

The histopathological spectrum of meningeal neoplasms

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Abstract

Background: Meningiomas are slow-growing and benign tumor of the meninges, which line the skull and enclose the brain.

Methods: We have studied 324 cases of meningeal lesions (clinically diagnosed and histologically proved) in Department of Pathology of a tertiary care hospital. We evaluated its frequency, age and sex distribution and documented as per the WHO histological grade of meningioma.

Results: The commonest age group affected was 41-60 years. Female predominance was seen. Headache being most common symptom with commonest site was intracranial (88.2%). The meningeal lesions consisted of meningioma (96.6%) and non-meningioma lesions (3.4%). The commonest histopathological type of meningioma was transitional (24.2%) followed by meningotheliomatous (22.8%). The 85.6% of the meningioma was WHO Grade I tumor. For WHO Grade II meningiomas, mitotic figures and high cellularity was helpful to diagnose the tumors. The non-meningioma lesions included hemangiopericytoma, solitary fibrous tumor, malignant melanoma and metastasis by carcinoma breast, lung and thyroid.

Conclusion: From our study, we can conclude that benign meningiomas WHO grade I are most common. Intracranial location is the most common for meningioma. Middle-aged group of 41-60 years was predominantly affected and it is uncommon in children.

Keywords: Meningeal neoplasms, Meningioma, WHO grade

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Introduction

Meningioma, so named by Harvey Cushing in 1922, is a group of heterogeneous tumors that arise from meningotheial cells. Meningiomas are predominantly benign tumors usually attached to the dura mater which are thought to derive from arachnoid cap cells in the meningeal coverings of the spinal cord and brain¹. The incidence varies from 13 to 26% of all intracranial neoplasms. The majority occurs in adult females in their reproductive years². Meningiomas are generally benign, slow growing tumours that may produce neurological symptoms and signs due to their space occupying property with compression of adjacent structures³.

In clinical practice, the diagnosis is based on light microscopy of routinely stained haematoxylin-eosin sections with criteria given by World Health Organization (WHO). The only change between the current WHO 2007 and previous 2000 edition is that otherwise benign meningiomas are classified as grade II depending on brain-infiltration⁴.

Even after complete removal, meningiomas have been estimated to recur in 10 to 32% of the cases within 10 years. Recurrence depends on histological malignancy grade, subtotal resection, young age, specific subtypes, brain infiltration and high proliferative rate^{5,6}.

The aim of the study was to analyse a large number of meningeal neoplasms, consecutively operated during a twenty-year period, to note the frequency of various subtypes and grades of meningioma according to the latest WHO classification (2007).

Material and Methods

Selection of specimens: Material collected by different methods like stereotactic biopsies, open biopsies, total resection of meningeal lesions had been studied in the Department of Pathology in Tertiary care hospital, Mumbai. A total 324 cases of meningeal neoplasms over a twenty year period, from 1.01.1995 to 31.12.2015, were studied, retrospectively (10 years) and prospectively (10 years).

Histopathological evaluation and clinical information: Routine H& E (Haematoxylin-Eosin) stained paraffin sections were reviewed. The tumors were classified into subtypes as per WHO classifications of 2007⁶.

Mitotic count was assessed in areas with high mitotic activity, by summing the highest number of mitotic figures in ten consecutive non-overlapping HPFs. Brain infiltration, defined as irregular, tongue like protrusions of tumour cells infiltrating underlying

brain parenchyma without an intervening layer of leptomeninges, was registered as either present, absent, or inaccessible when no brain parenchyma was observed. Increased cellularity was evaluated semi-quantitatively as present or not^{6,7}.

Recorded clinical data included sex, age at surgery, clinical presentation and tumour grade. Tumour location was noted based on surgical accessibility determined by CT or MR analyses, wherever available.

Results

Out of 1810 cases of CNS tumors studied over 20 years, meningeal neoplasms were seen in 324 patients (17.9%). Out of 324 Meningeal neoplasms, there were 313 cases of meningioma (96.6%) and 11 (3.4%) cases were of non- meningioma neoplasms.

Meningiomas: Meningioma being neoplasm of middle decade of life with peak incidence noted between 41-60 years- 44.1%. These are rare in children causing only 1.4%. The female: male ratio was 2.2:1. Spinal meningioma shows a marked female predominance, while male preponderance is seen in atypical and anaplastic meningiomas.

Out of 313 cases of meningioma, 88.2% were of intracranial meningioma, 8.6% cases were of spinal meningioma while orbital meningiomas seen in 3.2%. Of the intracranial meningiomas, Parafalcine (14.28%) followed by Fronto-parietal region (12.8%) was commonest sites.

Commonest clinical presentation for meningeal neoplasm was headache 45%, followed by convulsions (21%), same was seen in cases of Intracranial meningioma, headache 45.28%, and convulsions in 21.01% respectively. While spinal meningiomas, particularly thoracic meningioma presented with backache (81%) followed by paraplegias & parasthesias (74%). Majority of patients presented in our study were within 6 months (68%).

In our study, CT scan & MRI imaging was done in 75% cases, which showed Post contrast enhancement with tail sign and peri-lesional edema.

The histological grading of meningioma was done by WHO classification 2007. The frequency of grade I, II, and III meningiomas was 85.6 %, 11.5%, and 2.9%, respectively [Table 1].

Among Grade I meningiomas, the most common variants were transitional (24.2%), meningothelial (22.6%), while psammomatous meningioma was seen in 12.7%. There were 2 cases each of lymphoplasmacyte cell rich and microcystic meningioma. Also were seen 4 cases each of Angiomatous meningioma and Metaplastic meningioma. Out of 4 cases of metaplastic meningioma, there was a case of Xanthomatous meningioma with multiple multinucleated giant cells, which an uncommon finding. Due to presence of these giant cells, cytologically it was misdiagnosed as

tuberculous inflammation. Histiocytes were positive for CD68 & EMA positivity in whorls with low MIB index confirmed the diagnosis [Fig.1]. We had no case of secretory meningioma.

The Grade II meningioma comprised of 31 cases of atypical meningioma along with 3 cases of Clear cell and 2 cases of Chordoid meningioma. The mitotic count was the most commonly applied parameter for grading meningiomas as grade II (atypical). Other findings seen were sheeting, hypercellularity and macronucleoli.

There were 9 cases of Grade III Meningioma, which included 5 cases of anaplastic type exhibiting high mitotic figures (20 or more/10 HPF) along with necrosis and prominent nucleoli. Two cases (0.6%) each of Papillary & Rhabdoid meningioma were seen.[Fig. 2]

Non meningioma Neoplasms

There were total 11 cases of non- meningioma neoplasms in the study. Hemangiopericytoma was seen in two cases, both male, 28 & 65 year, supratentorial in location. Histologically shows characteristic features of hemangiopericytoma with “stag horn” pattern, immunohistochemistry shows diffuse Vimentine positivity.

Also is seen one case each of Solitary fibrous tumour, malignant melanoma & Meningeal Sarcoma with fibro-sarcoma like feature.

We had 6 cases of metastasis in meninges, 5 females with 3 of metastasis from Carcinoma breast (2 of Infiltrating Duct carcinoma & 1 case of Invasive lobular carcinoma) along with 1 case each of papillary carcinoma Thyroid & Choriocarcinoma. A 65 year old male had metastasis of Carcinoma lung in meninges. [Fig. 3]

Clinical outcome and follow up

Follow up was available only in 100 out of 324 cases of meningeal neoplasms. Total 7 cases had recurred, 6 meningiomas and one case of malignant melanoma. The median time of recurrence for meningioma cases was 4.5 years. While patient with Malignant melanoma recurred within 6 months after surgery.

Out of 268 grade I meningiomas, 79 cases had follow up. There was Olfactory groove meningioma (WHO Grade I), was partially resected as it involved underlying bone, it recurred with Grade I histology only.

Out of 31 cases of Grade II- Atypical meningioma, follow up was available in 20 cases. Out of which 5 were recurred. Three out of these 5 cases were of larger size and were partially resected at the time of initial surgery. On reviewing the slides, there were areas brain invasion in two cases, hence they recurred. Recurrent tumors on histology were of Grade II- atypical meningioma with increased mitosis.

None of grade III meningioma had followed up to comment upon recurrence.

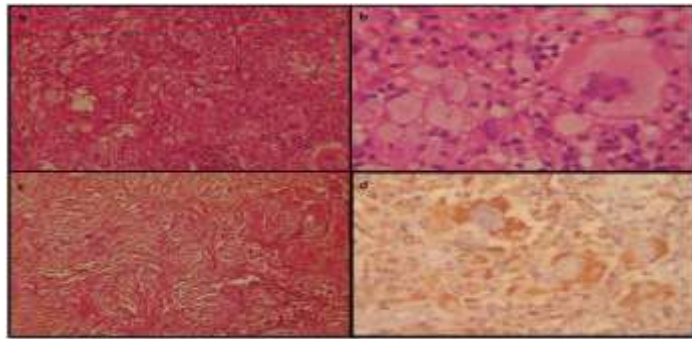


Fig. 1: Xanthomatous meningioma revealing, sheets of xanthomatous cell (a) admixed with multinucleated giant cells (b) which is rare feature, along with classical whorls of meningioma (c), the cells were immunoreactive for CD68 which confirms histocytic nature of cells

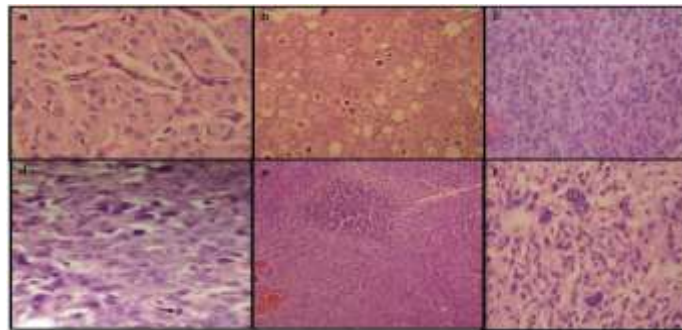


Fig. 2: Histological features of Grade I meningiomas viz. Meningothehal (a) and psammomatous meningioma(b). Grade II meningiomas shows hypercellularity with sheeting (c) along with mitotic fig. (d). Grade III meningioma exhibits small areas of necrosis (e) and nuclear pleomorphism and anaplasia (f)

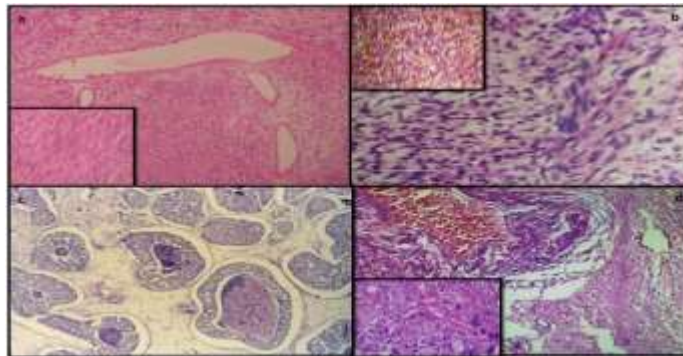


Fig. 3: Non meningioma lesions, show Hemangiopericytoma (a) with classical stag horn pattern with cellular spindle plump cells (incet). Meningeal sarcoma with fibrosarcoma like features exhibiting herringbone pattern (b) which showed Vimentin positivity (incet). Metastatic meningeal lesion seen as characteristic comedo necrosis in Metastasis of Infiltrative duct carcinoma breast (c) while syncytotrophoblasts & cytotrophoblasts replacing meningeal blood vessels seen in case of Metastatic Choriocarcinoma

Table 1: Histological subtypes of meningiomas

Tumor subtype	Frequency	Percentage	WHO Grade
Meningothelial	71	22.7	WHO Grade I
Psammomatous	40	12.7	268
Transitional	76	24.2	(85.6 %)
Fibroblastic	69	22.0	
Microcystic	02	0.6	
Lymphoplasmacell type	02	0.6	
Angiomatous	04	1.27	
Secretory	00	-	
Metaplastic	04	1.27	
Clear cell	03	9.6	
Chordoid	02	0.6	36
Atypical	31	9.9	(11.5%)
Papillary	02	0.6	WHO Grade III
Rhabdoid	02	0.6	9
Anaplastic	05	1.6	(2.9%)
Total	313	100	100

Discussion

The histological appearance of meningeal lesions is important predictor of tumour behaviour and is frequently a factor in decisions concerning therapy. The relationship between histological features and prognosis is formalized by in grading scheme such as the World Health Organization (WHO)⁸.

This study presents a review of 324 consecutively operated primary meningeal lesions classified according to the latest WHO classification of 2007, with the aim to analyse the frequency of various histopathological features and their mutual correlations.

Ionising radiation is a clear cause of meningiomas and there is a potential role of sex hormones, particularly the progesterone receptor. Meningiomas (besides schwannomas) are hallmark features of this autosomal dominant disorder caused by germline mutations in the NF2 gene on chromosome 22q12. Meningiomas have occasionally been reported in other hereditary syndromes, including Cowden, Gorlin, LiFraumeni, Turcot, Gardener, von Hippel-Lindau, and multiple endocrine neoplasia type I⁹. We confirmed median age at surgery and the higher frequency of benign meningioma in females compared to males, and a progesterone-dependent tumour growth is explained by Wolfsberger S¹⁰ and Perry et al¹¹.

Meningioma may occur anywhere in the central nervous system, however some predilections do exist, and intracranial site and parafalcine location was common location in our study. While Violaris¹² observed parasagittal (32.3%), convexity (23.8%), tentorium (12.4%) and sphenoid wing (9.6%) as common site of meningioma. Etiologic connections between a particular tumour grade and specific locations is not obvious, but may be related to the meninges' complex embryological origin¹³.

The histopathological classification is based on criteria given by World Health Organization (WHO) which provides guidelines for tumour grading and subtypes. The frequencies of different meningioma

subtypes in this study well correlated with Thomas¹⁴, Perry¹⁵ while meningotheliomatous was seen as the commonest histopathological type of meningioma by Patel¹ and Shah¹⁶. Distinguishing between benign subtypes of meningiomas is generally of minor importance, however, it is relevant as far as differential diagnoses and specific variants with a more aggressive behaviour are concerned^{7,12,14}.

The WHO 2000 classification was an improvement over the 1993 classification in that it brought about more objective and reproducible criteria, which led to higher recognition of atypical meningiomas^{14,17}. In the 2007 edition, all brain infiltrative specimens are classified as grade II. Since up to 25% of tumours with a benign histology recur, thus constant improvements of the classification criteria are required^{15,18} because patients with grade II will need closer radiological follow up and possible radiation therapy¹⁹.

We found that high mitotic count was the most important criterion for determining a meningioma as grade II similar as Vranic²⁰. Mitotic figures were often hard to detect, giving poor interobserver reproducibility^{21,22}. Therefore new techniques have been introduced that are intended to easily and reliably detect proliferative cells or identify mitotic figures, such as Ki-67/MIB-1 and PHH3 immunostaining^{23,24}.

Violaris¹² stated that overall percentage of recurrence was 21.52%. Grade 1 meningiomas (benign) recurred at a rate of 19.1%, grade 2 tumors (atypical) showed 41.7% rate of recurrence and grade 3 meningiomas (malignant) recurred at a rate of 75%, while Perry⁶ reported recurrence rates of grade I, II, and III meningiomas are 7- 25%, 29-52%, 50-94%, respectively. In our study 5 cases of atypical meningioma recurred, 2/5 had brain invasion, and 3 were of larger size. One case of olfactory meningioma (grade I) recurred due to involvement of underlying bone at the time of first surgery. Recurrence is the result of a direct extension attributable to incomplete resection of involved bone and regrowth at the edge of a previous

surgical field. Extensive resection of all suspicious underlying bone is a complement to radical removal of these lesions^{25,26}. Tumor size, mushroom shape, osteolysis, edema grade, proximity to a major sinus, cortical penetration and intensity on T2-weighted MRIs, pial-arterial supply on angiography, type of brain-tumor interface at surgery, Simpson Grade, and malignancy were significantly independent predictors for recurrence. Aggressive surgical therapy with wider dural removal should be considered when these findings are present preoperatively. Close radiological observation with shorter intervals or radiotherapy should be considered as an adjuvant therapy for patients with a high risk of recurrence in the early postoperative period^{12,27}.

In conclusion, The current grading system is based on histological features found in several clinicopathological studies to be of prognostic importance^{1,8}. However, a continuous revision of the histopathology of meningiomas is necessary to improve the accuracy and reproducibility of the histopathological diagnosis and grading of these tumours.

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