk than adults, having about 2:1 female to male ratio and a 10:1 intracranial-to spinal ratio. Meningiomas bring about neurological symptoms resulting from compression of surrounding structures; the particular depending on where the tumor is. Despite being benign, they exhibit a wide range of clinical traits and histologically different subgroups that are linked to a high risk of recurrence. There are established risk factors for recurrence, including grade of histological malignancy, young age, specific subtypes, brain infiltration, subtotal resection, and high proliferation rate. [3,7] The meningioma histological grading method used in the WHO 2021 classification labelled as (Table 1) tries to make better forecast of these varying meningioma features, which is crucial for patient care, prognosis, and follow-up. [8,9]

MRI is the investigation of choice for the diagnosis and characterization of meningiomas, as it is with the majority of other intracranial pathologies. The diagnosis may be determined with an extremely high degree of accuracy when both the look and location are usual. However, in other cases, the appearances are uncommon, necessitating careful interpretation in order to determine the proper preoperative diagnosis.

Typically, meningiomas take the form of extra-axial masses with a wide dural foundation. Although various variations are seen, they are typically homogenous and well-defined. Meningiomas' T2-weighted imaging signal intensity appears to be correlated with their histological subtypes.

Materials and methods

This study was conducted retrospectively in the pathology department of a tertiary care hospital in Pune from the year 2020 to 2022. A total of 39 biopsies were received for histopathological examination and some as frozen samples during this period. Those received routinely were fixed in 10% formalin and multiple serial sections of 3-4 micron thickness were obtained from paraffin-embedded blocks. Sections were stained with Hematoxylin and Eosin and IHC was done wherever needed.

Inclusion criteria: The study included all individuals with meningioma diagnosed both clinically and radiologically.

Exclusion criteria: Individuals with inadequate biopsies, autolyzed specimens, and specimens other than meningioma were excluded.

Ethical consideration and permission: This study was carried out as per ethical guidelines for biomedical research on human participants and ICMR.

Informed consent was taken from patients before the start of the study.

Results

There were 39 meningioma cases evaluated in total, of which 29 patients (74.35%) and 10 patients (25.65%) were male. [Table 1] Female predominance was seen in our study. [Table 2] Meningiomas most commonly presented in between 41-50 years (28.2%) which consisted of 11 cases, followed by 51 to 60 years (25.6%) consisting of 10 cases. Meningothelial meningioma was the most frequent histological form, occurring in 23 cases (58.9%), followed by transitional meningioma in 7 patients (17.9%).fibrous meningioma(7.6%) and atypical meningioma (7.6%) consists of 3 cases each.Least common variant consisted of angiomatous(2.5%), psammomatous (2.5%) and rhabdoid(2.5%) (WHO grade III) meningioma one case each. [Table 3]

In our study, 35 cases (89.7%) were classified by the World Health Organization (WHO) as Grade I, 03 instances as Grade II atypical meningiomas, and 1 case as Grade III rhabdoid meningiomas.In our study 35 cases were classified as grade I, 03 cases as grade II and 01 case as grade III. [Chart 1]

In our study, meningothelial meningioma was the most common form. Like normal arachnoid cap cells, the tumor cells were largely uniform, having delicate chromatin and nuclei which was oval having variable nuclear holes along with nuclear pseudo inclusions, eosinophilic cytoplasm. Reactive meningothelial hyperplasia occasionally resembles meningothelial meningioma because tumor cells closely mimic those of the normal arachnoid cap. Histologically, WHO grade I refers to meningothelial meningioma.

The second most common variant in our study was transitional meningioma. It contains a meningothelial and fibrous pattern with transitional features, lobular and fascicular foci appearing side by side with psammoma bodies, and tight conspicuous whorls. Transitional meningioma corresponds histologically to WHO grade I.

Fibrous meningioma is characterized by spindled cells forming parallel, storiform, and interlacing bundles in a collagen-rich matrix. Three cases of fibrous meningioma were included in our study. The tumor cells form fascicles with varying amounts of intercellular collagen. These fascicles may lead to a differential diagnosis of solitary fibrous tumor/hemangiopericytoma. Histologically, fibrous meningioma is correspondsto WHO grade II.

Angiomatous meningioma histologically shows numerous blood vessels that often make up a larger proportion of the tumor mass than the intermixed meningioma cells. Vascular channels vary from small to medium-sized, thin or thick-walled, and can be variably hyalinized. Vascular malformation and haemangioblastoma are two differential diagnoses of angiomatous meningioma. Angiomatous meningioma corresponds to WHO grade I histologically. One case of angiomatous meningioma was seen in our study.

Psammomatous meningioma histologically features a predominance of psammoma bodies over tumor cells. In psammomatous meningioma, the psammoma bodies frequently fuse, forming an irregular calcified mass and, on rare occasions bone. Middle-aged to elderly women are more susceptible to developing this kind of meningioma in the thoracic spinal area. One case of psammomatous meningioma was diagnosed in our study. It corresponds to WHO grade I histologically.

Atypical meningioma corresponds to WHO grade II histologically, these meningiomas are of intermediate grade between the malignant and benign forms, with other features variably seen in atypical meningioma like increased mitotic activity, increased cellularity, small cells with high nuclear to cytoplasmic ratio, sheeting, prominent nucleoli and in some cases foci of spontaneous necrosis. Three cases of atypical meningioma are included in our study.

One case of the rare meningioma variety termed as rhabdoid meningioma was included in our study showing large to medium sized nests of cells with syncytial appearance, many have round eccentric nuclei which sometimes show nucleoli in foci ,cells have abundant granular or clear cytoplasm, while in other areas there is fibroblastic appearance with scattred mitosis seen.This rare case falls into WHO grade III .

Table 1: Age incidence

AGE GROUP	NUMBER OF CASES
10-20 Years	01 (2.5%)
21-30 Years	02 (5.1%)
31-40 Years	09 (23.0%)
41-50 Years	11 (28.2%)
51-60 Years	10 (25.6%)
61-70 Years	03 (7.6%)
71-80 Years	03 (7.6%)

Table 2: Sex incidence

MALE	10 (25.65%)
FEMALE	29 (74.35%)

Table 3 : Meningioma classified according to WHO Classification

TYPES	CASES
Meningothelial (grade I)	23 (58.9%)
Transitional (grade I)	07 (17.9%)
Fibrous (grade I)	03 (7.6%)

Angiomatous (grade I)	01 (2.5%)
Psammomatous (grade I)	01 (2.5%)
Atypical (grade II)	03 (7.6%)
Rhabdoid (grade III)	01 (2.5%)

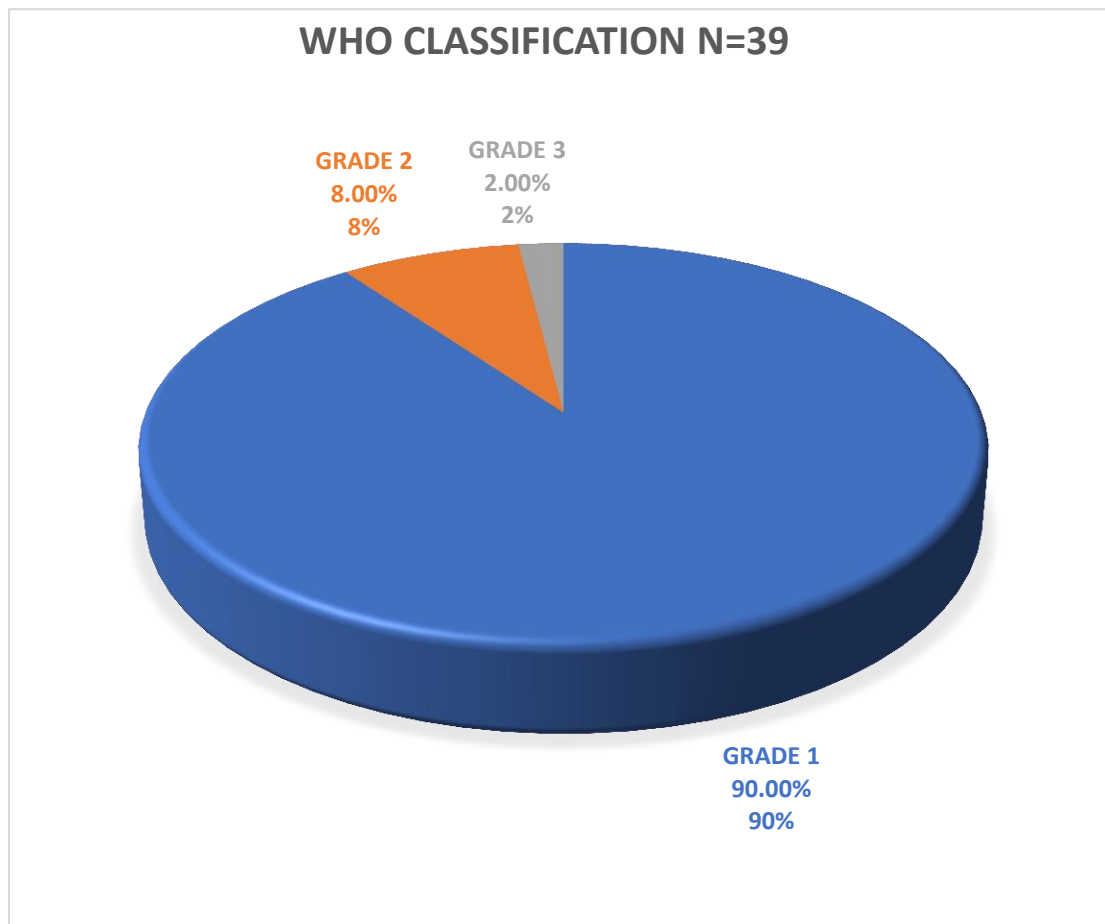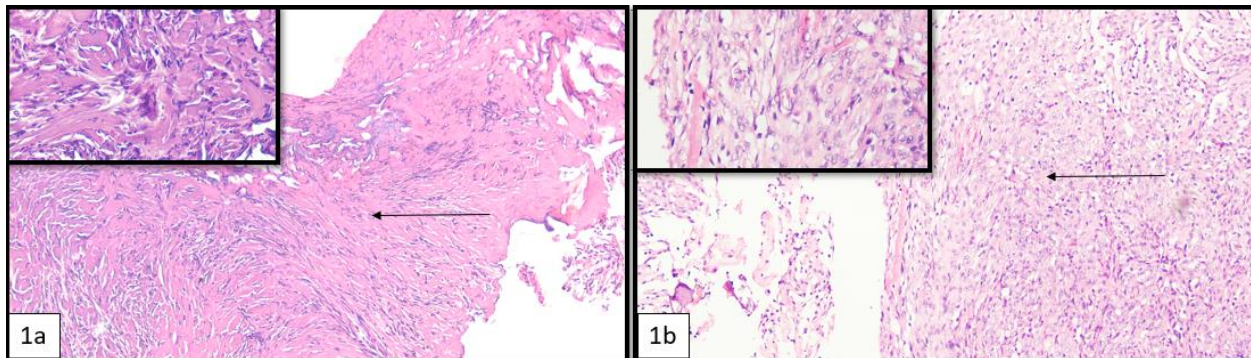**Chart 1: Meningioma incidence (WHO Classification)**

Fig 1A: Photomicrograph of Meningothelial meningioma: Tumor cells are arranged in lobules

which are separated by collagenous septae (thin black arrow) (H& E, 400X), inset showing tumor cells are largely uniform with oval nuclei, delicate chromatin (1000X).

Fig 1B: Photomicrograph of Transitional meningioma: shows cells arranged in lobular and fascicular foci,(thin black arrow)(H& E, 400X) inset showing whorls pattern(1000X).
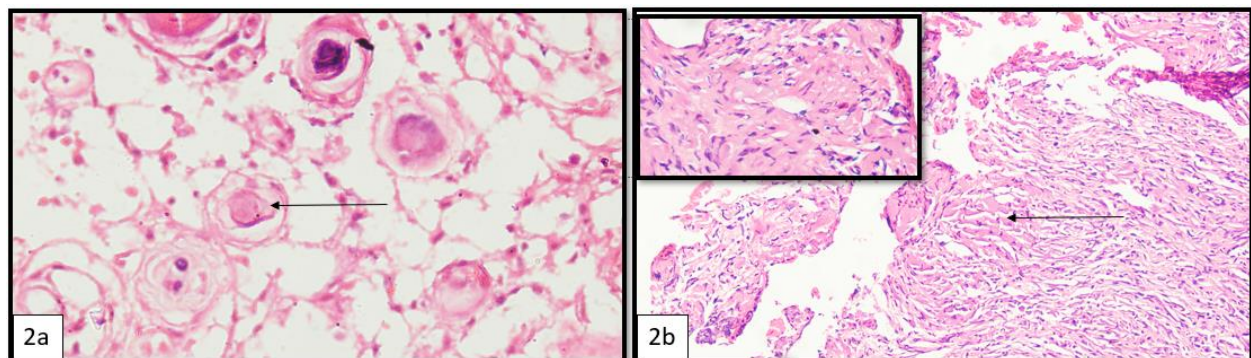

Fig 2A: Photomicrograph of Psammomatous meningioma: showing Psammoma bodies over tumor cells, often forming irregular calcified mass. (thin black arrow)(H& E, 400X).

Fig 2B: Photomicrograph of Fibrous meningioma: showing tumor cells arranged in fascicles and bundles. (thin black arrow)(H& E, 400X), inset showing thick bundles of collagen. (1000X).
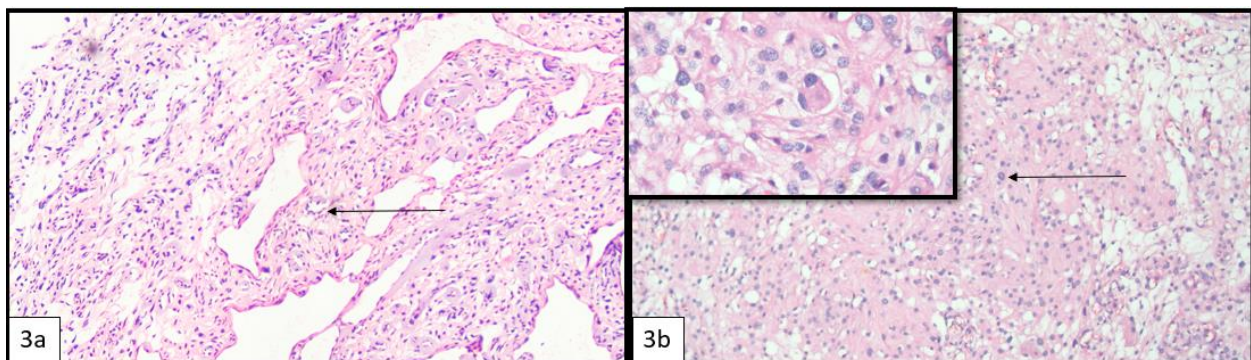

Fig 3A: Photomicrograph of Angiomatous meningioma: showing numerous blood vessels small to medium-sized, and moderate to marked degenerative nuclear atypia. (thin black arrow)(H& E, 400X).

Fig 3B: Photomicrograph of Rhabdoid meningioma: showing rhabdoid cells with abundant eosinophilic cytoplasm, eccentric nuclei. (thin black arrow)(H& E, 400X), inset showing vesicular nuclei with prominent nucleoli and mitosis. (1000X).
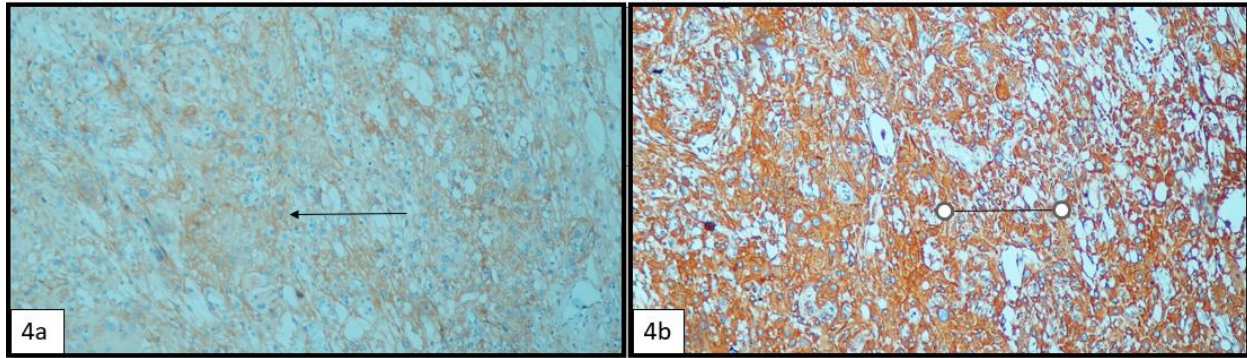
Fig 4A: IHC: EMA: positive in rhabdoid meningioma (EMA, 400X),

Fig 4B: IHC: Vimentin: positive in rhabdoid meningioma (Vimentin, 400X)

Discussion

Meningioma is the most common primary brain tumor and was well known before Harvey Cushing coined the term in 1922. [10] Meningiomas reveal heterogeneous histopathology, which may explain why classification schemes are constantly revised.

Females are affected more than males in our study, our study is in concordance with a study done by Perry et al [11] Shah SR et al. [12] Narmadha R et al [13] which showed similar results. Some meningiomas have frequent progesterone expression, occasionally estrogen or androgen, and quickly enlarging tumors during pregnancy or the luteal phase, which suggests a hormonal effect. [14]

The most common age group affected in our study came out to be 41-50 years of age followed by 51-60 years .Study done by Malik et al [15] found out that the average age that was affected was 47.6 years. Another study on meningioma done by Reddy et al [16] showed the maximum number of meningioma cases between the age group of 40 to 60 years.

Tumors are graded according to their morphological alterations, which can be either localized or diffuse for example grade I lesions occasionally exhibit mitotic figures and pleomorphic features. [17]

Atypical meningiomas, a grade II lesion, have more than four mitotic figures/10HPF and show three of the following characteristics: hypercellularity, patternless, macronuclei, sheet like growth, small cell component with a high nuclear: cytoplasmic ratio, and necrotic zones. Grade II also covers clear cell and choroid morphology. [17]

Grade III anaplastic meningiomas have more than 20 mitotic figures per high power field (HPF) and have a variety of distinct characteristics that give them melanoma, sarcoma, or carcinoma-like appearances. [18] Meningothelial cells in meningiomas and normal meningothelial cells can differentiate into mesenchymal and epithelial cells. Because tumor histology can vary, meningioma can exhibit many histomorphological spectrums. [19]

Desai P.B et al [20] conducted a study showing that the most common variant of meningioma was meningothelial meningioma which was 64% of the total cases,comparable to the findings in our study which showed that 59% of cases were of meningothelial type. According to WHO grading the most common grade in study done by Desai et al [20] was grade I in 90% of the cases in his study,in our study 89.7% of cases falls into grade I.

In another study by Gadgil NM et al [21] the commonest variant of meningioma found was transitional meningioma (24.2%) followed by meningotheliomatous meningioma (22.8%) and in his study 85.6% out of the total meningiomas were WHO grade I tumor.

The findings of studies by Shrilaxmi S et al [22], Jat KC et al [23], and Raza AKMM et al [24] are consistent with those of our own study.

Complete surgical removal of the tumor in all subtypes is the treatment for meningiomas. The use of radiation as a standard adjuvant is still debatable. However, recurrence depends not only on grade but also on location, size, accessibility, relationship to vital structures, and incomplete surgical resection. [25] Grade II and grade III meningiomas are more likely to recur.

Meningiomas of grades I, II, and III have been documented to recur at rates of 7–25%, 29–52%, and 50–94%, respectively. [26,27,28]

Conclusion

Meningiomas are tumors that are slow-growing and often develop in the meningeal layer of brain and spinal cord and are seen more common in women. Typically, older and middle-aged individuals are affected. There are several different forms of histology, with meningothelial meningiomas being the commonest. For WHO Grade I tumours and those who have had a complete surgical resection, the prognosis is favourable; however, for grade III tumours, it is less favourable. Accurate histological grading and typing are essential since a small number of histologic subtypes with higher WHO Grades have a higher rate of recurrence and a poorer outcome.

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