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# THE HISTOLOGICAL SPECTRUM OF MENINGIOMAS

Pathology

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## ABSTRACT

**Introduction:** Meningiomas are a group of slow-growing, primary intracranial neoplasms, that account for approximately 28 to 30% of the primary central nervous system (CNS) tumors1,2,3,4. They can occur at any age but are most common in middle-aged patients1. Headache is the most common symptom followed by seizures in the cases of intracranial meningiomas. Accurate histopathological diagnosis and grading of these tumors are essential for the management, prognosis, and follow-up of patients. **Aims and Objectives:** To study incidence, histomorphological types and grade meningiomas according to the WHO grading system. **Material and methods:** It is a retrospective study comprised of 46 cases of meningioma, which are diagnosed in the Pathology Department. **Result:** In the present study, the most common age group for presentation is 41-50 years. Male to Female ratio was 1:2.01. Among the chief presenting symptoms, headache is the most common symptom followed by seizures. Meningothelial meningioma was the most common subtype, followed by psammomatous meningioma. **Conclusion:** Meningiomas are rare slow-growing tumors which are more common in the adult female. A meningothelial variant is the most common variant which is WHO grade 1 meningioma, readily curable by resection. Grade 1 meningiomas have a good prognosis whereas grade 2 and 3 meningiomas have low frequency but come with a poor prognosis.

## KEYWORDS

Meningioma, Diagnosis, WHO Grading.

## INTRODUCTION

Meningiomas are a group of slow-growing, primary intracranial neoplasms, that account for approximately 28 to 30% of the primary central nervous system (CNS) tumors[1,2,3,4]. More than 90% of all meningiomas are solitary. Ionizing radiation is the only established environmental risk factor for meningioma[5,6]. Higher risk is seen in people who were exposed in childhood than adults. They can occur at any age, but are most common in middle-aged patients, with a peak during the sixth and seventh decades. The risk increases with increasing age. It shows an obvious female predominance[1].

According to WHO 2021, Grading changed to within the tumor grading system. Tumor grade is no longer identified by its subtype. Criteria designating meningiomas to grade 2 and grade 3 will be applicable to all subtypes. Though histological criteria will remain the mainstay for grading and subtyping of meningiomas, WHO CNS5 endorses molecular biomarkers to support diagnosis and prognostication of these tumors (TERT promoter mutation/ CDKN2A/B homozygous deletion, SMARCE1, BAP1, KLF4/ TRAF7, H3K27me3 loss). WHO classification of 2016 and 2007 are similar as far as the grading of meningioma is concerned.

**2021 WHO classification of meningiomas[7,8] -**

**Grade 1:**

Subtypes: Meningothelial, Fibrous, Transitional, Psammomatous, Angiomatous, Microcystic, Secretory, Lymphoplasmacyte-rich, and Metaplastic

Criteria: Pleomorphic, occasional mitosis, lacks features of anaplastic or atypical meningiomas.

**Grade 2:**

Subtypes: Atypical, Chordoid, and Clear cell

Criteria: 4-19 mitotic figures per 10 high-power microscopic fields/Brain invasion, with tumor breaching beyond the pia or

**Manifesting at least three of the following features:**

1) Hypercellularity 2) Uninterrupted patternless, sheet-like growth 3) Prominent nucleoli 4) Small cell components with high nuclear: cytoplasmic (N:C) ratio 5) Zones of spontaneous (i.e. non iatrogenic as seen after embolization) necrosis.

**Grade 3:**

Subtypes: Anaplastic, Rhabdoid, and Papillary

Criteria: 20 or more mitoses per 10 consecutive high-power microscopic fields or exhibiting a loss of differentiated features resulting in carcinoma-, melanoma-, or sarcoma-like appearances or TERT promoter mutation or Homozygous deletions of CDKN2A and/or CDKN2B.

A few histological features and variants are associated with aggressive behavior and a high risk of recurrence. Thus accurate histopathological diagnosis and grading of these tumors are essential for the management, prognosis, and follow-up of patients[9].

## AIMS AND OBJECTIVES

- To study the histomorphological types of meningiomas.
- To study the incidence of age, gender, anatomical location, and symptoms of meningiomas.
- To grade meningiomas according to the WHO (2021) grading system.

## MATERIAL AND METHODS

A retrospective analysis of the histopathology records and clinical case files of total 46 cases were done.

History was studied in detail in each case with respect to presenting complaints, site, age, and sex distribution. Specimens were fixed in 10% neutral buffered formalin followed by routine paraffin processing. Staining was done by using hematoxylin and eosin (H&E) stain. Mounting was done with DPX (distyrene, plasticizer, and xylene). Stained slides were examined under a light microscope. Reporting and diagnosis with the grading of meningiomas were done as per WHO 2021 criteria.

## RESULTS

In present study, a total of 46 cases of meningioma were studied histologically in which 31 patients were female (67.39%) and 15 patients were male (32.60%) (Table 1). Overall Male to Female ratio was 1:2.01. In the spinal location, Male to Female ratio was 1:6. Most common age group for the presentation of meningioma is 41-50 years (28.26%), which consists of a total of 13 cases, followed by 10 (21.73%) cases reported in 61-70 years, followed by 9 (20%) cases reported in 51-60 years. There were no cases reported in the age group of 0- 20 years (Table 2).

Among the chief presenting symptoms, headache is the most common symptom followed by seizures in the cases of intracranial meningiomas. Other symptoms are blurring of vision, weakness of limbs, difficulty in walking, and back pain.

**Table 1: Sex distribuation**

| Gender distribution | No of cases | Percentage |
|---|---|---|
| Male | 15 | 32.60% |
| Female | 31 | 67.39% |
| Total | 46 | 100% |

**Table 2: Age and gender distribution in meningioma cases**

| Age distribution | No of cases | | | Percentage |
|---|---|---|---|---|
| | Male | Female | Total | |
| 1-10 yr | 0 | 0 | 0 | 0% |
| 11-20 yr | 0 | 0 | 0 | 0% |
| 21-30 yr | 1 | 5 | 6 | 13.04% |
| 31-40 yr | 1 | 6 | 7 | 15.21% |
| 41-50 yr | 6 | 7 | 13 | 28.26% |
| 51-60 yr | 1 | 8 | 9 | 20.00% |
| 61-70 yr | 6 | 4 | 10 | 21.73% |
| 71-80 yr | 0 | 1 | 1 | 2.17% |
| 81-90 yr | 0 | 0 | 0 | 0% |
| 91-100 yr | 0 | 0 | 0 | 0% |
| Total | 15 | 31 | 46 | 100% |

Among all meningioma cases, meningothelial meningioma was the most common subtype, with 28 cases (60.86%), followed by psammomatous meningioma consisting of 6 cases (13.04%), anaplastic meningioma consisting of 4 cases (8.69%), atypical and angiomatous variant consisting of 2 cases each (4.34%), followed by microcystic, clear cell, histiocytic and transitional variant, one case each (2.17%) (Table 3).

**Table 3: Histological subtypes of meningioma cases**

| Histological subtypes | No of cases | | | Percentage |
|---|---|---|---|---|
| | Male | Female | Total | |
| Meningothelial | 6 | 22 | 28 | 60.86% |
| Psammomatous | 4 | 2 | 6 | 13.04% |
| Anaplastic | 2 | 2 | 4 | 8.69% |
| Atypical | 2 | 0 | 2 | 4.34% |
| Angiomatous | 0 | 2 | 2 | 4.34% |
| Clear cell | 0 | 1 | 1 | 2.17% |
| Microcystic | 1 | 0 | 1 | 2.17% |
| Histiocytic | 0 | 1 | 1 | 2.17% |
| Transitional | 0 | 1 | 1 | 2.17% |
| Total | 15 | 31 | 46 | 100% |

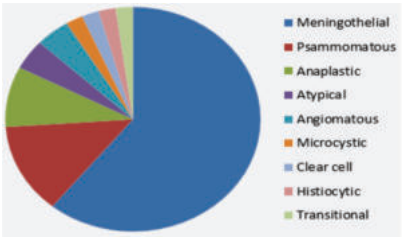


**Fig. 1 Pie chart showing the frequency of meningioma variants.**

According to the World Health Organization (WHO) grading, WHO grade 1 consists of 39 cases (84.78%), WHO grade 2 consists of 3 cases (6.52%), and WHO grade 3 consists of 4 cases (8.69%). Most meningiomas were benign grade I (Table 4).

**Table 4: WHO Grading**

| WHO | No of cases | Percentage |
|---|---|---|
| 1 | 39 | 84.78% |
| 2 | 3 | 6.52% |
| 3 | 4 | 8.69% |
| Total | 46 | 100% |

Among the 46 cases, 39 cases (84.78%) were found at the intracranial location, followed by 7 cases (15.21%) found at the intraspinal location. The most common site of meningioma in CNS is intracranial (Table 5).

**Table 5: Location**

| Location | No of cases | Percentage |
|---|---|---|
| Intracranial | 39 | 84.78% |
| Spinal | 7 | 15.21% |
| Total | 46 | 100% |

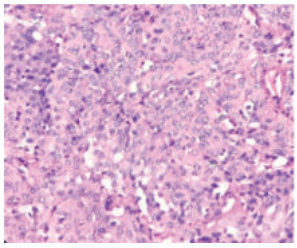

**Fig-2: Meningothelial meningioma showing meningothelial cells arranged in lobules (H&E, 40x)**

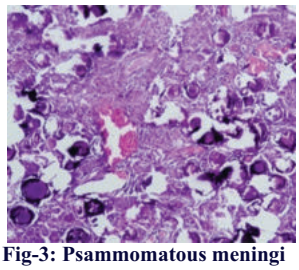

**Fig-3: Psammomatous meningioma showing numerous psammoma bodies with intervening tumor cells (H&E, 10x)**

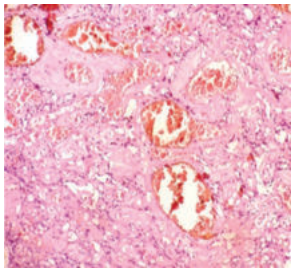

**Fig-4: Angiomatous meningioma showing numerous vascular channels (H&E, 40x)**

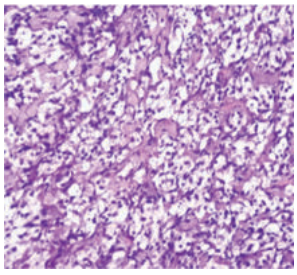

**Fig-5: Clear cell meningioma showing cells clear cytoplasm (H&E, 40x)**

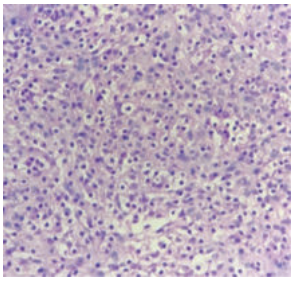

**Fig-6: Histiocytic meningioma showing cells with numerous foamy histiocytes (H&E, 40x)**

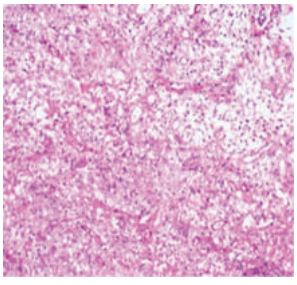

**Fig-7: Microcystic meningioma showing cells with microcysts and cobweb-like background (H&E, 10x)**

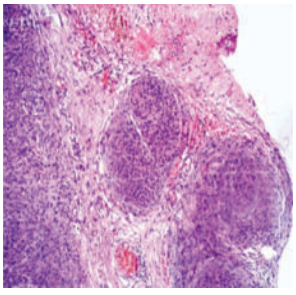

**Fig-8: Atypical meningioma shows brain invasion (H&E, 10x)**

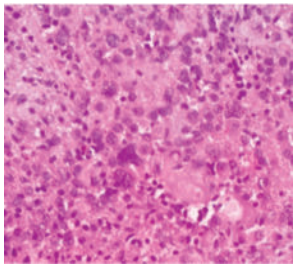

**Fig-9: Anaplastic meningioma showing markedly pleomorphic cells with increased mitotic activity (H&E, 40x)**

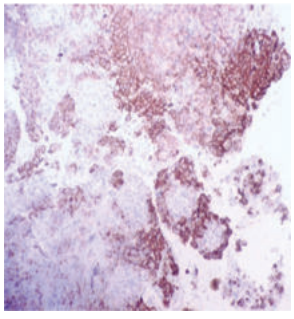

**Fig-10: Anaplastic meningioma showing EMA positivity (IHC, 10x)**

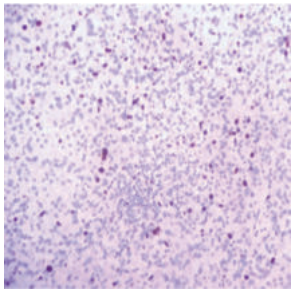

**Fig-11: Anaplastic meningioma showing increased Ki67 positivity (IHC, 40x)**

## DISCUSSION

Meningiomas are the single largest group of tumors arising from the meninges. Meningiomas are thought to arise from arachnoidal cap cells (meningothelial cells) of the brain and spinal cord meningeal coverings. It accounts for approximately 15% of intracranial tumors and about 25% of intraspinal tumors[1,2]. It was termed as meningioma by Harvey Cushing in 1922, based primarily on anatomy[1]. It was also recognized that the histopathology of meningiomas was similar to the cell clusters lining arachnoid villi, and after that, these arachnoidal cap cells have been considered the cell of origin for meningiomas[3]. Meningothelial cells have both epithelial and mesenchymal characteristics, reflected by the spectrum of meningiomas exhibiting diverse histological appearances.

The 5th edition of WHO 2021 CNS classification uses Arabic numericals for different grades of meningioma, a change in terminology, classifying all meningiomas as a single type and all 15 histological entities as subtypes. These changes maintained the grading of meningiomas as previous gradings, with atypical, chordoid, and clear cell meningiomas assigned to WHO grade 2 and anaplastic, rhabdoid, and papillary meningiomas assigned to WHO grade 3. This classification however advises that the WHO grade 2 and 3 should not be assigned solely based on the histological subtype but graded by applying the histological criteria for grade 2 and 3[6,8]. Many molecular biomarkers are also associated with the classification and grading of meningiomas. This includes *SMARCE1* for clear cell subtype, *BAP1 for* rhabdoid and papillary subtypes, and *KLF4/TRAF7* for secretory subtype mutations, *TERT* promoter mutation and/or homozygous deletion of *CDKN2A/B* for CNS WHO grade 3, H3K27me3 loss of nuclear expression signaling potentially worse prognosis, and methylome profiling for prognostic subtyping[6,7,8].

Meningiomas are most common in middle-aged to elderly adults, showing a peak incidence in the sixth and seventh decades[1]. Meningiomas are uncommon in pediatric populations. Female predominance was seen in meningiomas (Table 1). Most of the meningiomas arise in intracranial, intraspinal, or orbital locations. In cranial cavity, usual sites include the cerebral convexities, olfactory grooves, para/suprasellar regions, sphenoid ridges, petrous ridges, optic nerve sheath, tentorium, and posterior fossa[9,10]. Symptoms depend on the location of the tumor[11]. Since these are slow-growing tumors, usually the symptoms occur due to the compression of the adjacent structures like focal neurological deficits, increased intracranial pressure, headache and seizures[11,12,13].

Magnetic Resonance Imaging shows circumscribed, isodense, dural masses, which shows uniform contrast enhancement. Meningiomas may also show calcification and evidence of bone or cartilage. Calcification is better visualized on a CT scan. The characteristic radiologic feature of meningioma is the dural tail, a wedge-shaped extension of the tumor at the edge which is contrast-enhancing[1].

Grossly, meningiomas are rubbery, well-circumscribed, round, and firmly attached to the inner surface of the dura. Usually, t hese are solitary neoplasms, but sporadic cases may show multiple lesions. Occasionally, these are dumbbell-shaped[1]. The tumor is mostly smooth or bosselate.

The cut surface of the tumor is white, yellow-tan, which frequently shows white streaky bands of fibrous tissue. The cut surface is variable in different types. Cut surface is usually gritty in the psammomatous type, yellow in the xanthomatous type, and white in the metaplastic type due to cartilage and bone formation, a moist glistening surface usually indicates the microcystic type, whereas the secretory type has a tan red gland-like appearance. Atypical and anaplastic types shows foci of hemorrhage and necrosis on the cut surface[1].

### Histomorphological variants of meningioma

#### Meningothelial meningioma

It is the most common type of meningioma[14,15,16]. Histology shows lobules of different sizes formed by epithelioid cells, separated by collagenous septa. Most of the cases showed oval nuclei with delicate nuclear chromatin. Some cases show the presence of eosinophilic pseudo inclusions in the nucleus which are formed by intranuclear invaginations of the cytoplasm. The mimicker of meningothelial meningioma is melanocytoma[17].

#### Transitional meningioma

The transitional meningioma shows meningothelial and fibrous patterns, as well as frequent whorl formation and psammoma bodies.

#### Psammomatous meningioma

This is characterized by the predominance of lamellar calcifications-psammoma bodies more than tumor cells[2,6].

#### Angiomatous meningioma

The angiomatous subtype is rich in numerous hyalinized thick and thin-walled small blood vessels, often constituting a greater proportion (>50%) of the tumor mass[16]. This variant shares histological similarities with solitary fibrous tumors[14].

#### Microcystic meningioma

Microcystic meningiomas have thin, clear, elongated processes encompassing microcysts between cells bridged by wisps of cytoplasm, creating a “cobweb-like” appearance. This microcystic subtype is frequently found intermixed with angiomatous meningioma.

#### Clear cell meningioma

Clear-cell meningiomas are characterized by sheets of meningothelial cells with clear cytoplasm and round nuclei. The clear cytoplasm is imparted by glycogen content and can be confirmed with PAS and PAS-diastase staining. Hemangioblastoma[17] and clear cell renal cell carcinoma[14] are morphological mimickers of clear cell meningiomas. CD10, PAX8, and carbonic anhydrase IX immunohistochemical markers stained positive for clear cell renal cell carcinoma[14]and stained negative for Clear cell meningioma[14].

#### Atypical meningioma

Atypical meningiomas are tumors with increased mitotic activity-mitotic count >4 to 19/10 high power fields (HPF), brain invasion, and /or at least three of the following features: hypercellularity, patternless or sheet-like growth, prominent nucleoli, small cell components with high N:C ratio, zones of spontaneous (i.e. non iatrogenic as seen after embolization) necrosis[18]. The differential diagnosis are hemangiopericytoma, meningeal leiomyosarcoma, metastatic carcinoma, meningeal ES-PNET, and leptomeningeal medulloblastoma[17].

#### Anaplastic (malignant) meningioma

Anaplastic meningioma shows markedly pleomorphic cells arranged in sheets with prominent nucleoli, high mitotic count (>20/10 high power fields), and invasion into the brain[19]. It shows the presence of frank anaplasia defined as carcinoma, melanoma, and sarcoma-like histology. They have a high Ki67 index with poor prognosis and recurrence[2,6]. Mimickers are Metastatic carcinoma and leptomeningeal medulloblastoma[15,17].

Meningiomas are surgically treated neoplasms. Radiation is also a major treatment modality, especially for patients for whom surgery carries high risk. Adjuvant chemotherapy has been useful to reduce recurrence rates.

The present study shows female 37 (67.39%) predominance which is in concordance with all other studies Niranjan J et al 36 (64%)[2], Pant et al 221 (73.18%)[1], and Vijaya Gattu et al 30 (79%)[16].

**Table 6: Comparison of incidence of histological types and grades of meningiomas**

| Types of meningioma | | Lakshmi S. et al (11) | Iyengar S. et al (12) | Niranjan J et al (2) | Patil et al (21) | Shruti et al (9) | Malik et al. (20) | Present study |
|---|---|---|---|---|---|---|---|---|
| | Total cases | 128 | 117 | 57 | 87 | 50 | 126 | 46 |
| | | Percentage of cases | | | | | | |
| Meningothelial | | 23.44 | 62.42 | 33.3 | 43.68 | 32 | 17.3 | 60.86 |
| Psammomatous | | 21.88 | 12.82 | 8.77 | 10.34 | 22 | 3.9 | 13.04 |
| Anaplastic | | 1.75 | - | 1.75 | 3.45 | 2 | 1.6 | 8.69 |
| Atypical | | 4.69 | 1.70 | - | 2.30 | 6 | 11.1 | 4.34 |
| Angiomatous | | 2.34 | 10.53 | 10.53 | | 10 | 2.4 | 4.34 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Clear cell | | 2.34 | - | - | 2.30 | - | - | 2.17 |
| Microcystic | | 0.78 | 0.78 | 3.51 | | 2 | 5.7 | 2.17 |
| Histiocytic | | - | - | - | | - | - | 2.17 |
| Transitional | | 15.63 | 5.98 | 28.07 | 24.13 | 6 | 53.2 | 2.17 |

Incidence of meningothelial meningioma is highest in the present study, which is in concordance with the other studies Iyengar S. et al (62.42%), Patil et al (43.68%), Niranjan J et al (33.3%), Shruti et al (32%) and Lakshmi S. et al (23.44%). In the present study, Grade 2 and 3 variants constitute of few cases, which are comparable with other studies. In present study, the incidence of anaplastic (malignant) meningioma is slightly higher than other studies. This occurs may be due to less sample size.

## CONCLUSION

Meningiomas are uncommon slow-growing tumors originating from the meningeal layer of the brain and spinal cord. This is more common in adult females. The meningothelial variant is the most common variant which is WHO grade 1 meningioma, readily curable by resection. Grade 1 meningiomas have a good prognosis while grade 2 and 3 meningiomas have low frequency and poor prognosis.

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