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Original Article

Clinicopathological Study of Meningioma in a Sample of Iraqi Patients in Baghdad District

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BACKGROUND: Meningiomas are tumors that arise from the meningothelial cells that line the arachnoidal cell layer of meningeal coverings in the brain and the spinal cord. They constitute one of the most common types of primary intracranial tumors.

OBJECT: To evaluate a number of cases of meningiomas that have undergone surgical procedures in the past three years and to record the frequency of various histopathological variants and tumor grades according to 2016 World Health Organization (WHO) classification and their correlation with clinical parameters such as age, gender and tumor location.

METHODS: A retrospective case series study of 57 patients with meningioma surgically operated in the neurosurgery department of Ghazi Al-hariri hospital in Baghdad, Iraq, between January 2018 and December 2020. The epidemiology, clinical manifestations, tumor sites and histopathological variants were studied.

RESULTS: The mean age of patients in this study was 48.4 ± 12.5 years, with a male-to-female ratio of 1:4. Intracranial meningiomas represented 49/57 cases (86%). The most frequent clinical presentations for intracranial meningiomas were headache (61.2%), blurred vision (36.7%) and seizures (21.4%). WHO grade 1 meningiomas represented the vast majority of tumors in the present study with a total of 55/57 cases (96.5%). The most common histopathological variant was the meningothelial variant in 41/57 cases (71%).

CONCLUSION: Meningioma is a common primary intracranial tumor in adults. Females are more prone to developing this tumor than males. Most cases of meningioma behave as benign neoplasms; however, a considerable number presented as recurrent tumors, which implies that further research is required.

KEYWORDS: WHO grade, Intracranial, meningiomas.

INTRODUCTION

Meningioma is a tumor that arises from meningothelial cells which are dedicated cells that present in the arachnoidal layer of meninges, also covering the arachnoidal villi in the venous sinuses of the dural membrane and their branches.[1] It is the most common primary intracranial tumor in adults, comprising 20–30% of all primary brain tumors.[2] Most cases of meningioma are benign; however, aggressive cases with distant metastasis, especially to the lungs, have been reported.[3]

The incidence rate for meningioma in Iraq is 0.15 and 0.25 per 100,000 population for males and females, respectively.[4] The vast majority of cases of meningioma arise in middle or later adult life, and females are more susceptible to developing this tumor than males.[1] Two-thirds of intracranial meningiomas occur in females, and this ratio rises to 90% for spinal meningiomas.[2]

Some evidence suggests that there exists a female hormonal influence on the growth of meningiomas. The evidence suggests that they are expressed by the immunoreactivity of tumor cells to hormonal markers (especially to the progesterone receptor (PR) marker) in addition to a notably rapid growth of some meningiomas during pregnancy and during the luteal phase of the menstrual cycle.[1]

A meningioma grows as a firm, circumscribed or semi-circumscribed mass, widely attached to the dura mater. In most instances, it is easily separated from adjacent tissues.[1] Most meningiomas have an indolent growth; they can possess an indistinct or non-specific mass effect or can lead to specific signs and symptoms related to the part of the brain on which the tumor mass presses.[5]

The majority of intracranial meningiomas are located anteriorly, usually in close vicinity to the superior longitudinal sinus, and present as a dura-based mass covering the cerebral hemisphere or attached to the falx cerebri; however, they can also present as craniobasal masses, especially in the anterior part of the cranial cavity near the olfactory groove. Meningiomas arise less frequently in the posterior cranial fossa, such as the petroclival region, cerebellopontine angle and cerebellar convexity. Notably, cases have been reported of cranial meningioma arising from non-dural parts of the cranial cavity; however, these are rare.[3] The existence of a meningioma at a basal location in the cranial cavity

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comprises a negative prognostic factor, as it adds technical challenges in terms of access to it by a surgeon intending to perform complete excision.[1]

The extracranial meningioma in the spine favors the thoracic region and, less frequently, the cervical region of the spinal canal, whereas it rarely occurs in the lumber region of the spinal canal.[3] Meningiomas are not entirely craniospinal located tumors, as some have been reported in places like the orbital region, nasal sinuses, close to jugular vessels in the neck, skin, or – even further from the central nervous system – in the pulmonary tissues and other chest spaces.[1]

Meningiomas have been classified into various grades according to their risk of recurrence and distant metastasis. The 2016 World Health Organization (WHO) classification of meningiomas recognizes three grades of the tumor: grade 1, common meningioma with benign behavior; grade 2, intermediate or atypical meningioma; and grade 3, anaplastic meningioma or malignant meningioma, which occurs less commonly than the other two grades but is associated with aggressive biological behavior **(Table 1)**.[6]

Microscopically, meningiomas can be present in different histopathological patterns. WHO grade 1 meningiomas account for most of the cases and are represented by various histopathological patterns? The most common patterns are the meningothelial (syncytial) pattern, which represents small groups of cells that have indistinct cell membranes; the fibroblastic pattern, accounting for the elongated cells that are separated by many collagenous fibers; the transitional pattern, which is an intermediate between these first two patterns; and the psammomatous pattern, which is so-named because of the characteristic psammoma bodies that result from the calcifications of small groups of meningeal cells.[5]

Atypical or WHO grade 2 meningiomas account for approximately 25% of all cases of meningioma. Grade 2 meningiomas are characterized by a more aggressive growth and a higher risk of recurrence compared with grade 1 tumors. They are distinguished from other low-grade tumors by their increased mitotic rate in addition to central nervous system infiltration and other intrusive properties. Microscopically, grade 2 meningiomas appear as clear and chordoid patterns, which are distinct forms for this intermediate grade.[5]

Anaplastic or WHO grade 3 meningiomas, which represent the least frequent grade but have the most devastating effect, account for 1–3% of all meningioma cases. These high-grade tumors can be mistaken for epithelial or soft-tissue cancers. The tumor cells have notable mitotic activity and a propensity for tissue infiltration. The histological forms for this grade are papillary and rhabdoid.[5]

The risk of recurrence in meningioma is influenced by many factors, such as tumor grade and the degree of tumor resection. The higher the tumor's grade, the more likely it might recur. Moreover, tumors that are located in the cranial base, and therefore confer more challenges in terms of total resection, are more likely to recur than others.[7]

The Simpson grade of meningioma resection was described by Donald Simpson in 1957 and correlates the degree of completeness of surgical resection with symptomatic tumor recurrence, such that a more complete tumor resection is associated with a lower probability of symptomatic recurrence.[8]

Table 1: The 2016 WHO classification of meningiomas.[9]

Grade I: Benign	
Meningothelial	
Fibrous (fibroblastic)	
Transitional (mixed)	
Psammomatous	
Angiomatous	
Microcystic	
Secretory	
Lymphocyte rich	
Metaplastic	
Grade II: Atypical	
Clear cell	4–19 mitotic figures/10 HPF*
Chordoid	Or brain invasion
	Or three minor criteria: – increased cellularity – small cell with high N/C ratio – large and prominent nucleoli – patternless or sheet-like growth – foci of spontaneous or geographic necrosis
Grade III: Anaplastic	
Rhabdoid	≥20 mitotic figures/10 HPF
Papillary	Or frank sarcomatous carcinomatous histology

*HPF: High Power Field.

METHODS

A retrospective case series study included the analysis of data from 57 patients with meningioma collected from the neurosurgical department, Ghazi Al-hariri Hospital for Special Surgeries, Medical City, Baghdad, Iraq, between January 2018 and December 2020. The study was approved by the institutional review board (IRB) of the Scientific Council of Anatomical Pathology/Arab Board for Health Specialization in Iraq.

Inclusion criteria

All cases of meningioma that were operated upon in the neurosurgical department at Ghazi Al-hariri Hospital in Baghdad, with diagnosis confirmed by histopathological examination, have been included.

Exclusion criteria

Cases that were deficient in some of the clinical data relevant to the scope of this study (six cases) were not included in the study.

The cases were surgically operated upon in the neurosurgery department, and the tissue samples were formalin-fixed, paraffin-embedded, sectioned at 4–5 μm and stained with hematoxylin and eosin (H&E) stain, then the histopathological diagnosis was revised.

Statistical analysis was carried out using the frequency, percentage, mean, standard deviation and chi-square test to assess the different WHO grades and histopathological variants and to evaluate their correlation with age, gender and tumor location. A *p*-value of ≤0.05 was considered to be statistically significant.

RESULTS

The mean age of patients in the study was 48.4 ± 12.5 years. The age group with the highest number of patients was 41–50 years (32%), while the age group with the least number was <31 years (11%) **(Fig. 1)**. The majority of the patients were females and represented 46/57 patients (78.8%) in the studied group and the remainder were males (n = 11/57; 21.2%), giving a male-to-female ratio of 1:4 **(Fig. 2)**.

Regarding the sites of meningioma, intracranial meningiomas were found in 49/57 patients (86%), while spinal tumors were found in 5/57 patients (9%). Orbital meningiomas were present in 3/57 patients (5%) in our study **(Fig. 3)**. Regarding intracranial tumors, we found that the frontal lobe was the most common site and was present in 11/57 (19%) patients in the studied group, while the least common site of tumors was the occipital lobe, which was present in 2/57 (3.5%) patients. **Table 2** describes the frequency and site of all tumors in the studied group.

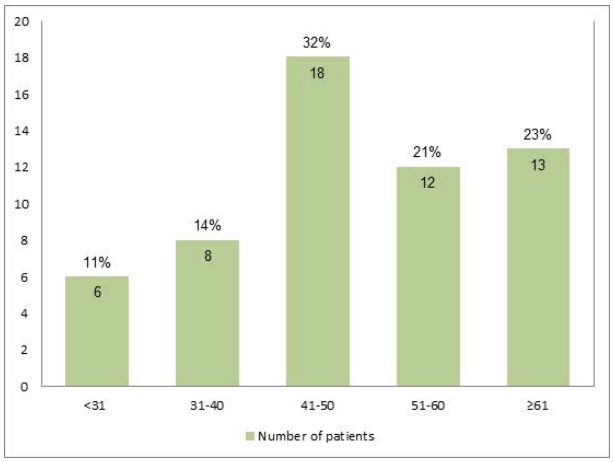

Fig 1: Age distribution of the patients in the study group.

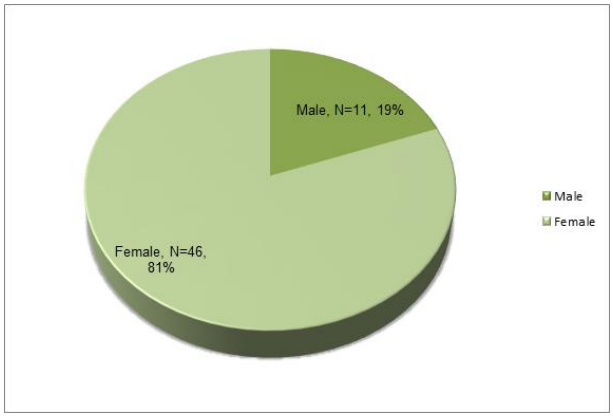

Fig 2: Gender distribution of the patients in the study group.

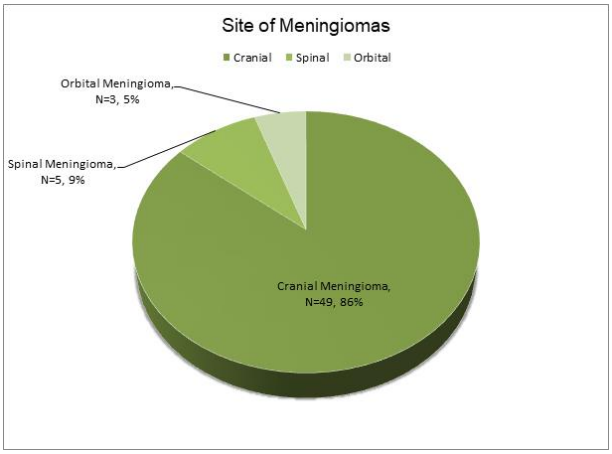

Fig 3: Site of meningiomas in the study group.

Table 2: Specific sites of meningioma in the study group

	Site of the Tumor	No.	%	Specific Site	No.
1	Cerebral convexity	30	53%	Frontal lobe	11
				Parietal lobe	8
				Temporal lobe	5
				Fronto-parietal lobe	4
				Occipital lobe	2
2	Skull base	12	21%	Middle cranial fossa	8
				Anterior cranial fossa (olfactory groove)	4
3	Posterior fossa	7	12%	Posterior cranial fossa	7
4	Spinal	5	9%	Dorsal spine	4
				Lumber spine	1
5	Orbital	3	5%	Orbital	3
	Total				57

Referring to the clinical presentation of intracranial meningiomas, headache was the most common symptom (61.2%), followed by blurred vision (36.7%) and seizures (22.4%), while the least common signs were bowel incontinence, personality changes and visual field loss (2% each) **(Table 3)**.

Table 3: Clinical presentation of patients with intracranial meningiomas in the study group*

Presentation	No.	%
Headache	30	61.2%
Blurred vision	18	36.7%
Seizure	11	22.4%
Limb numbness	7	14.3%
Dizziness	7	14.3%
Urinary incontinence	6	12.2%
Nausea	5	10.2%
Vomiting	5	10.2%
Vertigo	4	8.2%
Hearing loss	4	8.2%
Limb weakness	4	8.2%
Disturbed gait	3	6.1%
Loss of smell	3	6.1%
Loss of balance	2	4.1%
Slurred speech	2	4.1%
Difficulty in swallowing	2	4.1%
Facial numbness	2	4.1%
Bowel incontinence	1	2.0%
Personality changes	1	2.0%
Visual field loss	1	2.0%

*More than one presentation for each patient.

The distribution of histological variants and grades (WHO 2016) of meningioma in the studied group is shown in **Table 4**. The predominant tumor grade in the study was WHO grade 1 (n = 55; 96.5%), while the atypical variant (WHO grade 2) constituted a minority (n = 2; 3.5%) in the studied group **(Fig. 4).** The histopathological variants of cranial meningiomas were dominated by the meningothelial variant (n = 41; 72%), while the least common variant was the microcystic variant (n = 1; 1.7%).

Table 4: The distribution of histological variants of meningioma in the study group

	Histopathological Variant	WHO Grade	No.	%
1	Meningothelial	1	41	72%
2	Psammomatous	1	4	7.0%
3	Angiomatous	1	4	7.0%
4	Fibroblastic	1	3	5.3%
5	Transitional	1	2	3.5%
6	Atypical	2	2	3.5%
7	Microcystic	1	1	1.7%

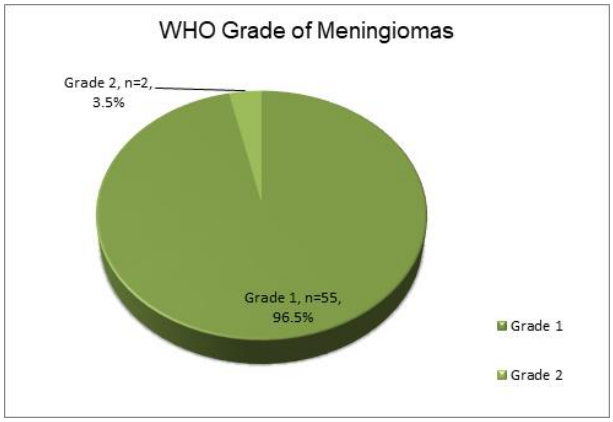

Fig 4: WHO grade of meningiomas in the study group.

The distribution of the histopathological variants in the present study according to age indicated that the highest number of patients with the meningothelial variant (32%) fell in the 41–50 years age group, followed by 22% in the ≥61 years group, 17% each in the 31–40 and 51–60 years groups, and 12% in the <31 years group. Up to 75% of the cases diagnosed with the psammomatous variant in this study were found in the age group ≥61 years. The atypical variant (WHO grade 2) meningioma presented in two different age groups: 31–40 years and 51–60 years, with a single case for each **(Table 5).**

Table 5: Distribution of the histopathological variants of meningioma according to the age

	Histopathological Variant (n = 57)	Age Group										
		<31		31–40		41–50		51–60		≥61		
		No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	Total
1	Meningothelial	5	12%	7	17%	13	32%	7	17%	9	22%	41
2	Angiomatous	0	0%	0	0%	3	75%	0	0%	1	25%	4
3	Psammomatous	0	0%	0	0%	1	25%	0	0%	3	75%	4
4	Fibroblastic	0	0%	0	0%	1	33%	2	67%	0	0%	3
5	Transitional	1	50%	0	0%	0	0%	1	50%	0	0%	2
6	Atypical (WHO grade 2)	0	0%	1	50%	0	0%	1	50%	0	0%	2
7	Microcystic	0	0%	0	0%	0	0%	1	100%	0	0%	1
	Total	6		8		18		12		13		57

P = 0.23*.

*A *p*-value of ≤0.05 was regarded as statistically significant.

The distribution of different histopathological variants of meningioma in the studied group according to gender is presented in **Table 6**.

Table 6. Distribution of histopathological variants of meningioma according to patients' gender

Histopathological Variant (n = 57)	Gender				Total
	Male (n = 11)		Female (n = 41)		
	No.	%	No.	%	
Meningothelial	8	20%	33	80%	41
Angiomatous	1	25%	3	75%	4
Psammomatous	0	0%	4	100%	4
Fibroblastic	1	33%	2	67%	3
Transitional	1	50%	1	50%	2
Atypical (WHO grade 2)	0	0%	2	100%	2
Microcystic	0	0%	1	100%	1
Total	11		46		57

P = 0.76*.

*A *p*-value of ≤0.05 was regarded to be statistically significant.

In reference to the correlation between histopathological variants and tumor site, the meningothelial variant was the most common variant located in the cerebral convexities and parafalcine area (22/30; 73%), skull base (10/12; 83%), posterior cranial fossa (5/7; 71%) and orbital area (2/3; 67%), while it presented in only 2/5 (40%) spinal tumors. The atypical variant (WHO grade 2) represented 1/3 (33%) orbital tumors and 1/30 (3.3%) cerebral convexity tumors in the present study. The psammomatous variant presented in 2/5 (40%) cases of the spinal meningioma **(Table 7)**.

Table 7: Frequency of the histopathological variants of meningioma according to the site of tumors

Site	Histopathological Variant: Meningothelial		Angiomatous		Psammomatous		Microcystic		Fibroblastic		Transitional		Atypical		Total
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.
Cerebral convexity and parafalcine area	22	73%	3	10%	1	3%	1	3%	0	0%	2	7%	1	3%	30
Skull base	10	83%	1	8%	0	0%	0	0%	1	8%	0	0%	0	0%	12
Posterior cranial fossa	5	71%	0	0%	1	14%	0	0%	1	14%	0	0%	0	0%	7
Spinal	2	40%	0	0%	2	40%	0	0%	1	20%	0	0%	0	0%	5
Orbital	2	67%	0	0%	0	0%	0	0%	0	0%	0	0%	1	33%	3
Total	41	72%	4	7%	4	7%	1	1.7%	3	5.3%	2	3.5%	2	3.5%	57

P = 0.23*.

*A *p*-value of <0.05 was regarded to be statistically significant.

In terms of tumor recurrences, 6 out of 57 (10.5%) cases presented as recurrent tumors, with the period of recurrences ranging from 8 months to 5 years. The average age of patients with recurrent tumors was 42.5 years, with a male-to-female ratio of 1:5. The histopathological variants of recurrent cases were meningothelial (n = 5/6; 83.4%) and atypical (n = 1/6; 16.6%) variants. The frontal lobe with falx cerebri was the most common site for the recurrent tumors (33.3%), followed by the middle cranial fossa (16.6%), temporal lobe (16.6%), spinal column (16.6%) and orbital region (16.6%), with a single case for each.

DISCUSSION

Harvey Cushing in 1922 was the first to apply the term "meningioma".[10] The mean age of patients in the present study was 48.4 ± 12.5 years, with the most frequent age group being 41–50 years and more than half of the patients were in their fifth or sixth decade of life. The male-to-female ratio was 1:4. Our study findings are aligned with Solanke et al. study in India, as the reported mean age of their sample was 48.46 (± 13.28) years, with more than half of the patients in their fifth or sixth decades of life. However, their male-to-female ratio was 1:2.[11] This gender ratio dissimilarity may be attributed to the sample size. In another previous study in Iraq (Ninawa), Abed et al. reported a mean age of meningioma at presentation of 44 ± 12 years; most patients were 40–49 years old, and the male-to-female ratio was 1:2.[12] This gender ratio inconsistency may be attributed to the small sample size in the present study and the different geographical distribution. The median age of meningioma in the United States is 65 years old, as reported by Ostrum et al. [13] This significant variation from our findings may be due to the different average age and ethnic group diversity in the United States in addition to the methods used for diagnosis, as the authors used radiographic tools as well as histopathological diagnosis as a confirmation method.

Regarding tumor site, according to our study, the intracranial cavity represented the most common site of meningioma (86% of cases), followed by spinal and extracranial sites (orbital), which represented 9% and 5% of the cases, respectively. Our results are comparable to those of Solanke et al. study in India, which reported that cranial and spinal tumors accounted for 88% and 11% of cases, respectively, in addition to a single extracranial case presented in the parotid gland.[11] According to our case series, the most common sites for intracranial tumors were the cerebral convexities and parafalcine areas (53%), followed by the skull base (21%) and posterior cranial fossa (12%). In a previous retrospective study of 126 patients with meningioma in India over a 10-year period, Malik et al. stated that intracranial sites represented 76.2% of all meningioma cases, and, of those, cerebral convexities were the most common site of presentation (42.1%), followed by the skull base and posterior fossa, with 15.0% and 11.9%, respectively, while spinal tumors represented 23.8%.[14] The most common site of spinal meningioma in the present study was the thoracic (dorsal) spines (80%). This is in agreement with the findings of Malik et al. study, which reported the thoracic region to represent the most common site of spinal meningioma, with 53.3% of all spinal cord tumors presenting in dorsal spines. [14] The percentage variation may be attributed to the small sample size.

Generally, meningioma tumors have indolent growth, and patients' complaints are commonly due to the tumors' effect of increasing intracranial pressure that leads to signs and symptoms such as headaches or seizures or may be due to the tumor's direct effect on a specific part of the brain that it displaces, leading to focal neurological symptoms.[5] According to the present study, headache, blurred vision and seizures were the most frequently encountered clinical presentations of intracranial tumors, where 32/49 patients (61.2%) complained of headache that was usually accompanied by one or more other symptoms. The second and third most common presenting symptoms were blurred vision (36.7%) and seizures (22.4%). This is in agreement with Shenoy et al. study in terms of reporting headache as the most frequent symptom (58.7%), while limb weakness (33.3%) and convulsions (23.8%) were the second and third most frequent presenting symptoms.[15] This variation may be attributed to sample size differences.

Regarding tumor grades, WHO grade 1 meningioma represented 96.5% of cases in the current study, while WHO grade 2 tumors represented 3.5% of cases. It is worth noting that no WHO grade 3 tumors were reported in the present study. These results support those of a previous study in India by Shenoy et al. [15] Furthermore, a study in Iraq by Al-Nuaimy et al. reported that 84%, 10% and 6% of meningioma cases were WHO grade 1, 2 and 3, respectively.[16] However, Abed et al. reported that 70.0%, 24.4% and 5.5% of tumors were WHO grade 1, 2 and 3, respectively.[12] Again, these variations may be due to small sample sizes and different geographical distribution in the studies. Regarding tumor variants in the present study, we found that the meningothelial variant constituted 41/52 (72%) cases of meningioma, while Al-Nuaimy et al. reported that meningothelial tumors represented 24/50 (48%) meningiomas.[16] The percentage difference may be attributed to the different geographical distribution of the patients' samples as well as small sample sizes.

Although statistically insignificant (p = 0.23), the correlation between histopathological variants and tumor site **(Table 7)** demonstrates the domination of the meningothelial variant in the cerebral convexities and parafalcine area (73%), posterior cranial fossa (71%), skull base (83%) and orbital area (66%). The psammomatous variant presented in spinal cord with a relatively higher percentage (40%) than other locations like cranial cavity, in agreement with a previous study by Lee et al, which reported the preference of the psammomatous variant to be presented in the spinal cord.[17] Moreover, we reported the thoracic spine to be

the most common site of spinal meningioma (80%), which supports the findings of a previous larger study of 131 patients with spinal meningiomas by Sandalcioglu et al.[18]

Recurrent tumors represented 10.5% of all cases in the present study, and the meningothelial variant was the most common (83.4%). Al-Nuaimy et al. [16] reported that 14% of tumors in their study were recurrent. These values were significantly higher than the recurrence rate value of 5.6% (7/126) reported by Malik et al. [14], who counted the transitional variant as the most common variant in recurrent cases, with a male-to-female ratio of 2.5:1. The previous variances may be attributed to different geographical distribution; however, our study is comparable to Malik et al. study [14] in that most of the recurrent tumors were WHO grade 1, with grade 1 tumors representing 83% (5/6 cases) and 71% (5/7) of the total recurrent cases in our study and Malik et al study, respectively.[14] It is relevant to note that Simpson grade was not included in the current study because of the shortage of data regarding the completeness of tumor resection, and this grading has an important role in predicting tumor recurrence after surgical resection.[8]

The study's obstacles and challenges included a scarcity of patients' clinical data (for instance, in relation to diagnostic imaging reports) in addition to the lack of a unified electronic national medical record system in Iraq. Here, we would like to allude to the importance of digital transformation in our hospitals to further support more comprehensive studies in the future.

Limitations of the study

Limitations included the small sample size and single center from which cases were collected and studied. The relatively low number of cases operated during 2020 in comparison with the previous years should be noted, and may be explained by the emergence of the Covid-19 pandemic in this year and its impact on health care provided by tertiary health centers.

The authors recommend undertaking larger prospective studies in multiple centers in different cities, collecting data for a longer period of time, comparing meningioma cases regarding clinical, pathological (using H&E examination, immunohistochemical markers, such as PR, Ki-67 and molecular genetics, such as NF-2, PIK3CA, FGFR3, AKT1, TERTp) and radiological imaging data, and, most importantly, studying the correlation between different meningioma variances.

The authors also recommend studying the long-term outcomes of surgically treated meningioma patients (different pathological grades and variants) in terms of recurrence, metastasis and overall survival, taking into account the Simpson grade in correlation with the tumor recurrence rate.

CONCLUSION

Meningiomas are common primary central nervous system neoplasms that have a clear predilection to women. Most of these tumors develop in the intracranial cavity from meningeal coverings of cerebral convexities and parasagittal area. They are usually presented with non-specific symptoms like headache. Meningioma present over wide histopathological variants and grades. Accurate histopathological assessment is crucial in predicting aggressive behavior and tumor recurrence. The most frequently encountered histopathological variant is the meningiothelial variant. Although with the relatively small number of cases in this case series, the psammomatous variant shows a higher propensity to affect the spinal cord than other sites; it also shows a greater tendency to develop in the old age group in comparison to other variants. Despite the majority of these neoplasms are grade 1 or benign tumors by definition, a significant number of them, however, present as recurrent growths which may reflect the importance of other factors like tumor site and completeness of surgical resection.

List of abbreviations

FGFR3: Fibroblast growth factor receptor

H & E: Hematoxylin and eosin

HPF: High power field.

IRB: Institutional Review Board

NF-2: Neurofibromatosis type 2

PIK3CA: Phosphoinositide-3-kinase, catalytic, alpha polypeptide

PR: Progesterone receptor

TERTp: Telomerase reverse transcriptase

WHO: World Health Organization

Disclosure

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