

Histopathological Correlation (World Health Organization Classification) of Meningiomas and Their Anatomical Localization: A Multicenter Epidemiological Study in Mexico

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OBJECTIVE: To determine the epidemiology of the localization and histological type of meningiomas in the Mexican population and the distribution of the different histological patterns and their relationship to tumor localization and patient demographics.

METHODS: A retrospective analysis was performed in 5 hospitals in Mexico from 2009 to 2019. For qualitative variables, mean values were compared using Pearson χ^2 test for the correlation between location and histological pattern as well as the clinical presentation and the patient's sex. Student *t* test was performed for age and its correlation with location and histology.

RESULTS: Analysis of 179 patients revealed significant differences in histopathological pattern, patient sex, and tumor location. No significant differences were found for age or clinical presentation in association with any specific histological pattern.

CONCLUSIONS: There was a correlation between the histology of the 15 histopathological varieties of meningiomas and the predilection site of appearance as well as certain demographic aspects, such as sex. This study lays the foundation for future studies in Mexico on the differentiation and typing of meningiomas regardless of the histological grade to which they belong, as the exact behavior of these tumors, including grade I tumors, remains unknown to date.

INTRODUCTION

Cushing coined the term meningioma in 1922 to define the most common dural-based tumor of the central nervous system, representing 15%–30% of all primary intracranial tumors.¹ Most meningiomas are intracranial, and 86%–90% are supratentorial in origin.² Prevalence is reported to 6.59 cases per 100,000.³ The prevalence has been reported to 0.9% in the general population undergoing magnetic resonance imaging.^{4,5} The prevalence is highest in the African American population, with up to almost 7.9 cases per 100,000.⁶

Meningiomas derive from arachnoid meningeothelial cells, and the most common location according to Mexican sources is the convexity in 34.4%, owing to the abundance of meningeothelial cells in Pacchionian granulations. There is also a clear higher incidence in women, who account for up to 72% of all cases. The vast majority of meningiomas are considered benign histologically (up to 92.8%); only 2.2% are considered atypical, and 5% are malignant.⁷ Some studies have found that male sex and convexity location are associated with a higher probability of atypical meningiomas.⁸ Moreover, tumors of the skull base are less likely to be a higher histological grade; in parasagittal tumors, the convexity and sickle have the greatest risk of having malignant features.⁹ Some studies claim a close correlation between the clinical course and histological pattern, while others have found no association.¹⁰ However, there is sufficient literature to suggest a link between histological subtypes of meningiomas and their location.¹¹ We conducted the largest retrospective study to date in Mexico to determine whether there is a relationship between the anatomical location of meningiomas within the central nervous system and the different histopathological variants according to the World Health

Key words

- Characterization of meningiomas
- Histopathological correlation
- Meningioma
- Meningioma localization

Abbreviations and Acronyms

WHO: World Health Organization

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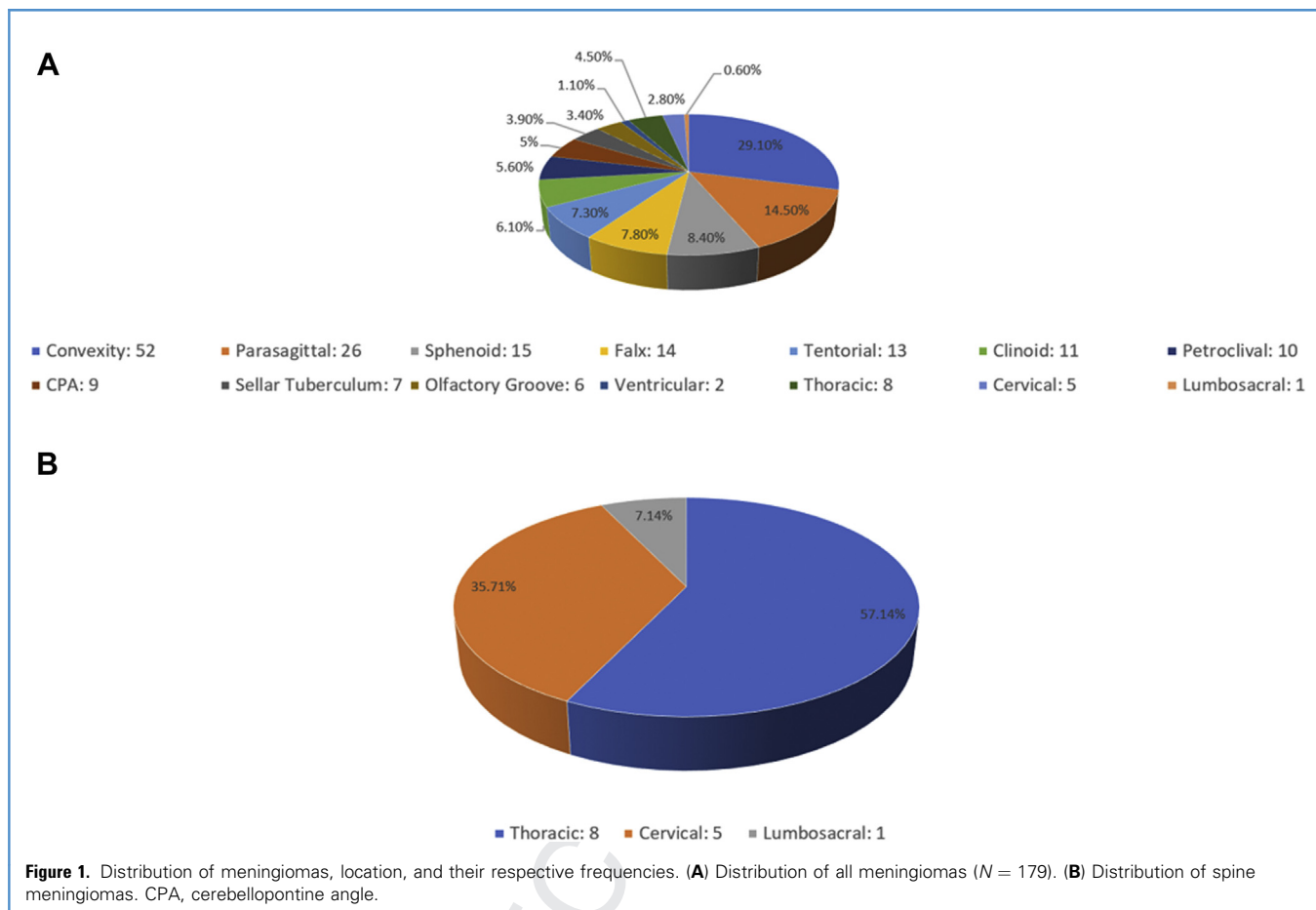
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Organization (WHO) classification as well as other features such as patient sex, clinical presentation, and patient age.

MATERIALS AND METHODS

In a period of 10 years, 2009–2019, a descriptive, analytical retrospective study was carried out in 3 high specialty hospitals and 2 regional hospitals in Mexico. All patients operated on for single intracranial or extracranial meningiomas in these 5 institutions during the study period who had at least 6 months of imaging and clinical follow-up were included. The probable anatomical site was determined on the preoperative imaging study; however, for the analysis, the decision of the main surgeon at the time of surgery was considered based on the implant site. Patients with a diagnosis of a genetic disease associated with meningiomas and patients in whom meningiomatosis was diagnosed during follow-up were excluded from the final analysis. All

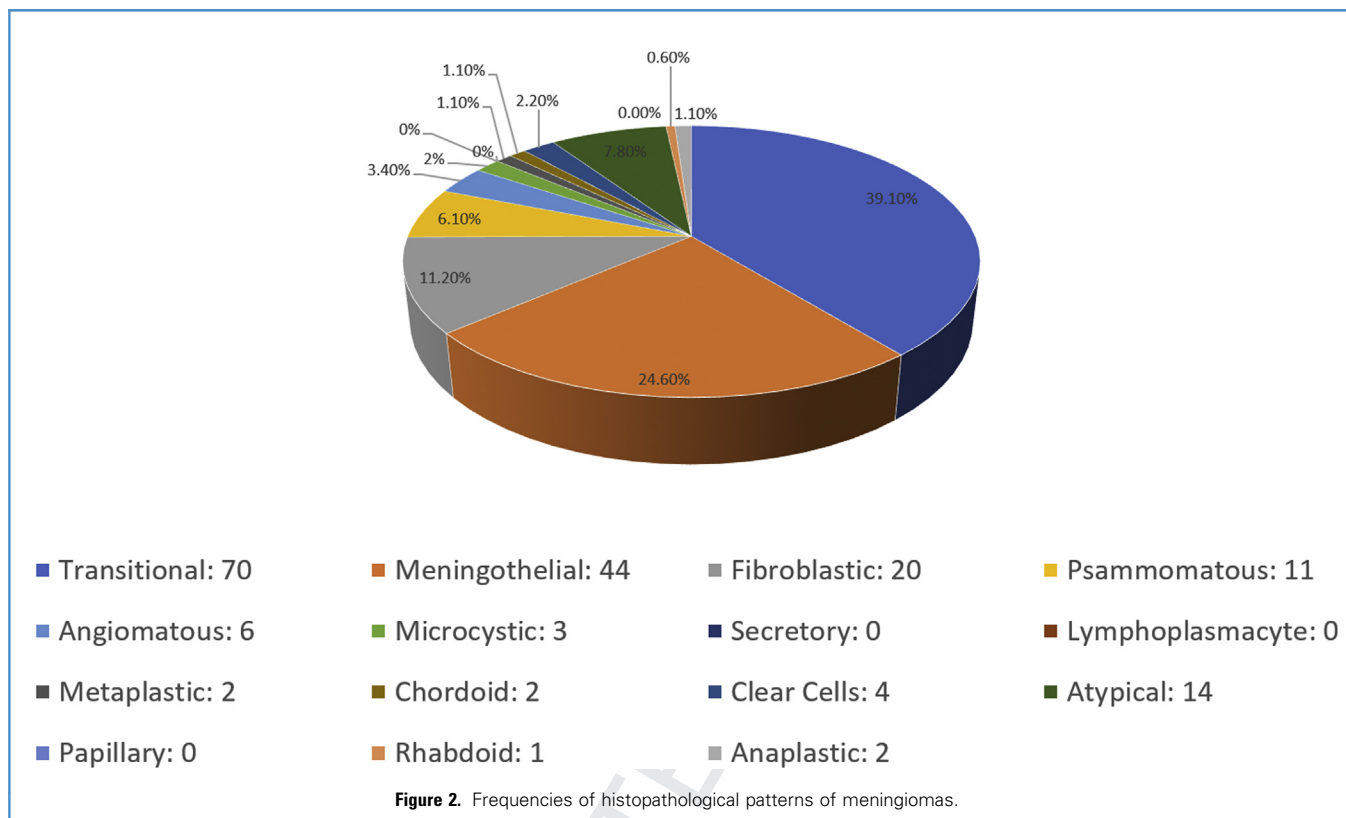
patient data (sociodemographic data, location, and histological type) were obtained from the electronic medical record. The images of histological sections were provided by the Pathology Department of the Hospital Central Sur de Alta Especialidad PEMEX.

Population

Of 183 patients analyzed, 4 were excluded from the analysis: 3 patients with a diagnosis of neurofibromatosis type 2, and 1 patient with a diagnosis of meningiomatosis. These patients were excluded from the final analysis to avoid biased data in terms of location and more aggressive histological variants. Thus, the final analysis included 179 patients.

Statistical Analysis

An analysis of measures of central tendency was performed to collect sociodemographic data, such as age, sex, location,



histological type, and clinical presentation. A comparison of means was carried out using contingency tables for the correlation of independent qualitative variables using Pearson χ^2 test and to obtain P values. The quantitative and qualitative independent variables analysis was performed using Student t test. IBM SPSS Version 21 statistical software (IBM Corporation, Armonk, New York, USA) was used, and graphs were made using Microsoft Office Excel (Microsoft Corporation, Redmond, Washington, USA).

RESULTS

Of 179 patients, 109 were women (60.9%) and 70 were men (39.1%) with a mean (SD) age of 56 (16) years. Meningioma locations included intracranial involvement in 92.2% and spine in 7.8%. Within the spine, the most frequently affected site was the thoracic spine in 57.14%, followed by the cervical spine in 35.71%. Complete location distribution is shown in [Figure 1](#).

The most frequently found histopathological pattern was the transitional (WHO grade I) in 39.1%, followed by the

meningothelial (WHO grade I) in 24.6%. None of the patients analyzed presented with the variants, such as secretory, lymphoplasmacyte-rich, or papillary; the complete distribution is shown in [Figure 2](#). These variants were omitted from the tables and graphs because they did not occur in any case, and so they were eliminated from the final analysis. Examples of the most frequent histological subtypes are shown in [Figure 3](#).

For the meningothelial variant, the mean (SD) age of patients was 54.18 (16.5) years ($P = 0.36$); for fibrous, 53.15 (18.47) years ($P = 0.38$); for transitional, 56.86 (15.15) years ($P = 0.615$); for psammomatous, 58.45 (15.57) years ($P = 0.61$); for angiomatous, 59.17 (17.17) years ($P = 0.63$); for microcystic, 61 (14.52) years ($P = 0.59$); for metaplastic, 58.50 (21.92) years ($P = 0.83$); for chordoid, 33.5 (28.99) years ($P = 0.045$); for clear cells, 55.75 (16.31) years ($P = 0.96$), for atypical, 63.36 (14.12) years ($P = 0.07$); for rhabdoid, 38 years (having obtained data for only 1 patient, no SD or P value was obtained); and for anaplastic, 51 (14.14) years ($P = 0.65$). There were practically no significant differences by age. When patients were analyzed by histological grade, patients with WHO grade I had a mean (SD) age of 55.9 (15.9) years and patients with WHO grades II and III had a mean (SD) age of 57.36

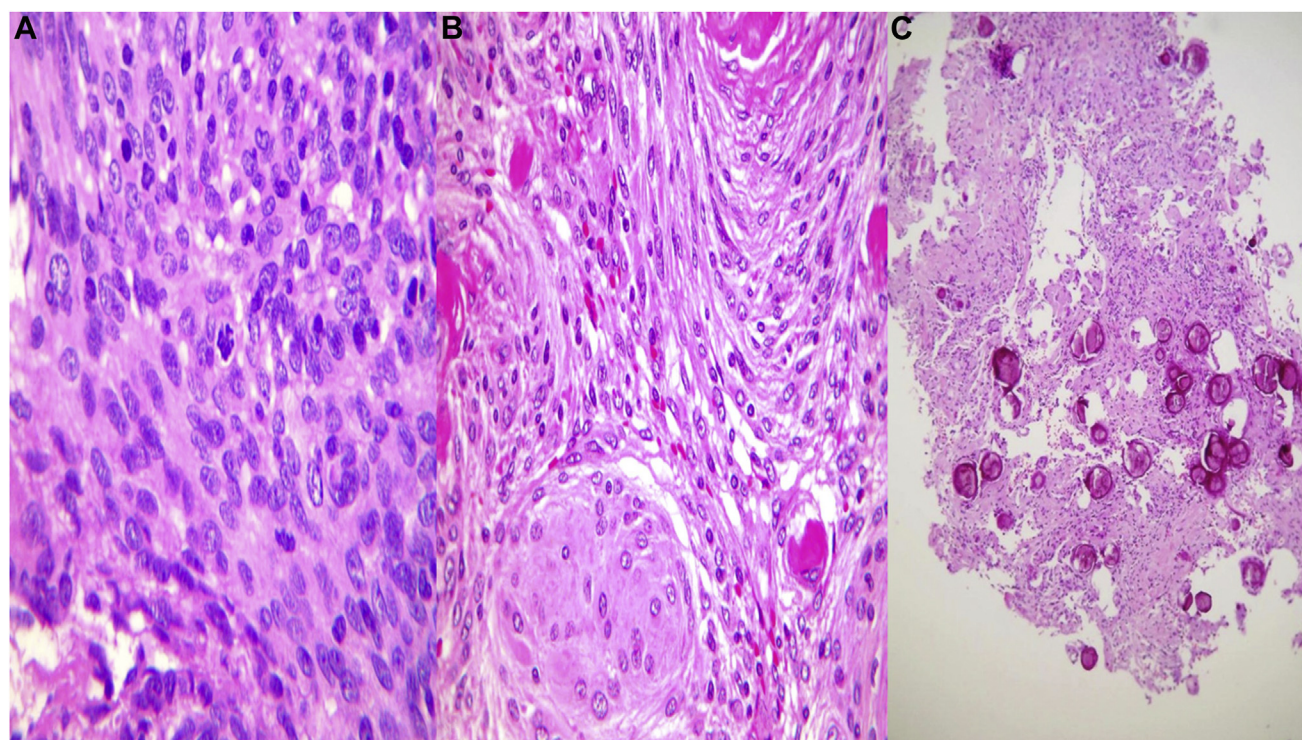


Figure 3. Examples of the most frequent histopathological patterns found. **(A)** Atypical meningioma: small neoplastic cells with nuclear atypia and prominent nucleoli. A figure of mitosis is observed in the center of the image. **(B)** Intertwined bundles of spindle cells and intercellular collagen bundles. Characteristic epithelioid cell lobes of meningothelial meningioma

are seen in the lower left corner. **(C)** Panoramic image showing abundant concentric calcifications or psammoma bodies as a result of calcification of meningothelial syncytial nests, compatible with psammomatous meningioma.

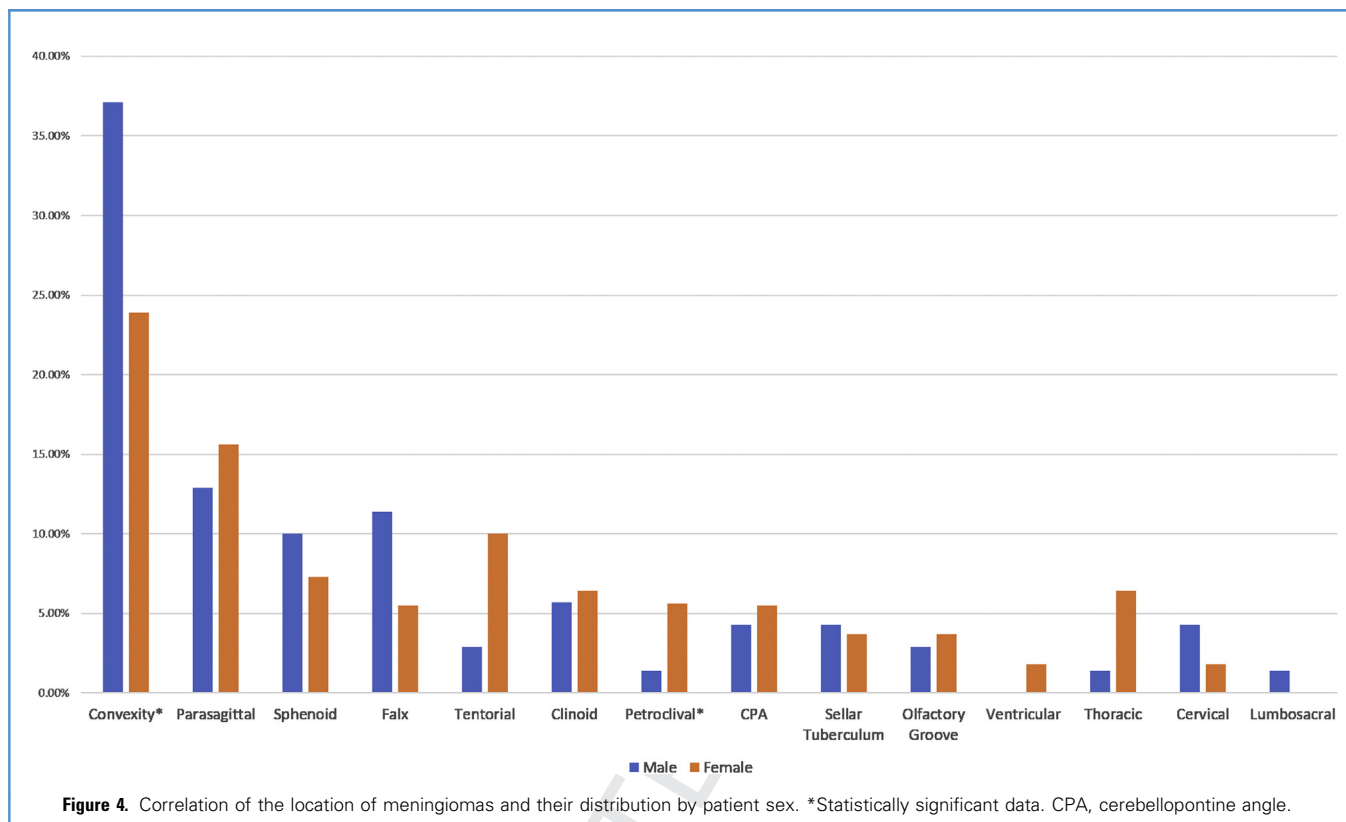
(17.1) years ($P = 0.67$), so there was no relationship between histological grade and age. Regarding age, it is probable that a relationship to specific anatomical sites of appearance of meningiomas exists. No significant differences were found between the groups.

For the distribution of meningiomas and their relationship to patient sex, significant differences were observed. In men, 37.1% of meningiomas manifested in the convexity, while in women, only 23.9% manifested in the convexity ($\chi^2 = 3.65$, $P = 0.05$). Among 10 patients with petroclival meningiomas, 9 were women (90%), and only 1 (10%) was a man ($\chi^2 = 3.76$, $P = 0.05$). The rest of the relationships are shown in **Figure 4**. **Table 1** shows Pearson χ^2 values and P values.

The most frequent presenting symptom was headache/pain, in 85 (47.5%) patients, followed by motor deficit in 54 (30.2%)

patients, sensory deficit in 17 (9.5%) patients, seizures in 39 (21.8%) patients, paresis of ≥ 1 cranial nerves in 45 (25.1%) patients, intracranial hypertension in 26 (14.5%) patients, and cerebellar symptoms in 4 (2.2%) patients (**Table 2**). An association analysis was carried out between the presenting symptoms and patient sex, and no statistically significant data were found between both groups.

Regarding symptoms and histological grade, of patients presenting with pain/headache, 85.9% had meningioma WHO grade I ($\chi^2 = 0.003$, $P = 0.956$), and 75.9% of patients presenting with motor deficit, had WHO grade I ($\chi^2 = 6.57$, $P = 0.01$). About 95% of the patients who presented with paresis of a cranial nerve had meningioma WHO grade I ($\chi^2 = 4.53$, $P = 0.03$); only 2 patients who presented with these clinical symptoms had meningioma WHO grade II or III. There was no association of intracranial

**Table 1.** Relationship of Meningioma Location to Patient Sex

Localization	Patient Sex	
	χ^2 Value	P Value
Convexity	3.65	0.05*
Parasagittal	0.25	0.61
Sphenoid	0.39	0.51
Falx	2.07	0.15
Tentorial	3.31	0.69
Clinoid	0.03	0.87
Petroclival	3.76	0.05*
CPA	0.13	0.71
Sellar tuberculum	0.04	0.83
Olfactory groove	0.08	0.76
Ventricular	0.06	0.56
Thoracic	2.48	0.11
Cervical	0.94	0.33
Lumbosacral	0.01	0.82

CPA, cerebellopontine angle.

hypertension as a presenting symptom with WHO grade II or III histological variants in our analysis. Also, we analyzed intracranial hypertension and tumor location, and no correlation was found of this type of clinical presentation with specific locations or with specific histological variants.

The correlation between histological type and patient sex that was obtained from the 20 fibroblastic types showed 17 (85%) were women and only 3 (15%) were in men ($\chi^2 = 5.49$, $P = 0.019$). Of the 11 psammomatous tumors, 10 (90.9%) were in women and only 1 (9.1%) was in men ($\chi^2 = 4.43$, $P = 0.035$). Of the 14 atypical tumors, 10 were in men (71.4%), and only 4 (28.6%) were in women ($\chi^2 = 6.66$, $P = 0.010$). The rest of the distribution is shown in Figure 5. Table 3 shows Pearson χ^2 values and P values.

Regarding the correlation between the histopathological pattern and the anatomical location, some significant results were obtained. For example, despite being a relatively frequent histological pattern, psammomatous meningiomas did not appear in the convexity ($\chi^2 = 4.79$, $P = 0.02$). The parasagittal location is a site of a high incidence of atypical variants, up to 23.1% ($\chi^2 = 9.82$, $P = 0.00$). The incidence of psammomatous meningiomas in the thoracic spine is up to 27% ($\chi^2 = 14.42$, $P = 0.00$). The rest of the results are shown in Table 4 and Figures 6 and 7.

Table 2. Clinical Presentations of Meningiomas

Clinical Presentation	Patients
Pain/headache	85 (47.5%)
Motor deficit	54 (30.2%)
Sensory deficit	17 (9.5%)
Epilepsy	39 (21.8%)
Cranial nerve	45 (25.1%)
Intracranial hypertension	26 (14.5%)
Cerebellar symptoms	4 (2.2%)

DISCUSSION

Meningiomas are generally slow-growing benign tumors that can produce neurological symptoms and signs owing to their property of space-occupying compression of adjacent structures.¹ The clinical presentation of meningiomas, as in many intracranial tumors, depends on their location.¹² Headache has been reported as the most common symptom, occurring in

approximately 36% of the cases, followed by paresis of a cranial nerve occurring in 31% and seizures occurring in 17%.⁹ As reported in other sources, the most frequent presentation of slow-growing lesions is still headache, followed by paresis or motor deficits (30%),¹² in contrast to malignant tumors with a histological pattern, where presentation is paresis in 50% with a higher percentage than in cases with nonmalignant pattern intracranial hypertension.¹³ These data contrast with the data provided by us, as we did not find an association between intracranial hypertension symptoms and histological grade, but motor and cranial nerve deficits were found with WHO grade I tumors. Physical examination is normal more frequently in patients with benign histological lesions (up to 26%), in contrast to patients with WHO grade II or III meningiomas, where only 14% are upright.¹⁴

The most frequent tumor location is the convexity. Of tumors in this location, 34% are WHO grade I. Meanwhile, 50% of WHO grade II or III tumors occur in the convexity, followed by the parasagittal plane and lesser sphenoid wing; these tumors are practically nonexistent in other locations, according to some studies.^{13,15-19} The histological pattern so far most frequently reported is the meningothelial in 38% of cases followed by transitional in 33%.¹⁹ In an Indian cohort, the meningothelial variant was reported as the most frequent histological variant, in 41.3% of cases.²⁰ Contrasting data in our population showed that the

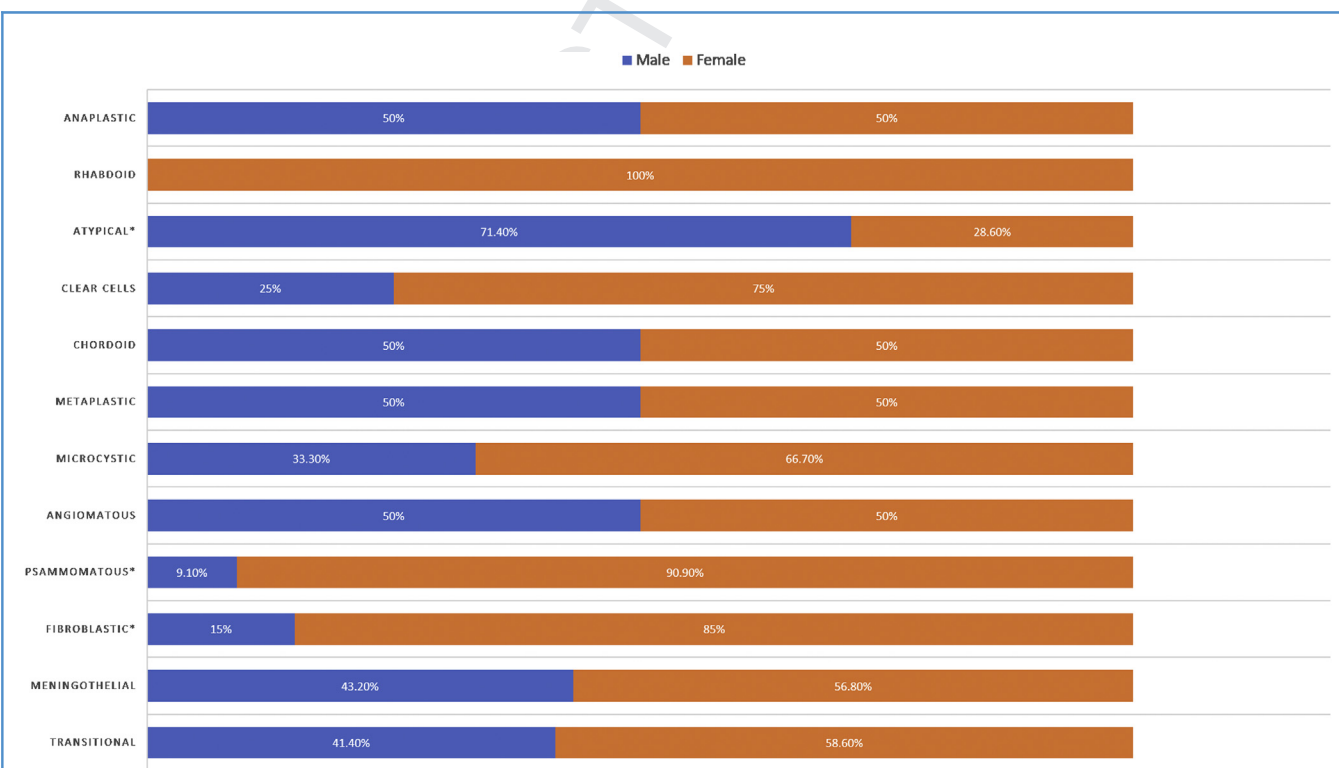


Figure 5. Correlation between patient sex and the histopathological variant of meningiomas by World Health Organization classification. *Statistically significant data.

Table 3. Relationship Between Histopathological Pattern and Patient Sex

Histological WHO Classification	Patient Sex	
	χ^2 Value	P Value
Transitional	0.260	0.610
Meningothelial	0.407	0.524
Fibroblastic	5.49	0.019*
Psammatous	4.43	0.035*
Angiomatous	0.30	0.578
Microcystic	0.04	0.836
Metaplastic	0.10	0.751
Chordoid	0.10	0.751
Clear cells	0.34	0.559
Atypical	6.66	0.010*
Rhabdoid	0.64	0.422
Anaplastic	0.10	0.751

WHO, World Health Organization.

most prevalent histological pattern was transitional in 39.1%, followed by meningothelial and fibroblastic patterns in 24.6% and 11.2%, respectively. Regarding involvement of the spine, 80% of the meningiomas that affect the spine are at a thoracic level.⁵ In our population, thoracic involvement was close to 50%. In a Dutch cohort that described the epidemiology of spinal meningiomas, the most frequent histological variant found was psammomatous in 42%, followed by transitional in 29%, with the thoracic spine being the most frequent location.²¹ Data that contrast with ours found that 57% of spinal meningiomas were at the thoracic level, and the histological variants with equal frequencies found were meningothelial and psammomatous with 28% each. According to some cohorts, there is a clear predisposition for spinal meningiomas in women, ranging from 80% to 94%.²¹⁻²³ Our cohort, although small, also shows a predisposition for women, although not as high as in other Eastern or European cohorts; in our cohort, 64% of the cases of spinal involvement were in women. Meningiomas can occur in any part of the central nervous system, however, there are some sites with a more specific predisposition. A continuous review of the histopathology of meningiomas is necessary to improve the precision and reproducibility of the histopathological diagnosis and classification of these tumors.²⁴

Concerning histological grade, some characteristics on magnetic resonance imaging, such as cerebral invasion, invasion of bone, and peritumoral edema, have been associated with meningiomas of

highest histological grade.²⁵ In the experience of some authors regarding the tumors, the larger the size, the greater the association with WHO grade II histological grade, with tumors >5–6 cm having the highest probability of being WHO grade II or WHO grade III.^{9,26} The reason why a site-specific meningioma shows a completely different histology probably depends on the cell of origin and the microenvironment of the original site of the meningioma. Wu et al.²⁷ hypothesized that angiomatous subtypes can be found only in the cerebellopontine angle, which is in stark contrast to the findings in our study, where the angiomatous subtypes could be found in virtually all locations—infratentorial, supratentorial, skull base, and even column. Chordoid meningiomas represent 0.5%–1.0% of all meningiomas and are frequently located in the supratentorial region. Marhx-Bracho et al.²⁸ reported a boy 3 years 6 months of age with a chordoid meningioma of foramen magnum. Chordoid meningiomas, although rare, occur in younger people, as found in other studies and supported by our research. The most common benign histological subtypes among meningiomas of the posterior fossa have been reported to be fibrous (37.79%) and psammomatous (24.13%).¹¹ In our study, the most frequent pattern found in the posterior fossa was the transitional pattern.

Regarding petroclival meningiomas, which represent a surgical challenge, some American series report a prevalence of WHO grade II petroclival meningiomas of 8%–12.5%,^{29,30} with WHO grade I being the most frequent variant, and of these, the fibroblastic variant was the most prevalent. However, in the Mexican population in the present study, it was found that all petroclival meningiomas are histologically benign (WHO grade I), and the meningothelial variant is the most frequent (up to 40%). In addition, this location was more common in women, found in up to 72% of cases according to Asian sources³⁰; in Mexicans, only 1 man (10%) had a tumor in this location, with women accounting for the remaining cases (90%).

An atypical meningioma is a tumor of intermediate grade between malignant and benign forms. Its diagnosis is based on increased mitotic activity, brain invasion, or at least 3 of the 5 histological characteristics (increased cellularity, change of small cells, sheet formation, prominent nucleoli, and foci of spontaneous necrosis).¹ Atypical meningiomas and anaplastic meningiomas usually occur at sites outside the base of the skull³¹ (i.e., toward the convexity, parafalcine, or falx). However, a high percentage of those meningiomas reported also occurred in cervical, sellar, and clinoid locations. The recognition of special variants and atypical meningiomas is of utmost importance owing to their more aggressive and recurrent nature.³² Histopathology has not shown a correlation between the degree of peritumoral edema, location, or size, as noted by Rohringer et al.¹⁹; however, they were found in larger cups recurrence patterns of histological WHO grade II or in grade I benign patterns.¹⁶ Some atypical locations, such as intraosseous or in the pineal region, are explained by sequestration of meningothelial cells during embryonic or pluripotent stem cell

Table 4. Relationship of Histopathological Subtype of Meningiomas to Their Intracranial and Extracranial Location

Histological Type/Location	Convexity	χ^2	P Value	Parasagittal	χ^2	P Value	Sphenoid	χ^2	P Value	Falx	χ^2	P Value	Tentorial	χ^2	P Value	Clinoid	χ^2	P Value	Petroclival	χ^2
Transitional	20	0.01	0.91	10	0.00	0.91	6	0.00	0.94	9	4.04	0.04*	6	0.29	0.58	4	0.03	0.84	2	1.62
Meningothelial	12	0.08	0.76	5	0.47	0.49	4	0.03	0.84	1	2.41	0.11	3	0.01	0.89	5	2.75	0.09	4	1.35
Fibroblastic	7	0.38	0.53	2	0.37	0.54	1	0.33	0.56	2	0.14	0.70	1	0.17	0.67	0	1.47	0.22	3	3.78
Psammomatous	0	4.79	0.02*	0	1.99	0.15	3	5.44	0.02*	0	0.99	0.31	2	2.07	0.15	0	0.76	0.38	1	0.27
Angiomatous	2	0.05	0.81	0	1.05	0.30	0	0.56	0.54	1	0.67	0.41	1	0.81	0.36	0	0.40	0.52	0	0.36
Microcystic	2	2.09	0.14	1	0.86	0.35	0	0.27	0.59	0	0.25	0.61	0	0.23	0.62	0	0.20	0.65	0	0.18
Metaplastic	0	0.82	0.36	0	0.34	0.55	0	0.18	0.66	1	4.99	0.02*	0	0.15	0.69	0	0.13	0.71	0	0.12
Chordoid	0	0.82	0.36	0	0.34	0.55	0	0.18	0.66	0	0.17	0.67	0	0.15	0.69	0	0.13	0.71	0	0.12
Clear cells	1	0.03	0.85	2	4.14	0.04*	0	0.37	0.54	0	0.34	0.55	0	0.32	0.57	1	2.52	0.11	0	0.24
Atypical	7	3.23	0.07*	6	9.82	0.00*	0	1.38	0.23	0	1.28	0.25	0	1.18	0.27	0	0.99	0.31	0	0.89
Rhabdoid	0	0.41	0.52	0	0.17	0.67	1	10.99	0.00*	0	0.08	0.77	0	0.07	0.77	0	0.06	0.79	0	0.06
Anaplastic	1	0.41	0.51	0	0.34	0.51	0	0.18	0.66	0	0.17	0.67	0	0.15	0.69	1	6.74	0.00*	0	0.12
Total	52	—	—	26	—	—	15	—	—	14	—	—	13	—	—	11	—	—	10	—

CPA, cerebellopontine angle; ST, sellar tuberculum; OG, olfactory groove.

*Statistically significant value.

development and mesenchymal transformation.³³ These locations have a greater relationship to malignancy.⁹ Finally, if the preoperative environment and the cell of origin of a meningioma are known, the treatment could be improved in the future owing to this established correlation,¹¹ as the prognosis of the disease depends not only on the histopathological classification of the lesion,³² but also on the site of the injury and the surgical challenge it represents.

CONCLUSIONS

Some histological patterns of low-grade meningiomas have a predilection for complex locations surgically speaking, and although their cellular behavior is considered benign, their anatomical location, clinical course, and prognosis are not. This is the first epidemiological and histopathological characterization study that has been done in Mexico that correlated each subtype of meningioma with the anatomical location. With this study, we lay the foundation for future prospective studies based on the survival of the patients depending on their location or histology, regardless of the grade.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Daniel Alejandro Vega-Moreno: Formal analysis, Methodology, Writing - original draft. **José Omar Santellán-Herández:** Conceptualization. **Héctor Eduardo Velázquez-Domínguez:** Data curation. **Alexis Oziel Martínez-Nava:** Data curation. **Rosa María Vicuña-González:** Resources. **Pamela Renéé Mendoza-Trillo:** Resources. **Víctor Andrés Reyes-Rodríguez:** Supervision. **Abraham Ibarra de la-Torre:** Supervision, Validation. **Iván Eduardo González-González:** Writing - review & editing. **Diego Ochoa-Cacique:** Writing - review & editing. **Rafael Sánchez-Mata:** Software. **Rodolfo Pedro Molina-Martínez:** Writing - review & editing. **Ulises García-González:** Project administration, Supervision.

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Table 4. Continued

P Value	CPA	χ^2	P Value	ST	χ^2	P Value	OG	χ^2	P Value	Ventricular	χ^2	P Value	Thoracic	χ^2	P Value	Cervical	χ^2	P Value	Lumbosacral	χ^2	P Value	Total
0.20	5	1.07	0.29	4	0.99	0.31	2	0.08	0.76	1	0.10	0.75	1	2.48	0.11	0	3.30	0.06	0	0.64	0.42	70
0.24	1	0.92	0.33	2	0.06	0.80	3	2.16	0.14	0	0.65	0.41	1	0.65	0.41	3	3.48	0.06	0	0.32	0.56	44
0.05*	2	1.16	0.28	0	0.91	0.33	1	0.18	0.66	0	0.25	0.61	1	0.01*	0.90	0	0.64	0.42	0	0.12	0.72	20
0.60	0	0.62	0.43	1	0.83	0.36	0	0.40	0.52	0	0.13	0.71	3	14.42	0.00*	1	1.71	0.19	0	0.06	0.79	11
0.54	1	1.76	0.18	0	0.25	0.61	0	0.21	0.64	0	0.07	0.79	1	2.16	0.14	0	0.17	0.67	0	0.03	0.85	6
0.67	0	0.16	0.68	0	0.12	0.72	0	0.10	0.74	0	0.03	0.85	0	0.14	0.70	0	0.08	0.76	0	0.01	0.89	3
0.72	0	0.10	0.74	0	0.08	0.77	0	0.07	0.79	0	0.02	0.88	1	9.82	0.00*	0	0.05	0.80	0	0.01	0.91	2
0.72	0	0.10	0.74	0	0.08	0.77	0	0.07	0.79	1	43.74	0.00*	0	0.09	0.75	0	0.05	0.80	1	88.99	0.00*	2
0.62	0	0.21	0.64	0	0.16	0.68	0	0.14	0.70	0	0.04	0.83	0	0.19	0.66	0	0.11	0.73	0	0.02	0.87	4
0.34	0	0.80	0.37	0	0.61	0.43	0	0.52	0.46	0	0.17	0.67	0	0.71	0.39	1	1.05	0.30	0	0.08	0.77	14
0.80	0	0.05	0.81	0	0.04	0.84	0	0.03	0.85	0	0.01	0.91	0	0.04	0.82	0	0.02	0.86	0	0.00	0.94	1
0.72	0	0.10	0.74	0	0.08	0.74	0	0.07	0.79	0	0.02	0.88	0	0.09	0.75	0	0.05	0.80	0	0.01	0.91	2
—	9	—	—	7	—	—	6	—	—	2	—	—	8	—	—	5	—	—	1	—	—	—

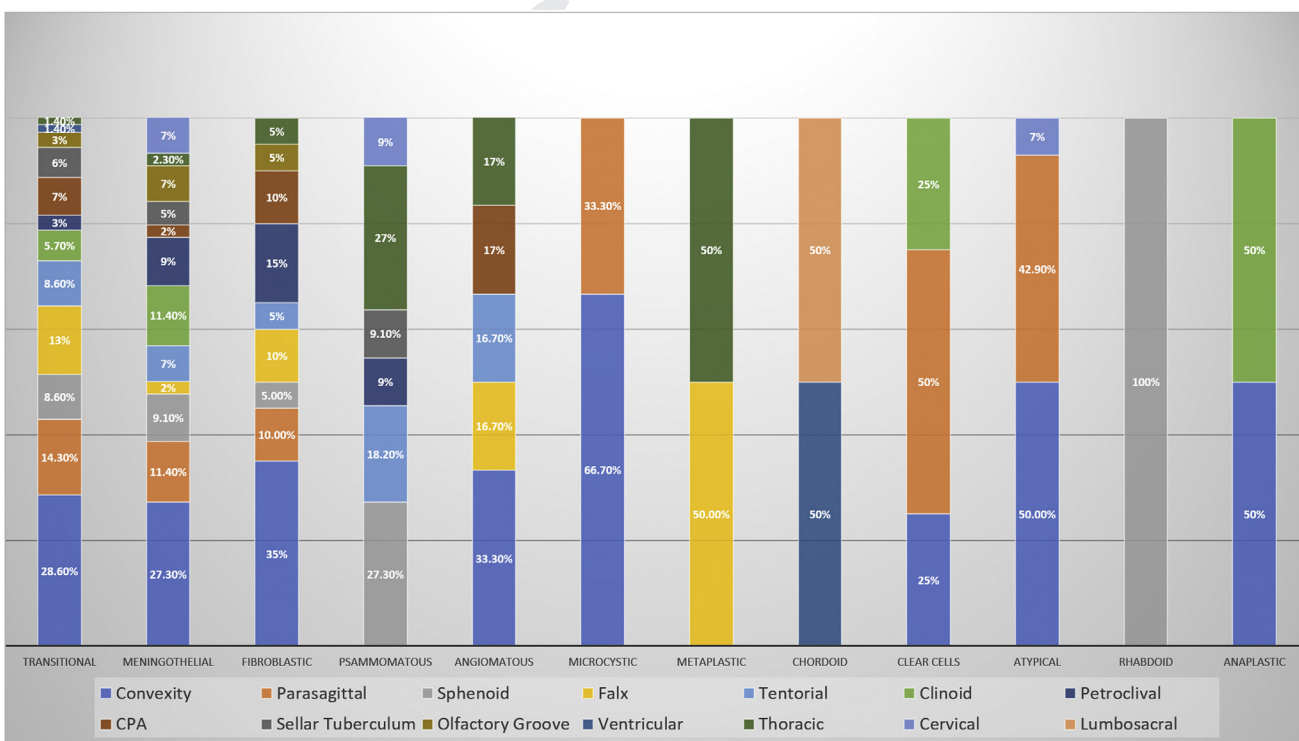


Figure 6. Location of meningiomas by histopathological variant. CPA, cerebellopontine angle.

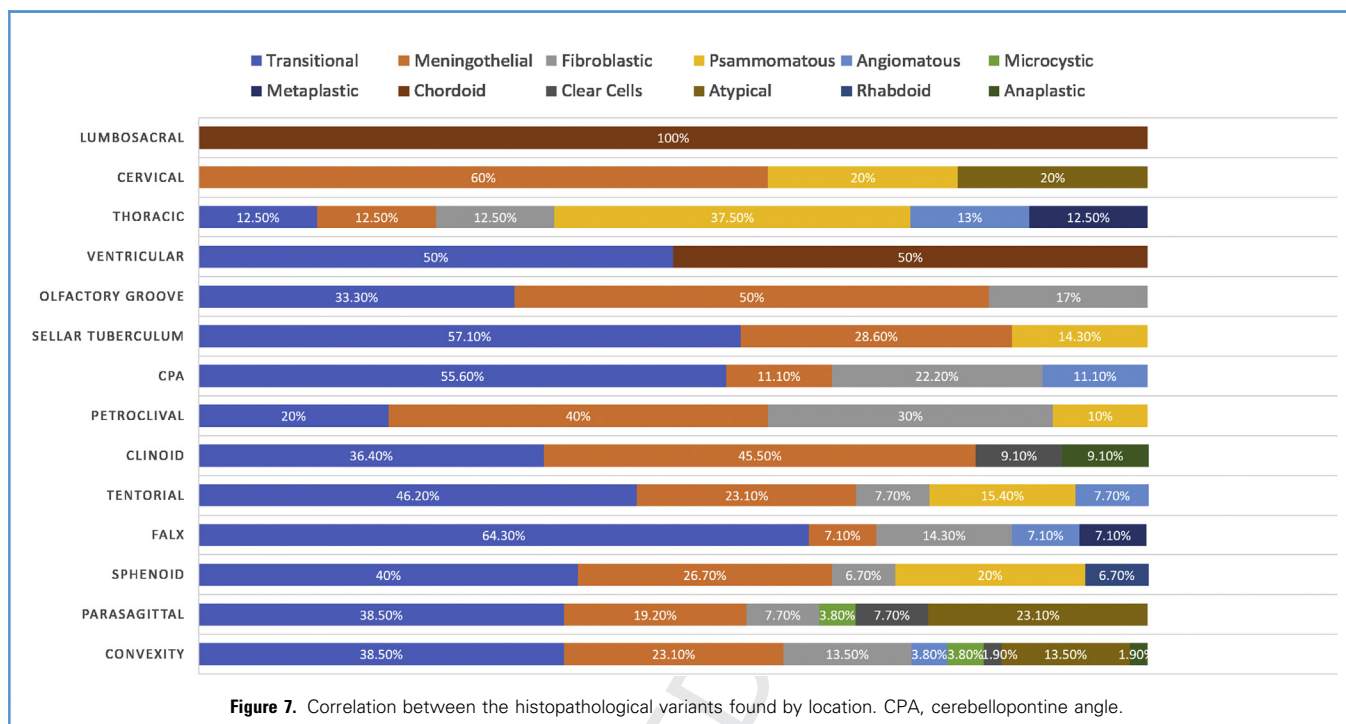


Figure 7. Correlation between the histopathological variants found by location. CPA, cerebellopontine angle.

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