

Clinical and therapeutic insights into intraventricular metastases from extracranial solid tumors: Patterns, prognosis and management

NAVEEN ARUNACHALAM SAKTHIYENDRAN, DANIEL SCONZO, ARYAN WADHWA and EMANUELA BINELLO

Department of Neurosurgery, Boston Medical Center, Boston University Chobanian and Avedisian School of Medicine, Boston, MA 02118, USA

Received June 2, 2025; Accepted July 3, 2025

DOI: 10.3892/mco.2025.2875

Abstract. Solid intraventricular metastasis from extracranial primary tumors (SIMs) are rare and their diagnosis and management remain poorly understood. A systematic review was conducted using the MEDLINE and Embase databases to identify relevant studies published until November 2024. Data such as presenting symptoms, treatments and survival outcomes were extracted from included articles on patients with SIMs. A total of 26 studies, involving 26 patients (34.6% female patients; median age, 64 years), met the inclusion criteria. The most common primary tumor was renal cell carcinoma (38.5%). Furthermore, 57.7% of patients had metastasis to one or both lateral ventricles, 19.2% had metastasis to the lateral and fourth ventricle, 11.5% had metastasis to the third ventricle alone, 7.7% had metastasis to the lateral and third ventricle, and 3.8% had metastasis to the fourth ventricle alone. Treatment approaches varied, with tumor resection (42.3%) being the most common intervention, followed by tumor resection with adjuvant chemo/radiation therapy (15.4%). The median post-treatment survival time was 4.3 months. Patients receiving tumor resection combined with radiation or chemotherapy had the longest survival (median, 24 months), compared with those undergoing tumor resection alone (median, 2 months). SIMs are rare but clinically significant, with variable treatment approaches and survival outcomes. Multimodal therapy offers the best prognosis, although survival remains generally poor. Further research is needed to better understand the pathophysiology, treatment strategies and outcomes of SIMs.

Introduction

Intraventricular metastases remain an unusual presentation of leptomeningeal metastatic disease. While parenchymal brain metastases from extracranial tumors are common and occur in almost one-third of adult patients with solid tumor malignancies, metastasis to the ventricles are infrequent, with a reported prevalence of only ~0.9-4.6% (1-3).

Intraventricular lesions arise from the ventricular wall, adjacent cerebral structures, or as metastases from extracranial cancers, with the trigone of the lateral ventricles being the most frequent site of involvement given the larger volume of choroid plexus in this region (3-5). Although rare, these lesions are prone to causing hydrocephalus and intracranial bleeding due to the disruption of normal cerebrospinal fluid (CSF) dynamics (5). Additionally, the similar appearance of these tumors to other brain lesions makes it challenging to reliably diagnose intraventricular metastasis (6,7).

Treatment options typically involve a combination of surgical resection and radiation therapy (3,5). While surgery can alleviate CSF obstruction and mass effect, it carries high risk given the invasive approach required (7). In contrast, radiation/chemotherapy (RCT) targets the lesion in a systemic manner while minimizing effects on surrounding structures. However, potential consequences include post-radiation swelling and a delayed tumor response, which may postpone symptom resolution (8-10).

The current literature of solid intraventricular metastasis from extracranial primary tumors (SIM) is predominantly present as individual case reports. While one prior study has evaluated general trends of presentation and management of SIMs (5), our study aims to take a more granular approach and conduct a systematic review of not only patient presentation, and tumor management strategies, but also evaluate the overall survival outcomes of SIMs. Through this approach, we hope to evaluate the most effective treatment strategy and guide patient outcomes for these rare and poorly understood lesions.

Materials and methods

Systematic literature search. A search was performed on MEDLINE, Cochrane and Embase bibliographic databases

Correspondence to: Dr Emanuela Binello, Department of Neurosurgery, Boston Medical Center, Boston University Chobanian and Avedisian School of Medicine, 725 Albany Street, Boston, MA 02218, USA
E-mail: emanuela.binello@bmc.org

Key words: metastases, choroid plexus, intraventricular, management, multimodal treatment

and in forward and backward citations for studies published between database inception and January 1, 2025. To systematically identify all pertinent articles related to SIMs, the following keywords were utilized: ('intraventricular metastasis') OR ('choroid plexus') OR ('lateral ventricle') OR ('third ventricle') OR ('fourth ventricle') AND ('extracranial') AND ('tumor') OR ('lung adenocarcinoma') OR ('renal cell carcinoma') OR ('prostate carcinoma') OR ('rectal carcinoma') OR ('hepatocellular carcinoma') OR ('breast cancer'). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed (Fig. 1). Full text articles that were available in English that specifically reported patient symptoms at presentation, treatment modalities used, and post-treatment outcomes were included. Articles that investigated primary central nervous system tumor metastases to the ventricles, non-intraventricular lesions, non-tumor intraventricular lesions, experimental *in vitro* studies or animal studies, and studies that did not report on presentation symptomatology, treatment modality, and post-treatment outcomes were excluded. Duplicate articles were identified and removed.

Data extraction. The screening process was conducted following the search strategy and using a data extraction form designed by the team. Initially, articles were screened based on titles, followed by abstracts and full texts to determine eligibility. Subsequently, three authors [N.A.S, D.S, A.W.] reviewed the full texts to finalize the inclusion of articles and extract relevant data. The bibliographies of included articles were also examined for additional relevant studies. Disagreements were resolved through consensus meetings. The following variables were extracted from the remaining articles: primary tumor classification, symptoms at presentation, treatment modalities utilized, and survival outcomes post-treatment. We also extracted survival outcomes post-treatment based on the length of time (in months) that patients were alive from completion of their respective treatment(s) to death or last follow-up of any cause. We acknowledge this is a limitation as this may include death due to SIM progression, treatment complications, or systemic disease burden. Comprehensive data extracted from each study is included in Table I.

Statistical analysis. Descriptive statistics were used to categorize patient demographics (age and sex), primary tumor type, location of the SIM within the ventricles, symptoms at presentation, treatment modalities used, outcomes post-treatment (survival duration in months following completion of treatment plan), and presence of hydrocephalus. Kaplan Meier (KM) survival analysis was conducted for prevalent primary tumor subtypes and management strategies and the KM curves are reported in the results section (however, this analysis was done qualitatively and there were no subsequent quantitative studies done for the KM survival analysis). All the analysis was performed on IBM SPSS (Version 29.0.2.0).

Results

Demographics. A total of 124 articles were identified. During screening, 28 records were removed as they were duplicates, 22 articles did not specifically evaluate SIMs, 9 articles were not available in English or full text review, 36 articles did not

report on patient outcomes post-treatment, and 3 articles did not report on patient symptoms at presentation (Fig. 1). In total, 26 articles met the final eligibility criteria, as summarized by Table I. Moreover, 22 of the articles also presented data on the presence or absence of obstructive hydrocephalus post-treatment (Table II).

There was a total of 26 patients (34.6% female) with a median age of 64 (range: 28-88) across all articles. Renal cell carcinoma (RCC) was the most prevalent primary tumor (38.5%) followed by thyroid carcinoma (23.1%), lung adenocarcinoma (19.2%), and 3.8% each of prostate carcinoma, rectal carcinoma, submandibular adenocarcinoma, breast cancer, and gastric cancer (Fig. 2A). Lesion measurement was available in 11 of the patients, with the median largest diameter of the SIMs being 34 mm (Table I). While specific characteristics of SIMs at presentation was only available in 10 studies, 7 of the SIMs were considered hypervascular lesions and 4 were considered to have a hemorrhagic component (with one patient having both) (Table I). Information regarding tumor content (solid vs. solid-cystic) was not available across studies.

The most common symptom at presentation was headaches which occurred in 16 patients (61.5%). This was followed by vomiting, nausea and/or diarrhea (VND) which occurred in 8 patients (30.8%), memory and/or cognitive deficits which also occurred in 8 patients (30.8%), gait disturbances which occurred in 7 patients (26.9%), altered mental status which occurred in 3 patients (11.5%), speech/language deficits which occurred in 2 patients (7.7%), and seizures, dysphagia, hearing loss, and weight loss, which occurred in 1 patient each (3.8%).

As shown in Fig. 2B, 12 patients (46.2%) had metastatic disease to only one lateral ventricle, while 3 patients had involvement of both lateral ventricles (11.5%). Additionally, 5 patients (19.2%) had metastasis to the lateral and fourth ventricle, 3 patients (11.5%) had metastasis to the third ventricle alone, 2 patients (7.7%) had involvement of the lateral and third ventricle, and 1 patient (3.8%) had involvement of the fourth ventricle alone (Fig. 2B).

Treatment modalities. Stand-alone tumor resection performed in 11 (42.3%) patients was the most common treatment, followed by tumor resection with adjuvant chemo/radiation therapy in 4 (15.4%), tumor resection in addition to a CSF/intraventricular bleeding (IVB) flow diversion procedure (external ventricular drain, ventriculoperitoneal shunt, or Ommaya reservoir placement) in 3 (11.5%), chemo/radiation therapy alone in 2 (7.7%), CSF/IVB flow diversion procedure alone in 2 (7.7%), tumor resection, chemo/radiation therapy, and CSF/IVB flow diversion procedure in 2 (7.7%) (Fig. 3). One patient (3.8%) had a tumor biopsy alone with no subsequent management, and one patient (3.8%) had chemo/radiation therapy and CSF/IVB flow diversion procedure. In the 20 patients that had surgical treatment, 15 patients had information on surgical approach: 7 (46.7%) patients underwent a transcortical approach, and 7 (46.7%) patients underwent a transcallosal approach. One (6.7%) patient underwent a Telovelar approach (Table II).

In the 8 patients that were treated with flow diversion procedure, 4 (50%) underwent external ventricular drain (EVD) placement for transient flow diversion of CSF or IVB. 3 (37.5%) underwent ventriculoperitoneal (VP) shunt placement and 1 underwent an Ommaya reservoir placement for

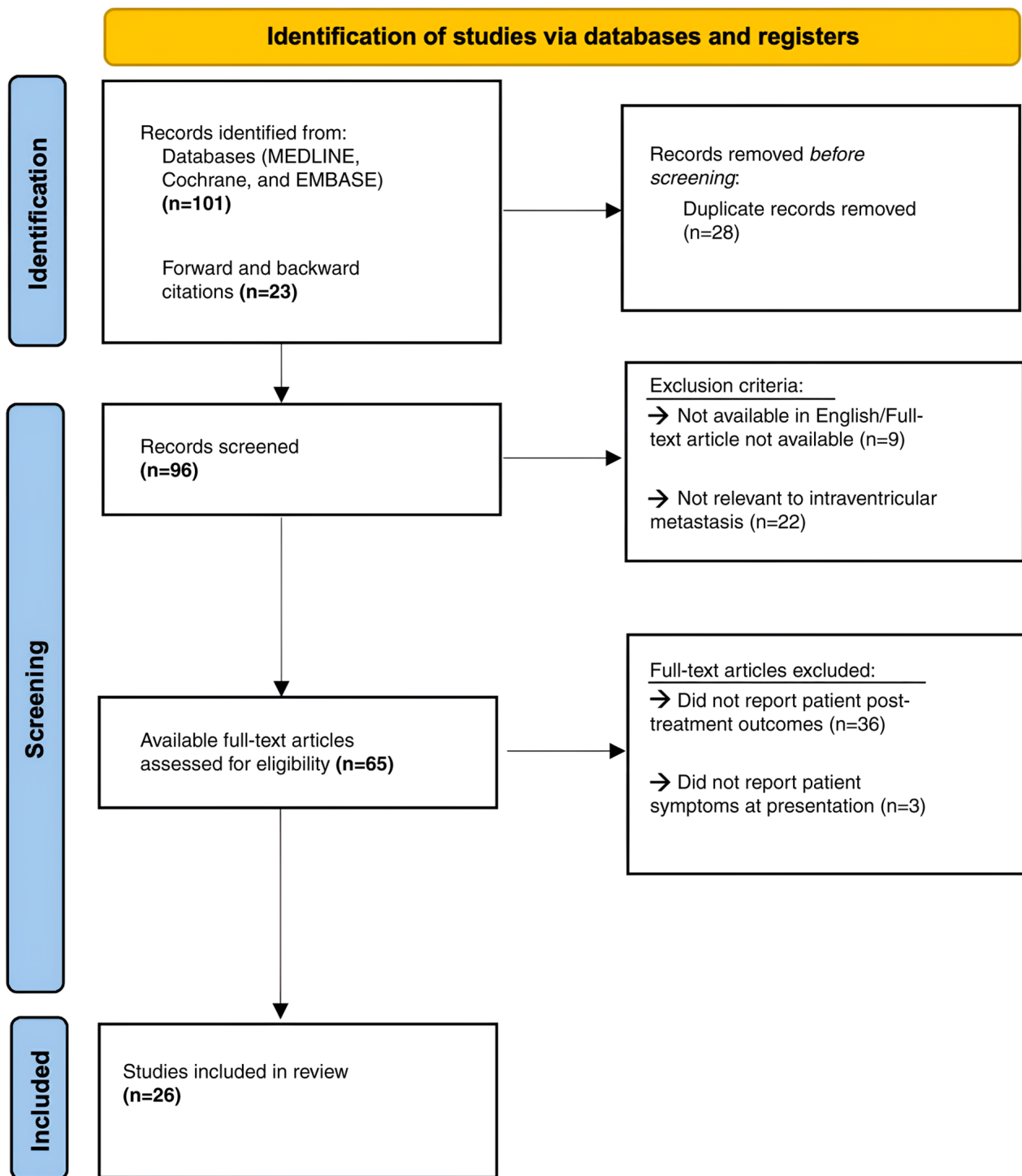


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram. A total of 26 articles were included in the final analysis.

permanent flow diversion. Post-treatment hydrocephalus was present in 14 (64%) patients. 9 (64%) of these patients specifically had obstructive hydrocephalus (Table II).

Post-treatment survival. The median post-treatment survival duration (PSD) across all patients was 4.3 months (0.03-60 months). Across the most prevalent primary tumors, RCC patients had a median PSD of 12 months (0.1-48 months), thyroid carcinoma patients had a median PSD of 13.5 months (0.75-24 months), and lung adenocarcinoma patient had a

median PSD of 1.5 months (0.03-12 months). In patients without fourth ventricular metastasis, the median PSD was 9.5 months (0.75-48 months), while patients with fourth ventricular involvement had a median PSD of 1.5 months (0.5-60 months) (Table III). In patients with presence of obstructive hydrocephalus post-treatment (OH), the median PSD was 4 months (0.4-48 months), whereas in patients without presence of OH, the median PSD was 6 months (0.03-60 months).

In 11 patients that underwent tumor resection alone, the median PSD was 2 months (0.5-48 months). In 4 patients that

Table I. Summary of articles: Patient demographic and clinical characteristics.

First author/s, year	Patient age, years/sex	Primary tumor	Location in ventricle	Size of SIM, mm	Symptoms at presentation	SIM characteristics	(Refs.)
Mizuno <i>et al</i> , 1992	59/female	RCC	Lateral ventricle	NA	Memory/cognitive, gait disturbance	NA	(8)
Sharifi <i>et al</i> , 2015	52/female	Thyroid	B/L lateral ventricles	NA	Headache, N/V/D, speech	Hypervascular and hemorrhagic component present	(4)
Gzell <i>et al</i> , 2013	67/male	Prostate	Fourth ventricle	50x35	Headache, gait disturbance	NA	(9)
Omofoye and Binello, 2019	72/male	Rectal	Lateral and fourth ventricle	NA	Headache, N/V/D, dysphagia	NA	(30)
Lauretti <i>et al</i> , 2005	65/female	RCC	Lateral and third ventricle	34	Headache, N/V/D	Hypervascular	(10)
Garrido <i>et al</i> , 2023	67/male	Lung adenocarcinoma	Lateral and fourth ventricle	NA	Headache, gait disturbance	NA	(5)
Shenoy and Shenoy, 2020	28/female	Breast	Lateral and fourth ventricle	30x28x37	Headache, N/V/D, seizures	Hypervascular	(24)
Matsumara <i>et al</i> , 1997	68/male	RCC	Lateral ventricle	NA	Headache	Hypervascular	(11)
Amirjamshidi <i>et al</i> , 2019	40/male	Adenocarcinoma of submandibular gland	Lateral and fourth ventricle	NA	Headache, N/V/D, transient hearing loss	NA	(28)
Healy and Rosenkrantz, 1980	73/female	Lung adenocarcinoma	B/L lateral ventricles	NA	Weight loss	NA	(31)
Killeberew <i>et al</i> , 1983	55/female	RCC	Lateral ventricle	25	Headache	Hypervascular	(21)
Tanimoto <i>et al</i> , 1991	64/male	Lung adenocarcinoma	Lateral ventricle	NA	Headache	NA	(17)
Nakabayashi <i>et al</i> , 1994	64/male	Gastric	Lateral ventricle	NA	AMS	NA	(29)
Raila <i>et al</i> , 1998	47/female	RCC	Lateral ventricle	NA	Headache, AMS	NA	(12)
Zhang <i>et al</i> , 2009	62/male	Thyroid	B/L lateral ventricles	35x35x40	Memory/cognitive	NA	(18)
Kart <i>et al</i> , 1986	61/male	Lung adenocarcinoma	B/L lateral ventricles	NA	Asymptomatic	NA	(32)
Wasita <i>et al</i> , 2010	75/male	Thyroid	Lateral ventricle	NA	Headache, N/V/D	NA	(27)
Tomiyaama <i>et al</i> , 2008	72/male	RCC	Third ventricle	60	Memory/cognitive	Hemorrhagic component present	(22)
Heery <i>et al</i> , 2012	88/male	Thyroid	Lateral ventricle	27x22	Memory/cognitive, dysarthria	NA	(19)
Beach <i>et al</i> , 2021	75/male	Thyroid	Lateral and fourth ventricle	16x9	Headache, AMS, memory/cognitive	Hemorrhagic component present	(7)
Kong <i>et al</i> , 2020	64/female	Lung adenocarcinoma	Lateral and fourth ventricle	NA	Gait disturbance, N/V/D	NA	(25)

Table I. Continued.

First author/s, year	Patient age, years/sex	Primary tumor	Location in ventricle	Size of SIM, mm	Symptoms at presentation	SIM characteristics	(Refs.)
Shigemori <i>et al.</i> , 1987	58/male	RCC	Lateral ventricle	NA	Headache, gait disturbance	NA	(15)
Karatay <i>et al.</i> , 2015	53/male	RCC	Third ventricle	22x19x27	Headache, N/V/D, memory/cognitive	NA	(13)
Sava <i>et al.</i> , 2013	48/male	RCC	Lateral and third ventricle	30x25x24	Headache, N/V/D	Hypervascular	(14)
Otani <i>et al.</i> , 2015	68/male	RCC	Third ventricle	NA	Memory/cognitive, gait disturbance	Hemorrhagic component present	(16)
Kitagawa <i>et al.</i> , 2013	74/female	Thyroid	Lateral ventricle	40	Memory/cognitive, gait disturbance	Hypervascular	(2)

RCC, renal cell carcinoma; B/L, bilateral; N/V/D, nausea, vomiting, diarrhea; NA, not available; AMS, altered mental status; SIM, solid intraventricular metastasis from extracranial primary tumors.

underwent tumor resection followed by adjuvant chemo/radiation therapy, the median PSD was 24 months (14-60 months). In 8 patients that underwent CSF/intraventricular bleeding flow diversion, the median PSD was 3.75 months (0.1-18 months). In 2 patients that underwent tumor resection, adjuvant chemo/radiation therapy and CSF/intraventricular bleeding flow diversion, the median PSD was 9.5 months (6-13 months). Lastly, in one patient that underwent CSF/intraventricular bleeding flow diversion along with chemo/radiation therapy, the PSD was 0.5 months (Table III). In 12 patients with follow-up imaging data available, 6 (60%) patients had either tumor recurrence or residual tumor in the ventricles. Specific post-surgical complications and/or hospital course data is available in 14 patients, of which 7 (50%) had neurological complications, and 6 (43%) had pulmonary complications (Table II). Additionally, out of the 17 patients that were deceased at the end of each case report, 11 (65%) patients passed from clinical deterioration related to SIM disease, 5 (29%) patients passed due to non-neurologic complications following the procedure, and one (6%) patient passed due to SIM hemorrhage. Comprehensive subgroup data on PSD has been detailed in Table III.

Kaplan Meier survival analysis. In the Kaplan Meier (KM) survival analysis comparing PSD for the most common primary tumors, thyroid carcinoma had the highest probability of survival up to 12 months post-treatment, followed by RCC, and lung adenocarcinoma. After the 12-month PSD, RCC had the highest probability of survival, followed by thyroid carcinoma, and lastly lung adenocarcinoma (Fig. 4A).

In the KM analysis comparing the most prevalent management strategies for SIMs, patients that received resection and chemo/radiation therapy had the highest survival probability at all timepoints post-treatment (Fig. 4B). Patients that received chemo/radiation therapy alone had the second highest probability of survival up to 15 months post-treatment. However, after 15 months post-treatment, patients that underwent resection alone had a moderately higher survival probability compared to the chemo/radiation cohort. Lastly, patients that received a CSF/IVB flow diversion procedure had the lowest survival probability across all timepoints.

Discussion

Renal cell carcinoma (RCC) emerged as the most common primary tumor in our cohort, consistent with prior literature (10-14). The predominance of RCC to metastasize to the ventricles may be attributed to its inherent hypervascularity and the choroid plexus' role as a site of filtration and vascular exchange, facilitating hematogenous spread (12). Additionally, studies have indicated that there are two subtypes within RCCs: one which is rapidly progressing and is often fatal soon after diagnosis, and one that is slower growing and is characterized as an indolent tumor (11,15,16). The longer timeline between initial diagnosis of RCC and diagnosis of the SIM in this analysis suggests that metastasis to the ventricles from RCC is more prevalent in the slower growing type (11). Although the mechanism behind this pattern is unknown, this may be due to slower-growing RCC subtypes allowing patients to survive longer, increasing the likelihood of detecting late-stage, unusual metastatic sites like the ventricles. Thyroid

Table II. Summary of articles: Management, clinical characteristics and outcomes.

First author/s, year	Management type	Surgical approach (if applicable)	PSD, months post-treatment completion	Hydrocephalus presence	Tumor seeding/recurrence seen at follow-up imaging	Post-surgical complications/hospital course	Alive/deceased/disabled at last follow-up (reason for death/disability if applicable)	(Refs.)
Mizuno <i>et al</i> , 1992	Tumor resection, VPS (permanent)	Transcallosal	18.00	No	Yes	Ventricular dilatation	Disabled (regrowth of the SIM)	(8)
Sharifi <i>et al</i> , 2015	Tumor resection, EVD (removed 2nd day), radiation	Transcortical	6.00	No	No	NA/A	Alive	(4)
Gzell <i>et al</i> , 2013	Tumor resection	NA/A	2.00	Yes (obstructive)	No	Urinary and fecal incontinence due to presacral lymphadenopathy	Deceased (clinical deterioration due to SIM)	(9)
Omofoye and Binello, 2019	Ommaya reservoir (permanent), radiation	NA/A	1.50	Yes (mild)	NA/A	Aspiration pneumonia and pulmonary embolism	Deceased (clinical deterioration due to SIM)	(30)
Lauretti <i>et al</i> , 2005	Tumor resection	Transcortical	46.00	Yes (non-obstructive)	NA/A	Pulmonary embolism (COD)	Deceased (died from pulmonary embolism)	(10)
Garrido <i>et al</i> , 2023	Tumor resection	Telovelar	0.50	Yes (obstructive)	NA/A	Neoplastic meningitis	Deceased (clinical deterioration due to SIM)	(5)
Shenoy and Shenoy, 2020	Tumor resection	Transcallosal	1.50	Yes (asymmetrical hydrocephalus)	Yes	Intratumoral bleeding, IVH and worsening hydrocephalus	Deceased (clinical deterioration due to SIM)	(24)
Matumara <i>et al</i> , 1997	Tumor resection	NA/A	30.00	No	NA/A	NA/A	Alive	(11)
Amirjamshidi <i>et al</i> , 2019	Tumor resection, radiation	NA/A	60.00	No	No	NA/A	Alive	(28)
Healy and Rosenkrantz, 1980	Chemotherapy, radiation	NA/A	0.03	No	NA/A	NA/A	Deceased (clinical deterioration due to SIM)	(31)
Killeberew <i>et al</i> , 1983	Tumor resection	Transcortical	48.00	Yes (obstructive)	No	Intratumoral bleeding	Alive	(21)
Tanimoto <i>et al</i> , 1991	Tumor resection	Transcortical	1.50	No	Yes	Acute myocardial infarction (COD)	Deceased (acute myocardial infarction)	(17)
Nakabayashi <i>et al</i> , 1994	Tumor resection	Transcallosal	2.50	No	NA/A	Respiratory complication (COD)	Deceased (respiratory complication)	(29)
Raila <i>et al</i> , 1998	Tumor resection	NA/A	0.75	Not reported	NA/A	NA/A	Deceased (clinical deterioration due to SIM)	(12)
Zhang <i>et al</i> , 2009	Tumor resection	Transcallosal	18.00	Not reported	Residual tumor	Bilateral pulmonary embolism	Alive	(18)

Table II. Continued.

First author/s, year	Management type	Surgical approach (if applicable)	PSD, months post-treatment completion	Hydrocephalus presence	Tumor seeding/recurrence seen at follow-up imaging	Post-surgical complications/hospital course	Alive/deceased/disabled at last follow-up (reason for death/disability if applicable)	(Refs.)
Kart <i>et al</i> , 1986	Stereotactic biopsy	NA/A	2.50	Not reported	NA/A	NA/A	Deceased (clinical deterioration due to SIM)	(32)
Wasita <i>et al</i> , 2010	Radiation, tumor resection	NA/A	24.00	Yes (mild, non-obstructive)	NA/A	NA/A	Alive	(27)
Tomiyama <i>et al</i> , 2008	VPS (permanent)	NA/A	6.00	Yes (obstructive)	NA/A	Sepsis (COD)	Deceased (sepsis)	(22)
Heery <i>et al</i> , 2012	Tumor resection, VPS, SRS	Transcortical	13.00	Yes (obstructive)	Yes	NA/A	Deceased (clinical deterioration due to SIM)	(19)
Beach <i>et al</i> , 2021	Tumor biopsy, EVD (removed post-operative day 7)	NA/A	0.75	Yes (obstructive)	NA/A	NA/A	Deceased (clinical deterioration due to SIM)	(7)
Kong <i>et al</i> , 2020	Chemotherapy	NA/A	12.00	Yes (obstructive)	Yes	NA/A	Deceased (clinical deterioration due to SIM)	(25)
Shigemori <i>et al</i> , 1987	Tumor resection, EVD (patient died quickly)	Transcortical	0.10	Not reported	NA/A	Left-hemisphere SDH	Deceased (clinical deterioration due to SIM)	(15)
Karatay <i>et al</i> , 2015	Tumor resection, EVD	Transcallosal	0.43	Yes (obstructive)	NA/A	IVH	Deceased (SIM hemorrhage)	(13)
Sava <i>et al</i> , 2013	Tumor resection	Transcallosal	0.40	Yes (mild, non-obstructive)	NA/A	Transependymal effusion and bronchopneumonia (COD)	Deceased (bronchopneumonia)	(14)
Otani <i>et al</i> , 2015	Tumor resection, radiation	Transcallosal	24.00	Yes (obstructive)	No	None	Alive	(16)
Kitagawa <i>et al</i> , 2013	Tumor resection, radiation	Transcortical	14.00	No	No	None	Alive	(2)

PSD, post-treatment survival duration; VPS, ventriculoperitoneal shunt; EVD, external ventricular drain; IVH, intraventricular hemorrhage; SDH, subdural hematoma; NA/A, not available/applicable; COD, cause of death; SIM, solid intraventricular metastasis from extracranial primary tumors; SRS, stereotactic radiosurgery.

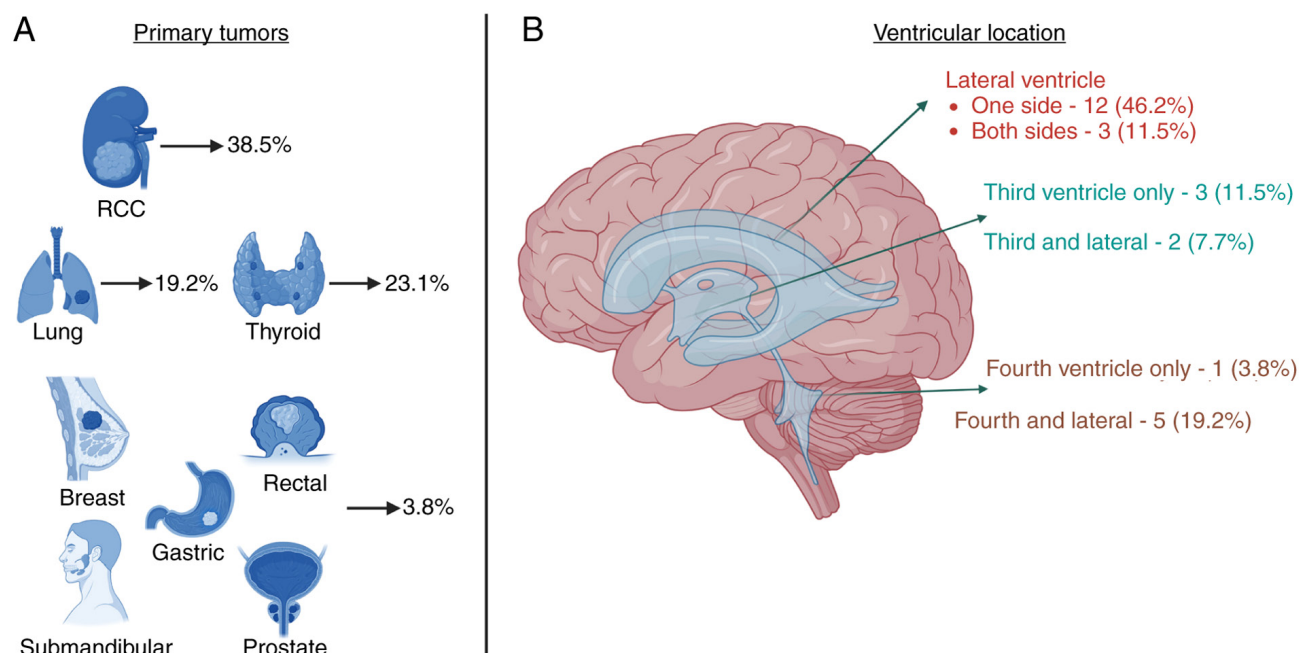


Figure 2. Prevalence of primary tumors and ventricular location of metastasis. (A) Prevalence of the different primary tumors in the present cohort, with patients with RCC having the highest prevalence, followed by those with thyroid carcinoma and lung adenocarcinoma. Other primary tumors, such as breast, gastric, rectal, submandibular and prostate carcinomas were found to be less likely to metastasize to the intraventricular space. (B) Prevalence of intraventricular metastasis based on ventricular location. The lateral ventricle was the most common site of metastatic spread, followed by metastasis to the fourth ventricle, and the least common site of metastasis was the third ventricle. Created in BioRender. Arunachalam Sakthiyendran, N. (2025). RCC, renal cell carcinoma.

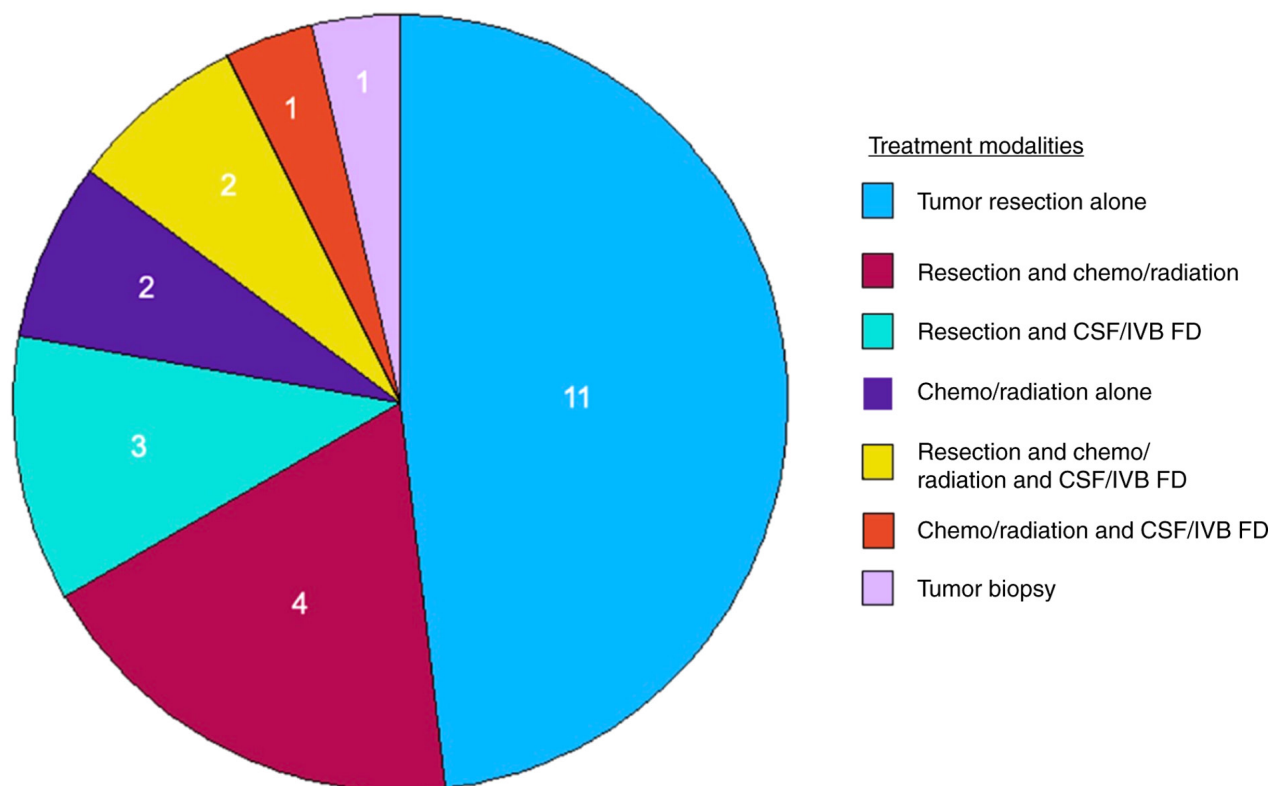


Figure 3. Pie chart of treatment modalities. Prevalence of the different management strategies employed to treat intraventricular metastasis in the present cohort of patients. CSF/IVB FD, cerebrospinal fluid/intraventricular bleeding flow diversion.

carcinoma and lung adenocarcinoma were also prevalent among patients in the included studies. This may be due to the propensity of these primary tumors to cause lymphatic or

hematogenous spread as indicated by the large percentage of SIMs characterized as hypervascular in this review, as well as their anatomical proximity to the brain (17-19).

Table III. Post-treatment survival duration for different subgroups.

Characteristic	Median post-treatment survival, months (range)
Sex	
Male (n=17)	2.50 (0.10-60.00)
Female (n=9)	12.00 (0.75-48.00)
Primary tumor type	
Renal cell carcinoma (n=10)	12.00 (0.10-48.00)
Thyroid carcinoma (n=6)	13.50 (0.75-24.00)
Lung adenocarcinoma (n=5)	1.50 (0.03-12.00)
Prostate carcinoma (n=1)	2.00
Rectal carcinoma (n=1)	1.50
Breast cancer (n=1)	1.50
Submandibular adenocarcinoma (n=1)	60.00
Gastric cancer (n=1)	2.50
Ventricular location	
One lateral ventricle only (n=11)	14.00 (0.1-48.00)
Both lateral ventricles (n=3)	2.50 (0.03-6.00)
Fourth ventricle only (n=1)	2.00
Third ventricle only (n=3)	6.00 (0.43-24.00)
Lateral and fourth ventricle (n=6)	1.50 (0.50-60.00)
Lateral and third ventricle (n=2)	23.20 (0.40-46.00)
Management type	
Standalone resection of IVM (n=11)	2.00 (0.50-48.00)
Chemo/radiation alone (n=2)	6.00 (0.03-12.00)
CSF flow diversion only (n=2)	3.40 (0.75-6.00)
Resection and chemo/radiation therapy (n=4)	24.00 (14.00-60.00)
Resection and CSF diversion (n=3)	0.40 (0.10-18.00)
Chemo/radiation and CSF diversion (n=1)	0.50
Resection, chemo/radiation, CSF diversion (n=2)	9.50 (6.00-13.00)
Biopsy only (n=1)	2.50
OH	
Presence of OH (n=16)	4.00 (0.40-48.00)
No presence of OH (n=6)	6.00 (0.03-60.00)

CSF, cerebrospinal fluid; IVM, intraventricular metastasis; OH, obstructive hydrocephalus.

The clinical presentation of SIMs varied widely, but frequently included headaches, nausea/vomiting/diarrhea, gait instability, and memory or cognitive disturbances. Additionally, while our analysis did not evaluate presentation symptoms based on SIM location, other studies have indicated that lateral or third ventricular tumors are more frequently associated with motor weakness and cognitive impairment, while tumors involving the fourth ventricle are more associated with ataxia and dizziness 5). While these symptoms are not exclusive to hydrocephalus and not all patients with SIMs develop OH, those presenting with these symptoms are typically evaluated with cranial imaging, which often reveals tumor-related causes. Tumors growing within the ventricles can obstruct CSF and blood flow, leading to increased ICP and OH (20-22). Even when OH or intracranial bleeding is not initially present, it is important to recognize the potential for

its progression as the tumor enlarges. Hence, patients should be informed about the possible development of hydrocephalus, hemorrhagic transformation, and the importance of persistent surveillance.

The heterogeneity in treatment strategies for SIMs reflect the complexity of balancing effective local control with the risks posed by the proximity of these tumors to vital structures. Tumor resection, either alone or in combination with adjuvant RCT, was the most frequently utilized approach in our analysis. The transcortical and transcallosal approaches were the most common surgical approaches used given the access it provides to the lateral and third ventricles (23). Patients who underwent tumor resection with adjuvant RCT also demonstrated the longest PSD, with a median of 24 months. This indicates that a multimodal and systemic approach to SIMs may provide superior local control and survival compared to

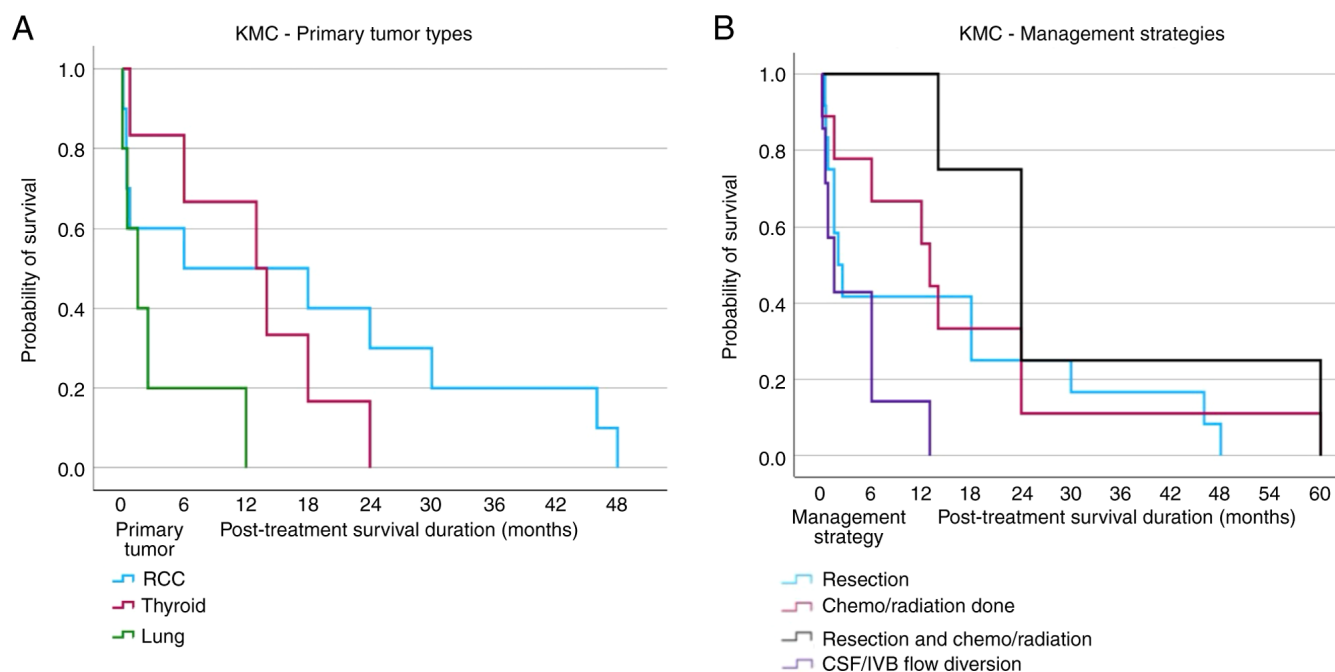


Figure 4. Kaplan-Meier analysis of the post-treatment survival duration for different primary tumors and treatment paradigms. (A) Kaplan Meier curve indicating that patients with thyroid carcinoma had the highest probability of survival up to 12 months post-treatment. However, after 12-months, patients with RCC had the highest probability of survival. Patients with lung adenocarcinoma had the shortest post-treatment survival duration across all timepoints. (B) Kaplan Meier curve indicating that patients who received resection and adjuvant chemo/radiation therapy had the highest survival probability at all timepoints post-treatment. Patients that received chemo/radiation therapy alone had the second highest probability of survival up to 15 months post-treatment. Patients that received a CSF/IVB flow diversion procedure (external ventricular drain, ventriculoperitoneal shunt or Ommaya reservoir) had the lowest survival probability across all post-treatment timepoints. CSF/IVB, cerebrospinal fluid/intraventricular bleeding; KMC, Kaplan Meier curves; RCC, renal cell carcinoma.

surgery alone (24,25). Performing surgical resection alone had a notably lower median PSD compared to the use of resection and chemo/radiation. Hence, while surgery may be done to relieve the debilitating symptoms related to mass effect in patients with large tumors or elevated ICP, surgical resection may be particularly complicated in SIM patients (26). This may likely be secondary to the increased risk of IVH due to the hyperemic nature of choroid plexus metastases, which needs to be adequately managed intraoperatively using irrigation, and CSF/bleeding diversion (27). Given these factors, the risk of surgery must be carefully weighed against the long-term benefits of quality survival. Traditionally, patients selected as surgical candidates are expected to have a reasonable performance function status, and stable metastatic disease, that is not characteristic in patients with SIMs (27,28). Hence, in patients (especially those that are elderly and/or frail) who prioritize quality of life, surgical resection may be contraindicated.

Interestingly, while 8 patients underwent CSF/IVB diversion procedures such as EVD placement, VP shunt, or Ommaya reservoirs, the PSD was lower than the overall median of the cohort. The reduced survival observed in patients undergoing CSF/IVB diversion suggests that these procedures are primarily palliative and reserved for patients with severe symptoms since CSF/IVB diversion does not alter the underlying disease process itself. Moreover, flow diversion such as EVD, Ommaya reservoirs, etc. carry risks such as infection, catheter occlusion, and ventriculitis, which can further compromise survival in this already vulnerable group (27). Therefore, surgical intervention and flow diversion should be considered in select cases to preserve neurologic

function and alleviate symptoms of hydrocephalus (20,29). In patients with extensive disease progression or limited systemic treatment options, CSF/IVB diversion may offer temporary relief, helping patients maintain a level of function and comfort during the course of their illness (20,30,31).

The unique microenvironment of the ventricular system poses distinct challenges for the treatment of SIMs. The nutrient-rich CSF, coupled with limited immune surveillance within the ventricles, creates an environment conducive to metastatic cell survival and proliferation (32,33). Moreover, the ventricular wall may act as a barrier to systemic therapies, including chemotherapy and targeted agents, further complicating management. While stereotactic radiosurgery (SRS) has shown promise in achieving local control for intraventricular metastases, its efficacy in SIMs is likely constrained by the shielding effect of the ventricular wall and the blood-brain barrier.

Our study also highlights the substantial variability in outcomes. Among the most prevalent primary tumors, patients with RCC demonstrated the longest median survival, whereas those with lung adenocarcinoma had a poorer prognosis. The shorter survival in lung adenocarcinoma likely reflects its aggressive nature and propensity for widespread systemic and intracranial disease progression (17,25). This observation highlights the relationship between tumor biology and disease progression, which may be crucial in tailoring therapeutic strategies.

Tumor location within the ventricles also appears to influence prognosis. Patients with fourth ventricular involvement had a shorter median survival compared to those with lateral or

third ventricle-only involvement. The anatomical and surgical challenges associated with fourth ventricular tumors, associated with operating in and around the posterior fossa, could contribute to increased perioperative morbidity. For instance, compression of the brainstem or cerebellum may accelerate functional decline and preclude aggressive therapy (26). While this was not statistically significant due to sample size, this trend warrants further investigation.

Importantly, the dismal overall median survival (4.3 months) for all patients with SIMs reflects the advanced nature of the disease and the limited therapeutic arsenal currently available. This aligns with previous reports that intraventricular metastases from extracranial tumors are associated with a worse prognosis compared to other brain metastases (7). The advanced disease stage at diagnosis and the anatomical complexity of the ventricular system are key contributors to these outcomes.

Emerging therapies, such as immunotherapy (e.g., tyrosine kinase inhibitors in RCC, checkpoint inhibitors in NSCLC) and advanced imaging modalities, offer hope for improving outcomes in this patient population. Immunotherapies targeting immune-suppressive mechanisms in the brain microenvironment are being actively explored and may hold promise for SIM treatment. Advancements in stereotactic radiosurgery (SRS) and intra-CSF drug delivery could enable more localized treatment with reduced systemic toxicity (28,29).

Additionally, novel imaging techniques, including molecular imaging and CSF biomarkers, could enhance the early detection and characterization of SIM, enabling more timely and tailored interventions. Future studies should explore the timing and efficacy of CSF diversion in improving both symptom management and overall survival. Given the lack of studies or clinical trials demonstrating the efficacy or safety of resection, shunt placement, chemotherapy, or immunotherapy for SIMs, treatment decisions must be approached cautiously due to the risk of peripheral structural damage and tumor-related hemorrhage (3). In addition, intraventricular metastases can grow larger, without clinical symptoms (31,32). If treatment is delayed, even slowly progressing tumors-such as RCC metastases-may increase in volume due to recurrent intratumoral hemorrhage. This bleeding can contribute to sudden expansion of the tumor, worsening mass effect, and OH. In cases where tumor burden extends into the third ventricle or hypothalamic region, progressive compression and infiltration may lead to hypothalamic dysfunction, resulting in neurological decline (11,14,16).

Our study is inherently limited by the rarity of SIMs, the heterogeneity in reported details of cases, and the retrospective nature of the included studies. The small sample sizes and variability in treatment approaches across studies limits definitive conclusions regarding prognostic factors and optimal management. Specifically, the retrospective nature of this review meant that we could not standardize treatment selection criteria. Hence, interventions reflect individual clinician judgment based on tumor location, patient performance status, and systemic disease. Additionally, due to the heterogeneity in outcome measures and lack of consistent reporting in timeline from primary tumor to SIM diagnosis, we had to use duration of survival post-treatment completion as the outcome measure.

PTD may reflect heterogeneous causes (SIM progression vs. procedural morbidity vs. systemic disease), which we could not disaggregate given case-report data. Given these limitations and the sample size being inadequately powered for significance analysis, we approached this systematic review through consolidating, analyzing, and describing the patterns across the literature on SIMs. As with all systematic reviews, our findings are limited and may reflect inherent biases of the studies included, although efforts were made to identify these biases.

Despite these limitations, our systematic review provides a comprehensive synthesis of the available literature on the presentation, management, and outcomes of SIMs. It also highlights key knowledge gaps and areas for future research, including the need for prospective studies to better define treatment outcomes and survival patterns in this rare patient population.

In conclusion, SIMs represent a rare but clinically significant manifestation of metastatic disease. Our findings underscore the importance of a multimodal treatment approach and highlight the challenges posed by the unique anatomical and biological features of the ventricular system. Continued research into the pathophysiology, early detection, and novel therapies for SIM is essential to improving outcomes for these patients.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

Not applicable.

Authors' contributions

NAS was involved in the conceptualization of the study, performing the analysis, writing the original draft and editing the manuscript. DS was involved in the conceptualization of the study, systematic review of the literature, reference management, writing the original draft, and editing the manuscript. AW was involved in the conceptualization of the study, systematic review of the literature, writing the original draft, editing the manuscript and data visualization. EB was involved in conceptualization of the study, editing the manuscript, project administration and supervision. All authors read and approved the final version of the manuscript. Data authentication is not applicable.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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