Original Article

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Histopathological Spectrum of Adult and Paediatric Meningiomas

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ABSTRACT

Introduction: Meningiomas are a group of neoplasms showing a spectrum of histopathological variants, mostly corresponding to World Health Organization (WHO) grade I. However, certain histologic variants correspond histologically to WHO grades II and III. In this study, the histopathological spectrum of the adult as well as paediatric meningiomas received in our department over the last 12 years is being revisited with the aim to analyse the various histopathological variants, to assess their grade as per WHO 2016 criteria, their epidemiology and localization.

Material and Methods: A retrospective analysis of the histopathology records and clinical case files was done in 336 cases of (adult and paediatric meningiomas) histopathologically diagnosed cases of intracranial and intraspinal meningiomas (WHO grade I, II and III) received over a period of 12 years (starting from 2009-2020) in our department.

Results: The commonest grade in adults and children was WHO Grade I while the commonest histopathological variant in adults and children was Transitional meningioma.

Conclusion: As per WHO classification of CNS Tumours 2016, grade I meningiomas are associated with low risk of recurrence and aggressive behaviour, while WHO grade II and III meningiomas are associated with greater likelihood of recurrence and aggressive behaviour, highlighting the importance of accurate typing and grading of meningiomas on histopathology.

Keywords: *Adult Meningiomas, Paediatric Meningiomas, Histopathology, Spectrum of Meningiomas*

Introduction

Meningiomas are generally slow growing, dural based tumours derived from meningothelial (arachnoid) cells in the leptomeninges. These cells have both epithelial and mesenchymal characteristics which are shown by meningiomas in a spectrum of diverse histologic appearances. As per the existing literature, approximately 20-30% of intracranial neoplasms are meningiomas, approximately 25% of intraspinal neoplasms are meningiomas and approximately 10% of meningiomas are multiple. Mostly meningiomas arise proximal to the duramater within the intracranial, orbital and intravertebral cavities.

Meningiomas may arise at any age but are most common in middle-aged to elderly adults with a female predominance, although high grade meningiomas are more commonly encountered in males. Paediatric meningiomas compared to the adult counterparts are distinctly rare, usually manifesting with large tumour size, cyst formation, lack of dural attachment, high-grade histology and aggressive behaviour. They lack any female predominance and are more likely to occur in unusual locations, such as lateral ventricles, posterior fossa, and spinal epidural regions.

In this study, the histopathological spectrum of the adult as well as paediatric meningiomas received in our department over the last 12 years is being revisited with the aim to analyse the various histopathological variants, to assess their grade as per WHO 2016 criteria, their epidemiology and localization.

Materials and Methods

A retrospective analysis of the histopathology records and clinical case files was done in 336 cases of histopathologically diagnosed cases of intracranial and intraspinal meningiomas (WHO grade I, II and III) received over a period of 12 years (starting from 2009-2020) in our department. These 336 cases included adult as well as paediatric meningiomas. The samples were from our own Institute and from the Neurosurgery Department of one of our neighbour government hospital. Haematoxylin and Eosin staining was done for histological typing and grading of the tumours and the cases were analyzed for histotopathological typing and grading as per WHO 2016 criterion. Immunohistochemical stains including Epithelial

Membrane Antigen (EMA), Vimentin, Pankeratin, S100 and Ki 67 were applied in relevant variants of meningiomas, wherever required. The inclusion criteria included: any variant where IHC was required for supplementing the diagnosis while the exclusion criteria included those cases where the variants were identifiable on HE only. Age and gender distribution along with the localization of the 336 cases was analyzed.

Results

Amongst the 336 cases of meningiomas, 322 cases (95.83%) were amongst adults while 14 cases (4.17%) were amongst paediatric population. According to the WHO 2016 grading criteria, amongst the 322 adult meningioma cases, grade I meningiomas (300 cases) were the commonest representing 93.17% of cases followed by 20 cases of grade II (6.21%) and 2 cases (0.62%) of grade III meningiomas. In 14 paediatric meningioma cases, grade I meningiomas (10 cases) were the commonest representing 71.43% of cases followed by 3 cases (21.43%) of grade III meningiomas and a single case of grade II (7.14%) meningioma [Table 1].

According to histological type, in adults amongst the grade I, 238 meningiomas were Transitional (79.33%), 13 Meningothelial (4.33%), 13 Angiomatous (4.33%), 12 Psammomatous (4%), 9 Fibroblastic (3%), 9 Microcystic (3%), 3 Metaplastic (1%), 2 Secretory (0.67%) and 1 Sclerosing (0.34). Amongst grade II, there were 19 cases of atypical meningiomas (95%), and 1case of clear cell variant (5%). Amongst the 2 cases of grade III meningiomas, both were anaplastic meningioma (100%). In the paediatric population, amongst the grade I, all 10 meningiomas were Transitional (100%). Amongst grade II there was only 1 case of Atypical meningioma (100%), while all the 3 cases of grade III meningiomas were Rhabdoid meningiomas (100%) [Table 1] [Figure 1].

Overall, the mean age in adults was 45.27 years (range: 20 to 78 years) and in children it was 15.50 years (range: 9 to 18 years). In adults, maximum 91 cases (28.26%) were reported in the fifth decade, followed by 75 cases (23.29%) in fourth decade, 67 cases (20.81%) in sixth decade, 49 cases (15.22%) in third decade, 33 cases (10.25%) in seventh decade, 04 cases (1.24%) in second decade, 3 cases (0.93%) in eighth decade. In children 13 cases (92.86%) were reported in second decade and only 01 case (7.14%) was reported in first decade [Figure 2].

In adults, there were 84 males (26.09%) and 238 female patients (73.91%), the male: female ratio being 1: 2.8 while in paediatric population, there were 7 male (50%) and 7 female (50%) patients, the male: female ratio being 1: 1[Figure 3].

Amongst the 322 cases in adults, 265 cases (82.30%) were found at the intracranial location, 49 cases (15.22%) were found at intraspinal location followed by 8 cases (2.48%) at intra ventricular location. Amongst the 14 cases in paediatric population, 10 cases (71.43%) were found at the intracranial location and 4 cases (28.57%) were found at intraspinal location. In adults, amongst the intracranial meningiomas, 177 cases (66.79%) were at the cerebral convexities followed by 44 cases at posterior fossa (16.60%), 22 cases (8.30%) at sphenoid ridges, 7 cases (2.64%) at parasellar/suprasellar regions, 7 cases (2.64%) at olfactory grooves, 5 cases (1.89%) at tentorium and 3 cases (1.13%) at optic nerve sheath. Amongst the intraspinal cases 39 cases (79.60%) involved the thoracic spine while 10 cases (20.40%) involved the cervical spine. Amongst the intraventricular cases 7 cases were within the lateral ventricles (87.5%) followed by a single case in the third ventricle (12.5%) [Table 3] [Figure 4a].

In the paediatric population amongst the intracranial meningiomas, 7 cases (70%) were at the cerebral convexities followed by 2 cases at posterior fossa (20%), and 1 case (10%) at sphenoid ridges. Regarding the intraspinal location, 2 cases (50%) were found in the thoracic region and 2 cases (50%) in the cervical region showing an equivocal distribution [Table 3] [Figure 4b].

In adults, amongst the grade I meningiomas, Transitional meningiomas had the age range from 20-78 years with a mean age of 45.81 years. Male: female ratio was 1:3.7 and the commonest location was cerebral convexities. Meningothelial meningiomas had the age range from 32-75 years with a mean age of 50.46 years. Male: female ratio was 1:1.4 and the commonest location was cerebral convexities. Angiomatous meningiomas had the age range from 25-60 years with a mean age of 39.46 years. Male: female ratio was 1:2.3 and the commonest location was cerebral convexities. Psammomatous meningiomas had the age range from 20-60 years with a mean age of 42.50 years. Male: female ratio was 1:3 and the commonest location was thoracic spine. Fibrous meningiomas had the age range from 22-50 years with a mean age of 37.33 years. Male: female ratio was 1:2 and the commonest location was cerebral convexities. Microcystic meningiomas had the age range from 28-64 years with a mean age of 48 years. Male: female ratio was 2:1 and the commonest location was cerebral convexities. Metaplastic meningiomas had the age range from 31-51 years with a mean age of 42 years. Male: female ratio was 2:1 and the commonest locations included cerebral convexities, posterior fossa and sphenoid ridges.

Secretory meningiomas manifested at the age of 50 years with a Male: female ratio of 0:2. Commonest locations included olfactory grooves and sphenoid ridges. Sclerosing meningiomas had a mean age of 27 years. Male: female ratio was 0:1 and the commonest location was cerebral convexities.

In the paediatric population, amongst the grade I meningiomas, Transitional meningiomas had the age range from 9-18 years with a mean age of 15 years. Male: female ratio was 2.3:1 and the commonest locations included cerebral convexities, thoracic and cervical spine.

In adults, amongst the grade II meningiomas, Atypical meningiomas had the age range from 20-70 years with a mean age of 44.95 years. Male: female ratio was 1: 1.1 and the commonest location was cerebral convexities. Clear cell meningiomas had a mean age of 30 years. Male: female ratio was 1:0 and the commonest location was thoracic spine. In the paediatric population, Atypical meningioma had a mean age of 18 years. Male: female ratio was 1:0 and the commonest location was cerebral convexities.

In adults, amongst the grade III meningiomas, Anaplastic meningiomas had the age range from 22-38 years with a mean age of 30 years. Male: female ratio was 1:0 and the commonest location was cerebral convexities. In the paediatric population, Rhabdoid meningiomas had the age range from 13-18 years with a mean age of 16.33years. Male: female ratio was 0:1 and the commonest location was cerebral convexities [Table 3].

Table 1: showing grade wise distribution in adult and paediatric population.

WHO Grade	Number of cases	% of cases
Adult population (n= 322; 95.83%)		
WHO Grade I	300	93.17%
• Transitional meningiomas	238	79.33%
• Meningothelial meningiomas	13	4.33%
• Angiomatous meningiomas	13	4.33%
• Psammomatous meningiomas	12	04%
• Fibroblastic meningiomas	09	03%
• Microcystic meningiomas	09	03%
• Metaplastic meningiomas	03	01%
• Secretory meningiomas	02	0.67%
• Sclerosing meningiomas	01	0.34%
WHO Grade II	20	6.21%
• Atypical meningiomas	19	95%
• Clear cell meningiomas	01	05%
WHO Grade III	02	0.62%
• Anaplastic	02	100%
Paediatric population (n= 14; 4.17%)		
WHO Grade I	10	71.43%
• Transitional meningiomas	10	100%
WHO Grade II	01	7.14%%
• Atypical meningiomas	01	100%
WHO Grade III	03	21.43%
• Rhabdoid meningiomas	03	100%

Table 2: showing location wise distribution of meningiomas in adult and paediatric population.

Adult meningiomas (n 322)	
Intracranial meningiomas • Cerebral convexities • Posterior fossa • Sphenoid ridges • Parasellar/Suprasellar regions • Olfactory grooves • Tentorium • Optic nerve sheath	**265 (82.30%)** 177 44 22 07 07 05 03
Intraspinal meningiomas • Cervical spine • Thoracic spine	**49 (15.22%)** 10 39
Intraventricular meningiomas • Lateral ventricles • Third ventricle	**08 (2.48%)** 07 01
Paediatric meningiomas (n 14)	
Intracranial meningiomas • Cerebral convexities • Posterior fossa • Sphenoid ridges	**10** 07 02 01
Intraspinal meningiomas • Cervical spine • Thoracic spine	**04** 02 02

Table 3: showing clinicopathological details of various variants of meningioma in adult and paediatric population

Histopathological variant (n)	Age range (in years)	Mean age (in years)	M: F ratio	Commonest location
In Adult population (n 322)				
Meningiomas (WHO grade I) with low risk of recurrence and aggressive behaviour				
Transitional meningiomas (238)	20-78	45.81	1: 3.7	Cerebral convexities
Meningothelial meningiomas (13)	32-75	50.46	1: 1.4	Cerebral convexities
Angiomatous meningioma (13)	25-60	39.46	1: 2.3	Cerebral convexities
Psammomatous meningioma (12)	20-60	42.50	1: 3	Thoracic spine
Fibrous (fibroblastic) meningioma (9)	22-50	37.33	1:2	Cerebral convexities
Microcystic meningioma (9)	28-64	48	2: 1	Cerebral convexities
Metaplastic meningioma (3)	31-51	42	2: 1	Cerebral convexities, posterior fossa, sphenoid ridges
Secretory meningioma (2)	50	50	0: 2	Olfactory grooves, sphenoid ridges
Sclerosing meningioma (01)	27	27	0:1	Cerebral convexities
Meningiomas (WHO grade II and grade III) with high risk of recurrence and aggressive behaviour				
Atypical meningioma (19)	20-70	44.95	1: 1.1	Cerebral convexities
Clear cell meningioma (1)	30	30	1: 0	Thoracic spine
Anaplastic meningioma (2)	22-38	30	1: 0	Cerebral convexities
In Pediatric population (n 14)				

Histopathological variant (n)	Age range (in years)	Mean age (in years)	M: F ratio	Commonest location
Meningiomas (WHO grade I) with low risk of recurrence and aggressive behaviour				
Transitional meningioma (10)	9-18	15	2.3:1	Cerebral convexities, Thoracic spine, Cervical spine
Meningiomas (WHO grade II and grade III) with high risk of recurrence and aggressive behaviour				
Atypical meningiomas (1)	18	18	1: 0	Cerebral convexities
Rhabdoid meningiomas (3)	13-18	16.33	0: 1	Cerebral convexities

Discussion

The term Meningioma was proposed by Harvey Cushing in 1922 based primarily on the anatomical features, followed by various hypotheses on the cell of origin including dural, endothelial, fibroblastic and epithelial cell types. After several discussions, a possibility was raised that these tumours might originate from the inner arachnoidal lining of the duramater, rather than the dense fibrous tissue of duramater. It was also stated that the histopathology of meningiomas was like the cell clusters that line arachnoid villi and since then these arachnoidal cap cells have been considered the cell of origin for meningiomas. [1].

A detailed monograph on 313 meningiomas providing a better understanding of these tumours was published by Harvey Cushing in 1938 with Louise Eisenhardt. [2] The second major monograph summarizing the major advances based on 1300 cases of meningiomas was published by John Kepes in 1982. [3] Later on few more aggressive variants were identified and added to the existing variants, grading system was extensively revised and gradually with the advent of molecular pathology the World Health Organization's (WHO) 2007 classification was introduced. [4] In 2016, WHO updated the classification and grading of tumours of the central nervous system incorporating well established molecular parameters and classified meningiomas into meningiomas with low risk of recurrence and aggressive behaviour (WHO grade I) and meningiomas with greater likelihood of recurrence and aggressive behaviour (WHO grade II and grade III) in adult and paediatric population. [5]

Meningiomas in adults account for about one third of the primary intracranial neoplasms. These are most common in middle aged to elderly adults, showing a peak in sixth and seventh decades. [6] Though meningiomas do manifest in the paediatric population [7], but the incidence in the first two decades is quite low. [8] In our study, in the adult meningiomas the peak was seen in the fifth decade, followed by fourth decade, concordant to the studies conducted by Shah et al, Shrilakshmi S and Patty S. [9-11] In the paediatric population, our study had 14 cases (4.17%) with a mean age of 15.5 years, results almost similar to the existing literature. [12-17]

According to the existing literature, meningiomas have been more common in women than men, with an approximate 1.7: 1 female/male ratio. In our study in adults the female/ male ratio was 2.8: 1, similar to the results of Thomas et al. [18] while in the paediatric population it was 1: 1. It has been observed that this difference is greatest prior to menopause with the highest female/male ratio of 3.15: 1, although, grade II and III meningiomas have been reported at higher rates in males. [19]

Meningiomas mostly arise proximal to the duramater within the intracranial, orbital and intravertebral cavities. Common sites within the cranial cavity include the cerebral convexities, olfactory grooves, sphenoid ridges, para/suprasellar regions, optic nerve sheath, petrous ridges, tentorium and posterior fossa. [7] In our study, in adult meningiomas, the commonest sites were intracranial (82.30%), intra spinal (15.2%) and intraventricular (2.48%). Amongst the intracranial meningiomas, maximal numbers were located over the cerebral convexities followed by posterior fossa, while amongst the intra spinal meningiomas the commonest location was the cervical spine, almost concordant with the existing literature and the study conducted by Shrilakshmi S. [10] Amongst the intraventricular cases, maximal cases were in lateral ventricles followed by 3rd ventricle. Usually intraventricular and epidural locations are uncommon and other than neural axis these tumours are rare. [18] However, in the paediatric population, there were 71.43% intracranial and 28.57% intraspinal meningiomas. Amongst the intracranial meningiomas, maximal numbers were located over the cerebral convexities followed by posterior fossa, while amongst the intra spinal meningiomas the distribution was equivocal between the cervical and thoracic spine.

Clinical manifestations in adult as well as paediatric meningiomas usually depend on the location of these tumours. Generally, these are slow growing tumours

manifesting with focal neurological deficits, increased intracranial pressure, headache and seizures mostly due to the compression of the adjacent structures. [19]

In adult and paediatric meningiomas, Magnetic Resonance Imaging (MRI) shows circumscribed, isodense, dural masses with uniform contrast enhancement. There may be areas of calcification, best seen on computed tomography (CT) scan. The characteristic radiologic feature of meningioma is the dural tail, a wedge-shaped extension of tumour at the edge and is contrast enhancing. [20] Higher grades may occasionally show peritumoural cerebral edema. [21]

Macroscopically, meningiomas in adults and children show a diverse range, depending upon the location, growth pattern and the histological variant. Commonly these are rubbery, well circumscribed, spherical and firmly attached to the inner surface of the dura. Usually these are solitary neoplasm, but in sporadic cases these may be multiple. Occasionally these are dumbbell shaped, and rarely these may be en plaque meningiomas, defined by a carpet like growth pattern, resulting in long stretches of thickened, sometimes rough or shaggy dura. [22] Tumour surface is usually smooth or bosselated while the cut surface is white, yellow or tan often showing white streaky bands of fibrous tissue. However, cut surface may be diverse in certain variants, like gritty in psammomatous variant, yellow in xanthomatous variant, white in metaplastic variant due to cartilage and bone formation, moist glistening surface in microcystic variant and a tan red gland like appearance in the secretory variant. Foci of haemorrhage and necrosis suggest variants like atypical and anaplastic.

WHO in 2016 grouped the Meningioma variants into (i) Meningiomas with low risk of recurrence and aggressive behaviour and (ii) Meningiomas with greater likelihood of recurrence and aggressive behaviour. The first group comprises of Meningothelial meningioma, Fibroblastic meningioma, Transitional meningioma, Psammomatous meningioma, Angiomatous meningioma, Microcystic meningioma, Secretory meningioma, Lymphocyte-rich meningioma and Metaplastic meningioma while the second group comprises of Chordoid meningioma, Clear cell meningioma, Atypical meningioma, Papillary meningioma, Rhabdoid meningioma, Anaplastic meningioma and meningiomas of any subtype with high proliferation index. In the first group all variants correspond to WHO grade I however, in the second group Chordoid meningioma, Clear cell meningioma, Atypical meningioma correspond to WHO grade II and Papillary meningioma, Rhabdoid meningioma, Anaplastic meningioma correspond to WHO grade III. [1] In our study, the commonest grade in adults and children was WHO Grade I while the commonest histopathological variant in adults and children was Transitional meningioma.

Meningiomas are basically a surgically treated disease. Concerning the management, the best therapeutic approach is gross tumour resection.

Both in adults and children, the extent of resection is an important prognostic factor as recurrence free rates improve significantly with an increasing extent of removal. It has been reported as a key prognostic factor for progression free survival in paediatric meningiomas by Kotecha et al in their study which concluded that children who undergo initial gross tumour resection have a significantly better progression-free survival than those with an initial subtotal resection. [23] Most paediatric CNS tumours (especially < 6 years of age) have a worse prognosis. Worse overall survival in this age group might be explained by congenital tumour development, which often results in tumours that are more aggressive in their biological behaviour. [23]

Conclusion

To conclude, meningiomas have a diverse spectrum of several histopathological variants corresponding to WHO grade I (meningiomas associated with low risk of recurrence and aggressive behaviour), grade II and III (meningiomas associated with greater likelihood of recurrence and aggressive behaviour). In a nutshell, this study highlights the histopathological spectrum of adult and paediatric meningiomas reported in our department.

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