Outcomes following surgical resection of cystic intracranial meningiomas

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Abstract

Introduction Cystic meningiomas are rare, accounting for 2–7% of all intracranial meningiomas. Little is known regarding whether these meningiomas behave differently compared to solid meningiomas. We sought to study this relatively uncommon imaging appearance of meningioma and to evaluate its clinical significance.

Methods A single-institution retrospective cohort study of surgically-treated meningioma patients between 2000 and 2019 was conducted. Cystic meningioma was defined as a tumor with an intratumoral or peritumoral cyst present on preoperative imaging. Demographics, preoperative imaging, histopathology characteristics, operative data, and surgical outcomes were reviewed. Imaging variables, histopathology and outcomes were reported for cystic meningiomas and compared with non-cystic meningiomas. Univariate/multivariable analyses were conducted.

Results Of 737 total meningiomas treated surgically, 38 (5.2%) were cystic. Gross total resection (GTR) was achieved in 84.2% of cystic meningioma patients. Eighty-two percent of cystic meningiomas were WHO grade I (n=31), 15.7% were grade II and 2.6% were grade III. Most cystic meningiomas had low Ki-67/MIB-1 proliferation index (n=24, 63.2%). A total of 18.4% (n=7) patients with cystic meningioma had recurrence compared to 12.2% (n=80) of patients with non-cystic meningioma (p=0.228). No significant difference in median time to recurrence was observed between cystic and non-cystic meningiomas (25.4, Q1:13.9, Q3:46.9 months vs. 13.4, Q1:8.6, Q3:35.5 months, p=0.080).

Conclusions A small portion of intracranial meningiomas have cystic characteristics on imaging. Cystic meningiomas are frequently WHO grade I, have low proliferation index, and had similar outcomes compared to non-cystic meningioma. Cysts in meningioma may not be a surrogate to determine aggressive meningioma behavior.

Keywords Cystic meningioma · Intracranial tumor · Recurrence · Clinical outcomes

Introduction

Meningiomas are one of the most common primary intracranial tumors, accounting for approximately one-third of all central nervous system tumors [1]. Meningiomas are commonly a solid-form tumor; far more rare are meningiomas that contain a cystic component [2]. Cystic meningiomas are described in only 2–7% of adult meningiomas [3, 4]. The more common intracranial tumors with cystic components are hemangiopericytomas, high-grade gliomas, hemangio- blastomas, and metastasis [5–7]. The cysts associated with meningiomas can be intratumoral with dominant fluid-filled compartments located within the tumor mass centrally or eccentrically, or they can be located in the periphery of the tumor in the adjacent brain parenchyma and subarachnoid space [5]. Nauta reported classification for cystic meningioma based on the characteristics of intratumoral and peritumoral cysts. This classification divides cystic meningioma into four categories: type I (centrally located intratumoral cyst), type II (peripherally located intratumoral cyst), type III (peritumoral cyst in adjacent parenchyma), type IV (peritumoral cyst between the tumor and adjacent parenchyma) [8].
The pathogenesis of cyst formation in meningioma is multifactorial. The cysts likely form from degeneration of tumor cells, necrosis due to lack of intratumoral blood supply, hemorrhage, direct secretion from tumor cells, or CSF from the subarachnoid spaces [5, 9]. Meningioma aggressiveness is defined based on WHO grading, proliferation index and recurrence after surgical resection [10, 11]. It is unclear, however, whether the presence of a cystic component would impact the behavior or aggressiveness of meningiomas.

Several studies have hypothesized that cystic change is more prevalent in atypical meningiomas [12, 13]. A few case reports have noted a higher propensity for recurrence in cystic meningiomas despite gross total resection (GTR) [14, 15]. Other case reports and case series have focused on radiological characteristics of cystic meningiomas [16–20]. No prior studies have reported comprehensive surgical outcomes following surgical resection of cystic meningiomas or compared outcomes with non-cystic meningiomas [12, 21]. To that end, the goal of this study was to report and compare the histopathology, imaging characteristics, and outcomes including extent of resection, readmission and recurrence following resection of cystic meningiomas to non-cystic meningioma.

**Methods**

A single-institution retrospective cohort study was conducted for patients who underwent operative treatment of meningioma from 2000 to 2019. Approval from the Vanderbilt University Medical Center Institutional Review Board (IRB #201263) was obtained. Patients aged 18 years and older who underwent surgical resection for meningioma were included in the study. Pediatric patients (< 18 years of age), those managed non-operatively, and those whose preoperative imaging or operative data were not available were excluded from the study.

Data was queried using the Research Derivative (RD) from the Vanderbilt Institute for Clinical and Translational Research (VICTR). Data including patient demographics, preoperative imaging characteristics such as presence of a cystic component, venous sinus involvement, necrosis, peritumoral edema, and tumor hemorrhage, as well as WHO grading, Ki-67/MIB-1 index, histopathological subtypes, and extent of resection were obtained via review of the electronic medical record. Patients were defined and divided into a cystic meningioma group and a non-cystic meningioma group based on presence of a cystic component upon review of preoperative radiographic computed tomography (CT) and magnetic resonance imaging (MRI) and review of radiology reports, which was supplemented by operative and pathology reports documenting presence of cyst. The cyst appeared hypointense or isointense on T1-weighted MRI and hyperintense on T2-weighted MRI. Presence of necrosis and hemorrhage was determined by the authors on review of radiographic and MRI reports, operative reports, and histopathology reports. Karnofsky Performance Score (KPS) was calculated based on the preoperative clinic or consult note and postoperative clinic note at last follow-up. Preoperative imaging characteristics, histopathological features, extent of resection, readmission, recurrence, and time to recurrence were reported for cystic meningiomas and presented for non-cystic counterparts.

**Statistical Analysis**

Descriptive statistics, including median and quartiles for continuous variables and frequency for categorical variables, were computed. Chi-square or Fisher’s exact test were used for categorical variables and Mann–Whitney U-test was used for continuous variables. Power calculations were performed. Kaplan–Meier analysis for recurrence-free survival probability in cystic meningioma was undertaken. Probabilities were compared between those undergoing GTR vs. non-GTR, those with WHO grade I vs. non-grade I meningioma, and those with low proliferation vs. high proliferation Ki-67/MIB-index. A separate Kaplan–Meier analysis was performed to demonstrate recurrence-free survival probabilities between cystic meningioma and their non-cystic counterparts. Mantel-Cox log rank test for Kaplan–Meier analysis was used. A multivariable Cox regression analysis was performed; the primary outcome of interest was time to recurrence. The number of variables included in the model were in accordance with the one in ten rule for cases of recurrence in the cohort[22, 23]. Time to recurrence was censored at last available follow-up. Statistical significance was set a priori at \( p = 0.05 \). All analysis were performed using IBM SPSS 27 and R-package.

**Results**

**Demographics**

A total of 737 patients with intracranial meningiomas who underwent surgical resection were reviewed. Of those, 38 patients had cystic meningiomas, representing 5.2% of the cohort. The median age of presentation was 57 years (Q1:49, Q3:66). Fifty-five percent of cystic meningiomas occurred in females \((n = 21)\), exhibiting greater tumor size than their male counterparts (53 mm vs. 39 mm, \( p = 0.009 \)).
Imaging and histopathology characteristics

Cystic meningiomas were primarily located along the skull convexity ($n = 28, 73.6\%$), while a smaller percentage arose at the skull base ($n = 10, 26.3\%$). There was no significant difference in tumor location between cystic meningiomas and non-cystic meningiomas ($p = 0.149$). Most cysts were intratumoral, either central ($n = 14$) or peripheral ($n = 15$). Seven cysts were located peripherally outside the tumor in the adjacent brain parenchyma and two were located between the tumor and adjacent brain parenchyma. Figure 1 demonstrates the various Nauta classification presentations of cystic meningiomas, including centrally located intratumoral cysts (Fig. 1A), peripherally located intratumoral cysts (Fig. 1B), cysts located peripherally within the adjacent parenchyma to the meningioma (Fig. 1C), and cysts

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**Fig. 1** Demonstration of various types of cystic meningiomas. A Axial T1-weighted post-contrast MRI demonstrating intratumoral cyst. B Axial T2-FLAIR post-contrast MRI demonstrating peripherally-located intratumoral cyst. C Axial T1-weighted post-contrast MRI demonstrating meningioma and cyst located peripherally within the adjacent parenchyma. D Axial T1-weighted post-contrast MRI demonstrating meningioma and cyst peripherally located between the tumor and normal parenchyma.
peripherally located between the tumor and normal parenchyma (Fig. 1D). Nearly half of all patients with cystic meningiomas exhibited preoperative edema on imaging (n = 18, 47.4%). These data are summarized in Table 1. A total of 7 cystic meningiomas were WHO grade II. The most common histopathological subtype of WHO grade I cystic meningioma was meningothezial (n = 17, 54.8%), followed by transitional (n = 4, 12.9%), psammomatous (n = 2, 6.4%), secretory (n = 2, 6.4%), fibroblastic (n = 2, 6.4%), microcystic (n = 2, 6.4%), and angiomatous (n = 2, 6.4%).

Surgical outcomes in cystic meningiomas

GTR was achieved in 84.2% of patients with cystic meningiomas. Eighty-two percent of cystic meningiomas were WHO grade I (n = 31), 15.7% were grade II, and 2.6% were grade III. The majority of cystic meningiomas had low Ki-67/MIB-1 proliferation index (n = 24, 63.2%), while nine tumors (27.3%) expressed high Ki-67/MIB-1 proliferation index. KPS improved in patients with cystic meningiomas from 78.7 ± 13.1 preoperatively to 86.7 ± 8.1 at the last follow-up visit postoperatively. A total of seven patients (18.4%) were readmitted within 90 days of surgery. Two patients with cystic meningiomas required shunt placements for postoperative pseudomeningocele and hydrocephalus, respectively. An additional patient was readmitted for pseudomeningocele development, which was managed conservatively. Other reasons for readmission included surgical site infection requiring debridement and presentation with new aphasia and somnolence.

Seven patients (18.4%) experienced recurrence at a median time of 25 months postoperatively (Q1:13.9, Q3:46.9). Of the seven cystic meningiomas that recurred, six were WHO grade I (85.7%) and one was grade II. Six recurrent meningioma patients had previously undergone GTR, while one had a subtotal resection. Two recurrent cystic tumors required reoperation, two were treated with stereotactic radiation to the resection cavity, and three were conservatively managed with observation. No meningioma-related deaths were reported in the cohort; at the time of data collection, two patients were deceased, approximately 9 and 17 years after their surgeries, respectively.

Cystic vs. non-cystic meningioma

Table 2 summarizes the imaging features, histopathological characteristics, surgical outcomes, and recurrence for cystic and non-cystic meningiomas. Compared with non-cystic tumors, cystic meningiomas exhibited higher frequency of tumor hemorrhage (n = 5, 13.2% vs. n = 15, 2.1%, p = 0.002) and necrosis (n = 5, 13.2% vs. n = 18, 2.6%, p < 0.001). The median maximal diameter of cystic meningiomas was significantly greater compared to their non-cystic counterparts (44, Q1:34, Q3:55 mm vs. 36, Q1:26, Q3:51 mm, p = 0.013). No statistically significant difference was observed in frequency of peritumoral edema (n = 18, 47.4% vs. n = 368, 52.6%, p = 0.602), calcification (n = 3, 7.9% vs. n = 64, 9.2%, p = 0.792) or intraventricular involvement (n = 11, 28.9% vs. n = 131, 18.7%, p = 0.120). No difference was observed in

| Table 1 Summary of demographic, clinical and outcome variables for cystic meningiomas |
|-------------------------------------------|--------|
| Variable of interest (n = 38) |        |
| Age at presentation in years, median (IQR) | 57 (49–66) |
| Gender, n (%) |        |
| Male | 17 (44.7) |
| Female | 21 (55.3) |
| Race, n (%) |        |
| White | 31 (81.6) |
| Black/African-American | 6 (15.8) |
| Hispanic | 1 (2.6) |
| Location, n (%) |        |
| Convexity | 24 (63.2) |
| Skull base | 10 (26.3) |
| Parasagittal/ventricular | 4 (10.5) |
| WHO Grade, n (%) |        |
| I | 31 (81.6) |
| Non-grade I | 7 (18.4) |
| MIB expression, n (%) |        |
| Low | 24 (72.7) |
| High | 9 (27.3) |
| Necrosis, n (%) |        |
| Yes | 5 (13.2) |
| No | 33 (86.8) |
| Preoperative edema, n (%) |        |
| Yes | 18 (47.4) |
| No | 20 (52.6) |
| Gross total resection, n (%) |        |
| Yes | 32 (84.2) |
| No | 6 (15.8) |
| 90-day postop neurosurgical readmission, n (%) |        |
| No | 31 (81.6) |
| Yes | 7 (18.4) |
| Adjuvant radiation therapy, n (%) |        |
| Yes | 3 (7.9) |
| No | 35 (92.1) |
| Postoperative complications |        |
| Total | 3 (7.9) |
| Pulmonary embolism | 1 (2.6) |
| Seizure | 1 (2.6) |
| Visual deficits | 1 (2.6) |
| Recurrence, n (%) |        |
| Yes | 7 (18.4) |
| No | 31 (81.6) |
Table 2  Comparison of imaging, histopathological and outcomes variables between cystic meningiomas with non-cystic meningiomas

| Variables                              | Cystic Meningiomas (N=38) | Non-Cystic Meningiomas (N=699) | p-value |
|----------------------------------------|---------------------------|--------------------------------|---------|
| Location, n (%)                        |                           |                                | 0.149   |
| Convexity/parasagittal/ventricular     | 28 (73.6)                 | 403 (57.7)                     |         |
| Skull base                             | 10 (27.4)                 | 295 (42.3)                     |         |
| Edema, n (%)                           | 18 (47.4)                 | 368 (52.6)                     | 0.602   |
| Calcification, n (%)                   | 3 (7.9)                   | 64 (9.2)                       | 0.792   |
| Hemorrhage, n (%)                      | 5 (13.2)                  | 15 (2.1)                       | < 0.001 |
| Necrosis, n (%)                        | 5 (13.2)                  | 18 (2.6)                       | < 0.001 |
| Tumor size, mm (IQR)                  | 44 (34–55)                | 36 (26–51)                     | 0.013   |
| Intraventricular, n (%)                | 11 (28.9)                 | 131 (18.7)                     | 0.120   |
| WHO Grade, n (%)                       | 31 (81.6)                 | 520 (74.4)                     |         |
| I                                      | 31 (81.6)                 | 520 (74.4)                     |         |
| Non-grade I                            | 7 (18.4)                  | 179 (25.6)                     |         |
| MIB expression, n (%)                  | N=33                      | N=549                          | 0.784   |
| Low                                    | 24 (72.7)                 | 387 (70.5)                     |         |
| High                                   | 9 (27.3)                  | 162 (29.5)                     |         |
| Gross total resection, n (%)           | 32 (84.2%)                | 581 (83.2%)                    | 0.876   |
| 90-day postop neurosurgical readmission, n (%) | 7 (18.4%) | 92 (13.2%)                     | 0.354   |
| Recurrence, n (%)                      | 7 (18.4%)                 | 80 (12.2%)                     | 0.228   |
| Time to recurrence, months (IQR)      | 25.4 (13.9–46.9)          | 13.4 (8.6–35.5)                | 0.080   |

Bold indicates significance <0.05 in our study

WHO World Health Organization

WHO grades (p = 0.318), MIB-1 expression (p = 0.784) and histologic subtype (n = 24, 63.2% vs. n = 383, 54.7% meningothelial subtype of meningioma, p = 0.309) between cystic and non-cystic meningiomas.

No statistically significant difference was observed in recurrence rate between cystic and non-cystic meningiomas (18.4%, n = 7 vs. 12.2%, n = 80, p = 0.228). Furthermore, no statistically significant difference was observed between the two cohorts in median time to recurrence (25.4 months, Q1:13.9, Q3:46.9 months vs. 13.4 months, Q1:8.6, Q3:35.5, p = 0.080). Figure 2 depicts the Kaplan–Meier curve for recurrence-free survival probability for cystic and non-cystic meningioma.

Fig. 2  Kaplan–Meier survival analysis for time to recurrence for cystic and non-cystic meningioma
meningiomas. There were no significant differences in time to recurrence between the groups \( (p=0.25) \). In multivariable Cox regression analysis, when adjusting for age at surgery, tumor size, presence of peritumor edema, extent of resection and WHO grading, the cystic meningioma was not associated with recurrence (Table 3).

**Discussion**

In a single-center large surgical series of operative meningiomas, cystic meningiomas accounted for a small subset of intracranial meningiomas. Imaging features, histopathological characteristics and outcomes following surgical resection of this relatively rare group of patients with cystic meningiomas is described. We found that the majority of cystic meningiomas were WHO grade I with low Ki-67/MIB-1 proliferation index. These results suggest that cysts in meningioma may not be as aggressive a feature as previously thought [12, 13, 15, 24]. In our study, cystic meningiomas were significantly larger than their non-cystic counterparts and exhibited higher rates of hemorrhage and necrosis. Cystic and non-cystic meningiomas demonstrated no statistically significant differences with regards to histopathological features and outcomes, including extent of resection, readmission, and recurrence. Although single-patient case reports of cystic meningiomas are common in the literature, only a few studies have reported longer term postoperative outcomes following resection of these tumors [25–27].

Prior studies have demonstrated that cystic meningiomas are often accompanied by edema [2, 28, 29]. Approximately half of cystic meningiomas in our study had peritumoral edema, a frequency similar to their non-cystic counterparts. This suggests that the presence of peritumoral edema in meningioma may be unrelated to the cystic component. We noted that cystic tumors had significantly larger median maximal diameter compared to non-cystic meningiomas. The increased tumor size may result in microvascular injury resulting in ischemic necrosis, which can evolve into an intratumoral cyst [30]. Most cysts were intratumoral, either central or peripheral [18, 31, 32]. In our analysis, cystic tumors were associated with higher frequency of necrosis and hemorrhage, which may demonstrate the various stages of cyst formation and shed light on the pathophysiology of intratumoral cyst formation in meningiomas [2, 16, 18, 33]. Further natural history studies are needed to evaluate a causal link between necrosis, hemorrhage, and tumor cyst formation in meningiomas. For peritumoral cysts, the larger tumor size may result in increased compression of the peritumoral brain parenchyma, causing reactive gliosis or entrapment of the CSF in subarachnoid spaces.

A prior study reported that tumor cells are often identified in the cyst wall of cystic meningiomas [25]. Therefore, GTR including removal of the cyst wall is recommended when possible. More than 84% of cystic tumor had GTR in our study. There was no difference in frequency of GTR between cystic and non-cystic meningiomas. This suggests that the presence of cyst may not affect the extent of meningioma resection. The presence of cyst is believed to be reflective of higher grade meningioma [12, 21, 34, 35]. Analogous to Weber et al. [29], we noted that most cystic meningiomas were WHO grade I and had low Ki-67/MIB proliferation index. This suggests that cysts associated with the tumor may not be an indicator of aggressive behavior. Recurrence of tumor after GTR is generally used as an additional indicator of aggressive tumor behavior. Our study was underpowered to demonstrate a statistically significant difference in recurrence rates between cystic and non-cystic meningiomas. Therefore, the negative association with recurrence should be interpreted with caution. Nonetheless, we noted that of the seven recurrent meningiomas, six were WHO grade I and underwent GTR at time of initial surgery.

Our study reviews the presentation and behavior of cystic meningiomas in one of the largest cohorts to date, but is not without limitation. The study cohort, although relatively large, was not powered to fully detect and compare recurrence or other outcomes between cystic and non-cystic meningiomas. Given the rarity of these tumors, multi-institutional studies with larger sample sizes could serve to provide additional clarity on the behavior and prognosis of these tumors. Further studies with higher sample size are required to determine the prognostic significance of cystic meningioma. Furthermore, the single-center retrospective study design contributes its associated biases. In addition, the use of billing codes to identify patients may have resulted in missing patients in both cystic and non-cystic meningioma groups. Finally, cystic meningiomas were identified based on review of imaging and radiology reports by the authors, who are neurosurgeons, and not reevaluated by a neuroradiologist for this study [36].

### Table 3: Multivariable Cox regression analysis for time to recurrence

|                          | HR\(^a\) | 95% CI\(^b\) | p-value |
|--------------------------|---------|-------------|---------|
| Age                      | 1.01    | 0.98, 1.02  | 0.89    |
| Edema                    | 0.98    | 0.62, 1.56  | 0.94    |
| Cystic                   | 1.58    | 0.72, 3.49  | 0.25    |
| Size                     | 1.01    | 0.99, 1.02  | 0.13    |
| GTR                      | 0.75    | 0.45, 1.23  | 0.26    |
| WHO grading              | 1.74    | 1.08, 2.81  | **0.02**|

Bold indicates significance <0.05 in our study

\(^a\)HR: Hazard ratio

\(^b\)CI: Confidence interval
Conclusions

A small portion of intracranial meningiomas have cystic characteristics on imaging. Cystic meningiomas are frequently WHO grade I, have low proliferation index, and had similar outcomes compared to non-cystic meningioma. The cysts in meningioma may not be a surrogate to determine aggressive meningioma behavior.

Author contributions All authors contributed to the conception and design of the study. Material preparation and data collection were performed by ART, SC, CJG, BSG, and JRM. Statistical analysis was performed by SC. Manuscript preparation was performed by ART, SC and reviewed by all authors. PJM, RCT and LBC provided supervision for the study. All authors read and approved the final manuscript.

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Declarations

Conflict of interest The authors declare no competing interests.

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