

Clinicopathological Study of Meningioma

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Abstract

Background: Meningiomas are tumours originating from meningotheial cells. They are commonly located at intracranial, intraspinal or occasionally ectopic site. They show histological diversity and are categorized into three grades by WHO 2007 Classification .This grading helps in predicting their behaviour and deciding treatment strategy. Objective: To study the frequency, clinical details, topographic distribution, histological typing and grading of 87 cases of meningioma. Diagnostic accuracy of radio-imaging and utility of squash cytology for their intraoperative diagnosis was also assessed.**Methods:** Total 87 histopathologically confirmed cases of meningioma were studied with above mentioned aims and objectives. Analysis of histological features, typing and grading of all cases was done according to WHO 2007 classification of meningioma. **Result:** Meningioma constituted 15.60% of all CNS neoplasms. It was the most common extra-axial tumour and contributed to 37.09% all extra-axial intracranial neoplasms. 90.8% of the meningiomas were intracranial where convexity was the most favored location. 6 out of 8 spinal meningiomas were located at thoracic level. Headache was the most frequent presentation. Obvious female predominance was observed. The most common histological subtype was meningotheial followed by transitional. Majority 87.36% were benign grade I tumours .3.45% cases showed recurrence. In 74.41% cases radiological diagnosis matched exactly with histopathological diagnosis while squash cytology provided exact diagnosis in 91.15% cases. **Conclusion:** Meningiomas are slow growing extra-axial tumours majority being intracranial, benign grade I neoplasms occurring commonly in elderly females and squash cytology plays a great role in their intraoperative diagnosis.

Key words: Meningioma, Intracranial, Tumour, Extraaxial, Grading, Squash cytology

Introduction

In 1922, Harvey Cushing proposed the term meningioma [1] for the tumours arising from the arachnoid cells present in arachnoid villi and granulations and in stroma of perivascular spaces and choroid plexus [2]. Meningiomas constitute about 28–30% of primary Central Nervous System (CNS) tumours [3]. They exhibit typical dural attachment and account for 15 % of intracranial tumours and about 25% of intraspinal tumours [3]. Though they are tumours of adulthood and are commonly seen in middle-aged and elderly patients, paediatric cases are not very rare. When occur in middle-aged patients, there is a marked female predominance with the approximate female:

male ratio being 1.7:1[4]; the ratio peaks at 3.5:1 in the patients 40–44 years of age [5]. Atypical and particularly anaplastic meningiomas are somewhat more frequently encountered in males [6]. Few genetic as well as environmental risk factors are described for development of meningioma [7,8,9]. Cerebral convexities, sphenoid ridge, parasagittal, olfactory groove, tuberculum sella and cerebellopontine angle are some of the favourite sites of intracranial meningioma. Spinal meningiomas occur more commonly in the thoracic region. Intraventricular and epidural meningiomas are rare. Pediatric meningiomas tend to occur at unusual locations, including the ventricles, posterior fossa and spinal dural regions [10]. Meningiomas are generally solitary, slowly growing tumours producing neurological signs and symptoms

Manuscript received: 11th March 2016
Reviewed: 24th March 2016
Author Corrected: 3rd April 2016
Accepted for Publication 19th April 2016

due to compression of surrounding structures; specific deficits depend upon the location of tumour. Imaging has an important role in characterizing these lesions and helping in presurgical differential diagnosis, which is essential for optimizing treatment strategies [11]. The CT scan and MRI evaluate the lesion with respect to the following points: Location (supra/infratentorial) and site, periregional edema, intensity compared to grey matter, contrast enhancement and type of enhancement, presence of extra axial signs viz, CSF cleft, displaced subarachnoid vessels, buckling of cortical grey matter between the mass and the white matter, displaced and expanded subarachnoid space, broad dural base and bony reaction, presence of mass effect, presence of signal voids on T1WI and T2WI (calcification or fibrosis or vessels), presence of haemorrhage, heterogeneity, presence of necrosis or cystic change, presence of calcifications, margins: Sharp & well defined or ill-defined. On MRI, meningiomas are typically isodense, contrast-enhancing dural masses. "Dural tail" is a distinctive although non-specific feature of meningioma. Angiography often displays a characteristic tumour blush, reflecting their high vascularity [11].

Most meningiomas are globular discrete masses with broad dural attachment. An exception to this is an en plaque variant which is a carpet like mass usually found over sphenoid wing. External surface appears cobblestone or bosselated while cut surface is often lobular but may be variable, often reflecting the predominant histological variant, such as gritty texture with abundant psammoma bodies or a more lipidic quality with the secretory type. Squash smears from meningiomas show cohesive syncytial clusters as well as single intact meningotheial cells having moderate amount of cytoplasm, slightly oval nuclei with evenly dispersed fine to coarse chromatin. Most characteristic feature is formation of cell whorls and variable presence of psammoma bodies. Intra-operative frozen section is helpful for correct diagnosis of meningioma differentiating it from other dura based tumours [12]. As meningiomas show microscopic diversity, various histological variants are described. WHO 2007 classification of meningioma takes an account of different histological variants of meningioma and categorise them into three grades a Grade I (benign), II (atypical) and III (malignant). Higher Grade meningiomas tend to behave more aggressively and recur [13]. Hence grade of meningioma is key factor in deciding treatment policy [13]. Vimentin positivity is found in all meningiomas. The vast majority of

meningiomas stain for epithelial membrane antigen (EMA), although EMA immunoreactivity is less consistent in atypical and malignant lesions. S-100 protein positivity is not usually prominent [14]. In most cases, grade I meningiomas are treated only surgically while grade II and III tumours are far more likely to recur and follow a more aggressive clinical course including metastasis [13].

The present study was undertaken in a tertiary referral centre with separate Neurosurgery and Neuropathology speciality. This meta-analysis study was done over two and half years to determine the frequency of meningioma among all CNS tumours, to study clinical aspects of presentation, age and sex correlation, topological distribution, histological subtyping, grading of meningiomas. Also the radiological diagnosis was correlated with histological diagnosis and accuracy of intra operative diagnosis by squash smear was judged.

Materials and Methods

This was a prospective study of patients with primary intracranial and intraspinal meningiomas operated at Grant Government Medical College and Sir J J Group of Hospitals, Mumbai. Only cases of clinically and radiologically suspected meningiomas which were confirmed on histology in the Department of Pathology during the period Jan 2012- June 2014 were enrolled in the study. There were total 87 such cases. The study was approved by the institutional ethics committee. The details of the each patient were taken from medical records i.e. age, gender; clinical presentation, radiological evaluation (MRI and/or CT scan), location, brain infiltration and recurrence were noted. Intra operative consultation was done by squash smears for which sample was received in isotonic normal saline. Squash diagnosis was noted and was correlated with final histological diagnosis which was considered as gold standard for diagnosis of meningioma. The histological sections were viewed and all tumours were subtyped graded by experienced pathologist according to WHO 2007 criteria.

In all cases, the specimens received following surgery were fixed in 10% buffered neutral formalin for 24 hours. If the resected tissue was received as fragmented bits, all the tissues were submitted for processing. If the tumour was removed in toto and exceeded 4-5 cms, representative sections were taken. These tissue blocks were processed and embedded in paraffin wax. The paraffin embedded blocks were cut into 4-5 micron

sections and stained with routine Haematoxylin and Eosin stain (H&E). Subtyping and grading was done according to WHO (2007) grading system [Table 1].

Immunohistochemical (IHC) staining was performed on few cases.

Result

Of total 568 CNS tumours diagnosed during study period, Meningiomas constituted 87 (15.60%). The most common affected age group was 41 – 50 years, with more than 60% cases falling between 31 - 60 years (Table 2). Females 62 (71.26%) were more commonly affected compared to males 25 (28.75%). In all age groups females were more commonly affected except in the older age group of 71- 80 years where male predominance was seen. The lowest and highest age of occurrence for meningioma was 7 and 74 years respectively. The mean age was 46.1 years (male- 47.8 years and female- 45.4 years). Meningiomas were less common in the extremes of age with 3 cases each in the 1-20 years and 71-80 years age group. Most of the meningiomas were found in cranial region 79 (90.80%). Cerebral convexity was the most favoured site 37 (42.52%) followed in frequency by sphenoid wing and planum sphenoidale (14.94%). Intraspinal meningiomas were only 8 (9.19%) cases with thoracic spine being most commonly involved 6 (75%) [Table 2]. The most common clinical symptoms were headache, vomiting and seizures related to raised intracranial pressure in cases of intracranial meningioma. The more common radiological findings were dura based mass lesions with pressure effect on adjacent structures and peritumoral edema. Based on WHO 2007 grading criteria, Grade I meningiomas were most common 76 cases (87.36%) followed by grade II 7 cases (8.04%) and grade III only 4 cases (4.60%). Meningothelial meningioma 38 (43.68%) was the commonest subtype followed by transitional 21 (24.13%), psammomatous 9 (10.34%), fibroblastic 5 (5.75%), metaplastic 1 (2.7%) and others. Grade II meningiomas included atypical 2 (2.30 %), clear cell 2 (2.30 %) whereas grade III included all the cases of papillary 1 (1.15 %) and anaplastic 3 (3.45%) meningiomas [Table-4]. 3 out of 87 cases were recurrent contributing to 3.45% cases. Radiological impression matched completely with histologic diagnosis in 75 cases (86.22%). Accurate diagnosis on intra operative squash smears was given in 81 cases (91.95%).

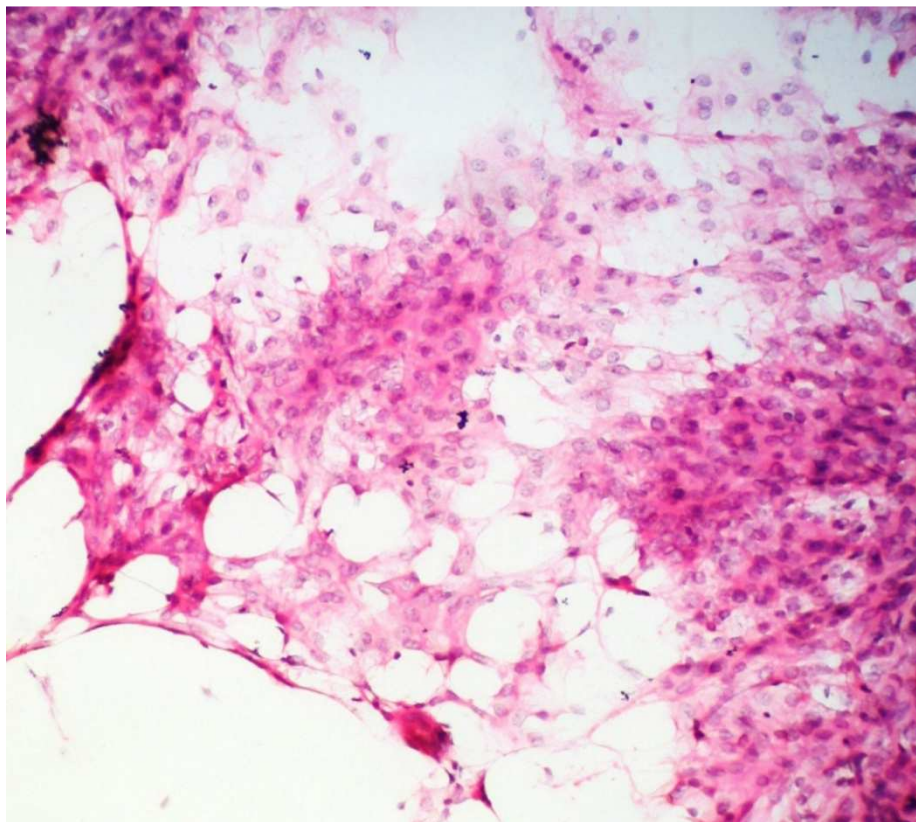


Figure-1: Meningothelial meningioma – Squash Smear showing syncytial clusters of meningothelial cells (H&E, X100)

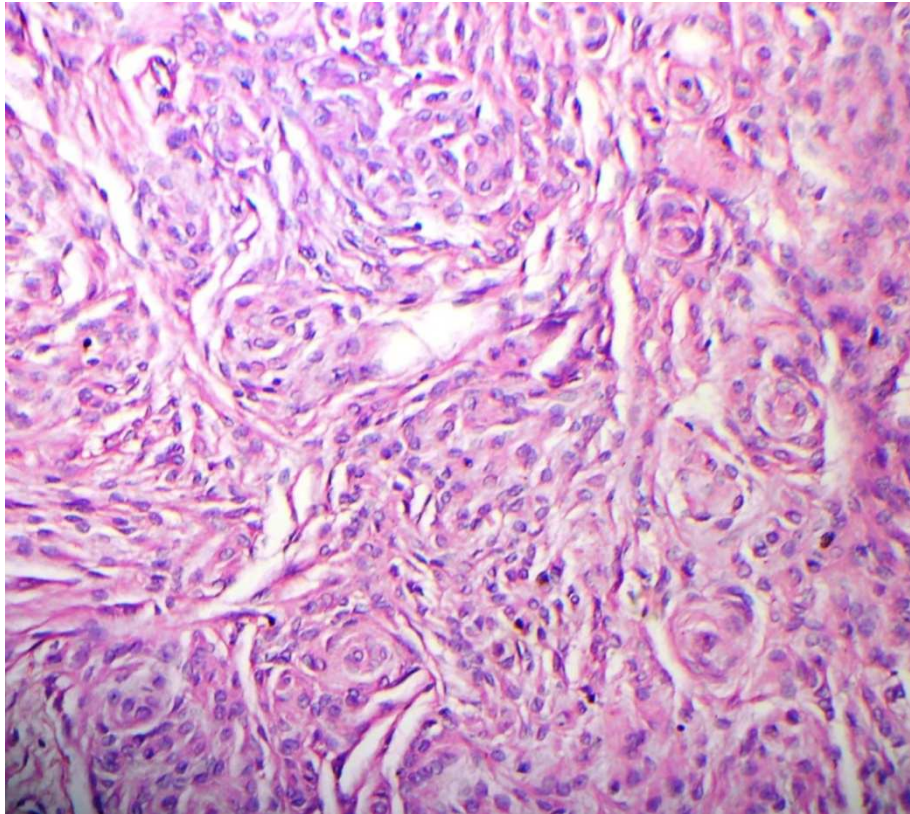


Figure 2: Meningothelial meningioma –showing whorls of meningothelialcells (H&E, X100)

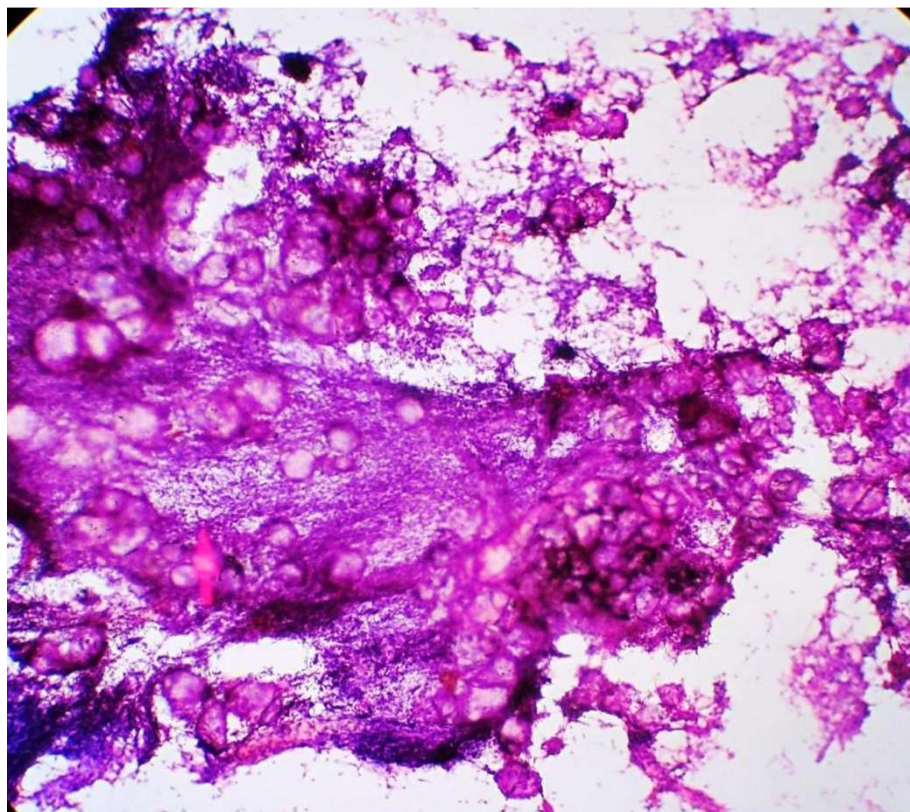


Figure-3: Psammomatous meningioma – squasmsmear showing numerous psammoma bodies along with clusters of meningothelial cells (H&E, X40)

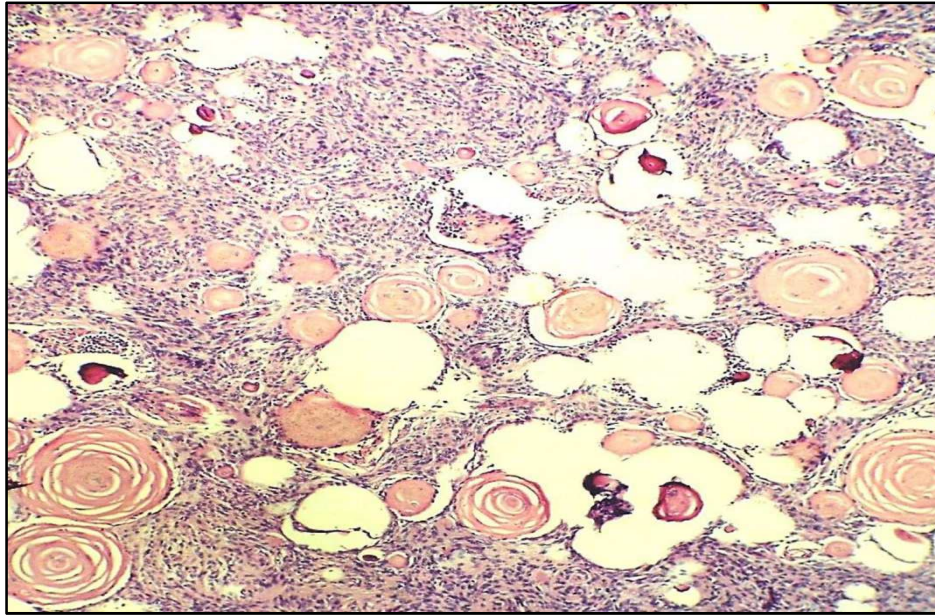


Figure-4: Psammomatous meningioma - numerous psammoma bodies with sheets of meningothelial cells (H&E, X100)

Table-1: WHO 2007 [3]Histomorphologic criteria for grading of meningioma

WHO grade	Criteria
I	Mitosis <4/10 high power field (HPF)
II	a) Mitosis 4 - 19/10 HPF
	or
	b) 3 or more of the following five features:
	1. Increased cellularity
	2. Uninterrupted patternless or sheet-like growth
	3. Small cells with a high nuclear/cytoplasmic ratio
4. Prominent nucleoli	
5. Foci of 'spontaneous' or 'geographic' necrosis	
III	a) Mitosis \geq 20/10 HPF
	or
	b) Exhibiting loss of differentiated features resulting in carcinoma, melanoma or sarcoma like appearances.

Table 2: Age and sex incidence of Meningioma

Age	Male	Female	Total	% (n=87)
0-10	--	01	01	1.15
11-20	--	02	02	2.30
21-30	01	02	03	3.45
31-40	08	20	28	32.19
41-50	08	21	29	33.33
51-60	04	06	10	11.49
61-70	01	10	11	12.64
71-80	03	--	03	3.45
Total	25	62	87	
%	28.74	71.26	100	

Table 3: Regional distribution of meningioma (n=87)

Cranial region		No.	%	Spinal region		No.	%
Cerebral convexity	Frontal (14)	37	42.52	Cervico-thoracic	01	1.15	
	Fronto-parietal (06)			Thoracic	06	6.89	
	Parietal (06)			Lumbar	01	1.15	
	Parieto-temporal (04)						
	Temporal (02)						
	Parieto-occipital (02)						
	Occipital (03)						
Parafalcine	08	9.20					
Tentorium cerebelli	07	8.05					
Sellar, suprasellar, parasellar	04	4.60					
Sphenoid wing, Planumsphenoidale	13	14.94					
Posterior cranial fossa	02	2.30					
Cerebellar	01	1.15					
Cerebellopontine angle	04	4.60					
Cranio-vertebral junction	01	1.15					
Cavernous sinus	01	1.15					
Intraventricular	01	1.15					
Total	79	90.81	Total	08	9.19		

Table 4: Histological sub-types of meningioma

Type	No. (n=87)	%
Meningothelial	38	43.68
Transitional	21	24.13
Fibrous	05	5.75
Psammomatous	09	10.34
Microcystic	02	2.30
Secretory	01	1.15
Lipomatous& secretory	01	1.15
Metaplastic	01	1.15
Chordoid	01	1.15
Clear cell	02	2.30
Atypical	02	2.30
Papillary	01	1.15
Anaplastic	03	3.45
Total	87	100

Discussion

Though Harvey Cushing used the term “meningioma” in 1922 for the first time, this tumour was known under various names since the 17th century. Actually it was Felix Plater, a professor of medicine who described the earliest known case of meningioma in the literature in 1614. [1]John Cleland in 1864 was first to hypothesize the origin of meningiomas from pacchionian granulations [1]. Meningiomas are the most common nonglial primary tumours of the central nervous system accounting for nearly 15-30% of all CNS neoplasms[3]. They comprise of approximately 15% of all intracranial tumours and are most common extra axial neoplasms. Symptomatic meningiomas observed two to three times more frequently in female patients, especially those in the middle age (40-60 years) group and generally slow growing benign neoplasms[3] presenting with signs and symptoms of raised intracranial tension. Radioimaging has important role in characterizing these tumours in terms of location and helping in presurgical differential diagnosis. Intra operative smear squash provides

rapid, reliable intraoperative diagnosis and guidance to the neurosurgeon during surgical resection and lesion targeting. The various highly diversified histologic patterns of meningioma have been described, reflecting the mesenchymal and epithelial histogenetic potential of arachnoid cells [2]. Meningothelial and transitional meningiomas exhibit most typical meningothelial appearance while mesenchymal and epithelial phenotypes of the arachnoid cells are better reflected in other forms such as fibrous and metaplastic forms comprise the mesenchymal variants while the epithelial variant of meningiomas is expressed by the microcystic, secretory, clear cell and papillary variants [2].

The most common patterns of growth are meningothelial, fibrous and transitional meningiomas [2]. Although most meningiomas are benign, they have a surprisingly broad spectrum of clinical characteristics, and histologically distinct subsets are associated with high risk of recurrence, even after seemingly complete resection. In rare instances, meningiomas are malignant. The WHO 2007 classification aims to better predict the divergent clinical characteristics of meningiomas with a histological grading system based on statistically significant clinicopathological correlations [3]. There are three types of meningiomas according to malignancy grades: benign (WHO grade I), atypical (WHO grade II), and anaplastic or malignant (WHO grade III) meningiomas. Epithelial Membrane Antigen [EMA], Vimentin, S100 are immunostains used for meningioma. MIB 1 and P53 expression is observed correlating with increasing histological grade and biological behaviour of meningioma [15]. Surgical resection is treatment of choice in benign meningioma while higher grade tumours need additional radiotherapy. Recurrence occurs in higher grade tumours as well as benign tumours when removed incompletely.

Table 5: Comparison of incidence of histological subtypes of Meningioma

Study	Meningothelial	Transitional	Fibroblastic	Psammomatous
Smita Shah et al[22]	37%	-	16%	19%
Thomas Backer et al[25]	17%	40%	7%	-
Joseph Wanjeri et al[26]	22.5%	25.4%	25.4%	-
Haradhan et al[23]	32%	20%	20%	-
Shri Lakshmi S. et al [21]	23.44%	15.63%	23.44%	21.88%
Present study	43.67%	24.14%	5.74%	10.34%

Table 6: Comparison of incidence of different WHO grades of meningioma

Study	WHO grade I	WHO grade II	WHO grade III
Smita Shah et al[22]	92%	8%	0%
Joseph Wanjeri et al[26]	94.7%	4%	1.3%
Akyildiz EU et al[24]	82%	6%	-
Shri Lakshmi S. et al [21]	90.63%	7.03%	2.34%
Nasrin Samadi et al [29]	86.1%	8%	5.9%
Konstaninos Viplaris et al[30]	89.82%	5.82%	4.36%
Present study	87.36%	8.04%	4.6%

In present study, 87 cases of meningioma constituted 15.60% (87 out of 588) of all 588 CNS neoplasms which was lower than study done by Zalata et al[16], AB Shah et al[17], Ruberti R F[18], Intisar SH Patty et al[19] and Ejaz Butt et al.[20], ShriLaxmi[21] who reported 25.6%.

We found about 65.52 % cases were in age group 31-50 years which were similar to Smita Shah et al^[22] found 59% and Haradhan et al^[23] found 60% cases in 40-59 years. Low frequency of meningioma 3.45% in pediatric age group which was in the similar range as noted by ShriLaxmi et al[21].

Our study confirmed preponderance of female sex which may be explained by progesterone dependent tumour growth. The male: female ratio was 1:2.5 and females constituted about 71.76 % cases. This figure approximately matches with all of the studies [21,22,23]. The most common presenting symptom was headache seen in 70.11% (61 out of 87) cases which was similar to studies done by Smita shah et al[22] and Haradhan et al[23] who found it in 75% and 72% cases

respectively. There was seen obvious majority of intracranial meningioma than spinal meningioma. Incidence of intracranial meningiomas was 90.8% which was comparable with Smita Shah et al[22] and Akyildiz EU et al[24] in which it was 90.2 % and 96% respectively.

The present study supported usual sites of predilection of meningiomas as about 37.93% cases were convexity meningiomas followed by sphenoid meningioma (14.93%). This was in accordance with studies done by Smita et al[22] and Thomas Backer et al[25] in which convexity meningioma constituted 51% and 39.3% respectively. We did find meningioma at unusual sites such as orbital meningioma, intraventricular meningiomas. 6 out of 8 (75%) spinal meningiomas were located at thoracic spinal level. Various studies like Traul et al[27] and Chamberlain et al[28] had similar observations suggesting thoracic segment as commonest spinal site.

Histological appearance of meningioma is an important predictor of tumour behaviour and is frequently a factor in decisions concerning therapy. Though incidence of histological subtypes varies in different studies meningothelial and transitional meningiomas were most common subtypes in most studies. This was followed by fibrous and psammomatous variants [Table-5]. Interestingly we got rare cases of secretory, clear cell, microcystic, secretory and lipomatous, metaplastic, papillary, chordoid, atypical, anaplastic variants of meningioma thus covering almost whole spectrum of histological subtypes.

Incidences of different WHO grades of meningioma in present study parallel others [Table-6]. There was an obvious predominance of Grade I meningiomas. Of the Grade II meningiomas (total 7 cases) 2 cases were atypical meningioma, 2 of clear cell meningioma and 1 was chordoid meningioma. While notably 2 cases showing brain invasion but otherwise benign histology were included as per WHO 2007 criteria. Three cases of anaplastic meningioma and one case of papillary meningioma constituted Grade III meningioma. As per institutional treatment protocol all cases of Grade I meningioma were treated surgically where extent of resection depended upon location, relationship with surrounding structures and expertise of operating neurosurgeon. Grade II and Grade III meningioma cases were sent for postoperative radiotherapy. Due to financial constraint we performed immunohistochemistry in only two cases of clear cell meningioma and lipomatous meningioma which showed positivity for EMA and Vimentin.

3 out of 87 cases were recurrent, contributing to 3.45% of the total, which is lower than the recurrent rate of 5.46 % observed by Shri Laxmi et al [21] 2 cases of anaplastic meningioma and one case of benign meningioma showed recurrence which was attributed to incomplete removal. In present study we considered the cases as radiologically and pathologically correlated only if the radiological impression matched exactly with final histopathological diagnosis. MRI and / CT scan findings were noted in all 87 cases of which 75 cases (86.22%) showed complete correlation with final histological diagnosis. In 4 cases (3.48%) diagnosis offered was glioma of which one case was called high grade glioma which turned out as anaplastic meningioma on histopathology. In 6 cases (6.89%) radiology could not pinpoint the diagnosis of meningioma and differential diagnosis was given of schwannoma of which 4 cases were in cerebello - pontine angle causing location bias. In 2 cases (1.74%) radiological diagnosis of only schwannoma was offered. Our experience was similar to Mary A.K et al [30] showing that though imaging can reliably diagnose meningiomas, histopathological subtypes of meningiomas could not be differentiated from each other based on radiological features. CT and MR imaging play indispensable role in the localization & characterization of these tumours, and MR have virtually yielded its position of dominance in characterizing these tumours [30]. When correlated with intra-operative squash finding, 91.95% accuracy (81 out of 87 cases) was observed. This was in parallel with study by Gabriela D et al [31] who found 93.54% concordance. We experienced difficulty in differentiating fibroblastic meningioma from schwannoma in 4 cases and diagnosis of benign spindle cell tumour with differential diagnosis of meningioma and schwannoma was given on squash cytology. Thomas P et al[33] have encountered similar difficulties in their study on overall lesions in CNS. In remaining 2 cases high grade tumour was the diagnosis offered on cytology. Smears showed anaplastic cells with increase mitotic activity but lacked in syncytial appearance or no other pointers indicating to meningothelial differentiation. On histology these cases turned out to anaplastic meningioma.

Thus, even though we missed exact diagnosis in 6 cases (6.46%) on squash smears cytology, it did not cause any adverse impact on immediate surgical management of the patient, proving that squash smear cytology is a rapid, reliable and simple technique for intraoperative consultation for diagnosis of meningioma.

Conclusion

Meningiomas are slow growing tumours arising from the meningotheelial cells accounting for 15.60% of all CNS neoplasms with a wide variety of histological patterns. These tumours are more common in women and Grade I tumours are predominant; Grade II and Grade III tumours are less frequent. Recurrence of tumours depends on histological grade and extent of surgery. Radiological localization helps in preoperative diagnosis while squash cytology is simple, cost effective and reasonably accurate method for intra-operative rapid diagnosis of meningioma.

List of Abbreviations Used

H&E - Haematoxylin and eosin, CNS- Central nervous system, CT- Computerised tomography, MRI- Magnetic resonance imaging, WHO- World Health Organisation, CP angle- cerebellopontine angle.

Funding: Nil,

Conflict of interest: None.

Permission of IRB: Yes

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How to cite this article?

Patil P.R., Sondankar D, Clinicopathological Study of Meningioma: *Int J Med Res Rev* 2016;4(4):592-601. doi: 10.17511/ijmrr.2016.i04.20.

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