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Case report

Complete remission of brain metastasis from thymic carcinoma following hypofractionated gamma knife radiosurgery: Case report and a review of literature

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ABSTRACT

Introduction: Thymic carcinoma is a rare, aggressive neoplasm that frequently metastasizes to the lungs, liver, and bones, but rarely to the central nervous system. Less than 50 cases of brain metastases from thymic carcinoma have been documented in the literature, and no consensus exists regarding their optimal management and follow-up.

Case presentation: Here, we report the case of a 54-year-old male who developed a solitary metastasis in the right temporal region nearly four years after the diagnosis of metastatic thymic carcinoma. The lesion was discovered incidentally on follow-up PET-CT scan. He was treated with hypofractionated stereotactic radiosurgery (hSRS) alone. No surgical intervention or whole brain radiotherapy (WBRT) was performed. MRI showed near-complete regression of the lesion and cavity collapse at the first month, and complete remission was achieved at 4th months. The patient remains alive and recurrence-free at 17 months of follow-up.

Clinical discussion: To date, only five cases have been reported in which stereotactic radiosurgery (SRS) was used as part of a multimodal approach, typically in combination with surgical resection, to achieve intracranial disease control. Notably, hSRS was employed in only two of these cases, both alongside surgery; however, neither achieved progression-free survival.

Conclusion: This case demonstrates that Gamma Knife-based hSRS may achieve durable control of solitary brain metastases from thymic carcinoma without the need for surgery or WBRT. It also emphasizes the importance of long-term neuroimaging surveillance in thymic carcinoma due to the potential for delayed central nervous system dissemination.

1. Introduction

Thymic epithelial tumors (TETs), comprising thymomas and thymic carcinomas (TCs), are rare malignancies with an annual incidence of 0.15 per 100,000 individuals. They typically arise in adults over the age of 30, without a gender predilection. Notably, over half are asymptomatic and found incidentally during unrelated evaluations [1,2]. Although less common than thymomas, TCs are more aggressive and metastasize more readily, particularly to the pleura, lungs, liver, and bones. In contrast, central nervous system (CNS) involvement is exceedingly rare [3], with less than 50 cases were reported. Moreover, it is generally associated with a poor prognosis [4–6]. Surgical resection, WBRT, and stereotactic radiosurgery (SRS) have all been employed with varying degrees of success [4,5]. Nevertheless, the literature on

Abbreviations: CBCT, cone-beam computed tomography; CNS, central nervous system; CT, computed tomography; F, female; GKRS, gamma knife radiosurgery; Gy, gray; hfRS, hypofractionated radiosurgery; LINAC, linear accelerator; M, male; MRI, magnetic resonance imaging; NA, not available; PET-CT, positron emission tomography–computed tomography; SIADH, syndrome of inappropriate antidiuretic hormone secretion; SRS, stereotactic radiosurgery; TC, thymic carcinoma; TET, thymic epithelial tumor; WBRT, whole brain radiotherapy.

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radiosurgical treatment, particularly hypofractionated radiosurgery (hfRS), is scarce [4]. Here, we present the first documented case of solitary brain metastasis from TC successfully treated with Gamma Knife hfRS alone, contributing to the limited data on CNS dissemination in the TC and highlighting the efficacy of radiosurgery as a standalone treatment.

2. Case report

A 54-year-old male presented with a two-month history of progressive cough in 2020. He had no regular medication use, known comorbidities or family history of malignancy, and denied alcohol-tobacco use. Thoracic and abdominal computed tomography (CT) revealed multiple metastatic lesions in the lungs and liver, along with an anterior mediastinal mass. A fine needle aspiration biopsy of a hepatic lesion demonstrated a poorly differentiated carcinoma with basaloid morphology and squamous differentiation, arranged in a nested growth pattern, findings consistent with metastatic TC, Masaoka stage IVb. Subsequent positron emission tomography–computed tomography (PET-CT) revealed a hypermetabolic anterior mediastinal mass, bilateral pulmonary nodules, liver metastases, and lymph nodes.

Concurrently, the patient was commenced on systemic chemotherapy, including Doxorubicin, Cyclophosphamide and Cisplatin in the first course with 8 cycles and Paclitaxel and Carboplatin in the second course with 4 cycles, alongside external radiotherapy to the mediastinal mass. Targeted therapies, including Imatinib during the first course, Pembrolizumab and Sunitinib during the second course, were added due to disease progression. Four months after the completion of all systemic therapies, follow-up PET-CT showed hypometabolic activity in the right temporal lobe (Fig. 1a). Magnetic resonance imaging (MRI) confirmed a novel right temporal metastasis with cystic/necrotic foci and slight perilesional edema (Fig. 1b-d).

The multidisciplinary tumor board recommended hfRS as a standalone treatment and referred the patient to the Gamma Knife Center. He underwent planning with MRI, perfusion MRI, CT, and cone-beam computed tomography (CBCT) imaging on the first treatment day. The Leksell GammaPlan® v11.3 (Elekta AB, Stockholm, Sweden) was utilized for planning (Fig. 2). The metastatic lesion volume was measured as 33.8 cm^3. Multishot dose delivery with various collimator dimensions was employed to shape a toroidal isodose contour and achieve a high target coverage (0.99), selectivity (0.83) and Paddick conformity index (0.83), while remaining within accepted V24 brain tolerance limits (volume of brain tissue exposed beyond 24 Gy), ensuring both safety and efficacy [7]. Thermoplastic mask application was performed, and hfRS was delivered to the right temporal metastasis via The Leksell Gamma Knife® Icon™ (Elekta AB, Stockholm, Sweden). A fractionation scheme of 25 Gy in five daily fractions (5 × 5 Gy) to the 50 % isodose line was selected to balance tumor control with reduced risk of radiation necrosis, particularly given the lesion size and proximity to critical structures. The beam on time was 50.3 min per fraction. The patient underwent all sessions of hfRS as an outpatient procedure without the need for hospital admission.

The first follow-up MRI showed an excellent response: near-complete regression of the lesion, cavity collapse, and contrast-enhancing margins suggestive of radiation necrosis, without new metastasis (Fig. 3a, b). At the four-month follow-up, MRI confirmed complete regression of the treated lesion with established radiation necrosis (Fig. 3c). Subsequent imaging at the 11th and 17th months demonstrated sustained resolution and no new metastatic foci (Fig. 3d, e).

The work has been reported in line with the SCARE criteria [8].

3. Discussion

TCs are rare but biologically aggressive neoplasms with a pronounced tendency for distant metastasis [3]. However, central nervous system involvement remains exceptionally rare, with fewer than 50 cases reported in the literature, resulting in limited clinical experience and a lack of standardized treatment guidelines. Among the reported cases, SRS has been used sparingly, only five cases have described its application to date, and no case has documented the use of hfRS as a standalone treatment. This rarity presents unique diagnostic and therapeutic challenges, particularly in determining the optimal management approach for isolated brain metastases from TC. In the present case, a 54-year-old male developed a solitary right temporal lobe metastasis nearly four years after his initial diagnosis and multiple systemic treatments, a timeline consistent with prior reports indicating that CNS metastases from TC may emerge late in the disease course [4,9]. Remarkably, Gamma Knife hfRS alone achieved complete remission, underscoring its potential as a noninvasive and effective therapeutic option in select cases.

The Masaoka staging system is commonly used to classify TCs. The 5-year survival rate for stage IV TETs across all histological subtypes is approximately 50 %, whereas it declines to 30 % for stage IVb TCs [4]. CNS involvement, especially multiple metastases, indicates significantly worse prognosis [10]. Accordingly, patients should undergo vigilant and routine surveillance for potential brain metastases, preferably incorporating brain MRI into follow-up protocols. In the present case, one of the key factors contributing to the successful outcome of SRS was the patient's adherence to regular follow-up with PET-CT imaging, which enabled early detection of the brain metastasis before the onset of neurological symptoms or the involvement of eloquent and functionally critical brain regions.

The management of TETs is highly stage dependent. Surgical resection remains the cornerstone of treatment for stages I and II, whereas stage III-IV disease is typically managed with platinum-based chemotherapy. Radiotherapy is generally reserved for incomplete surgical resection, high-grade histology, or evidence of local invasion [1]. For unresectable stage III and IVa tumors, a multimodal approach, incorporating chemotherapy, radiotherapy, and, when possible, delayed surgery, is favored [1]. Despite advances in systemic therapies, the prognosis for stage IVb TC remains poor [4,10]. Although cisplatin-based chemotherapy has shown responsiveness in TC, its impact on overall survival, particularly in the setting of brain metastases, remains limited. Recent studies advocate for a multimodal therapeutic approach: early surgical resection of accessible lesions, followed by timely initiation of radiotherapy and systemic chemotherapy [6]. However, the

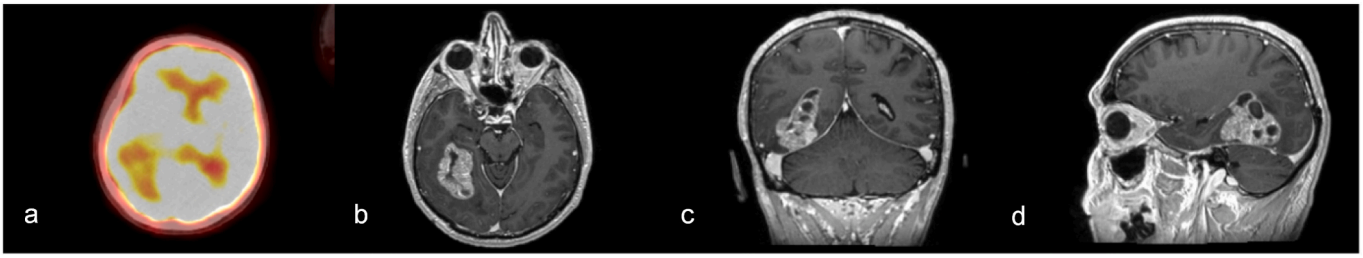


Fig. 1. PET-CT revealing new hypometabolic activity in the right temporal lobe (a). Brain MRI confirming a right temporal metastatic lesion (b, c, d).

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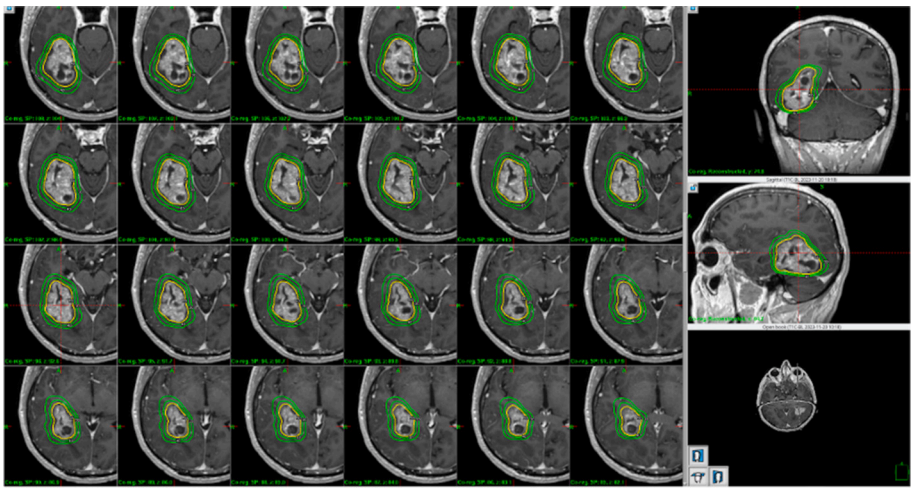


Fig. 2. Treatment plan created using the Leksell GammaPlan® v11.3 (Elekta AB, Stockholm, Sweden).

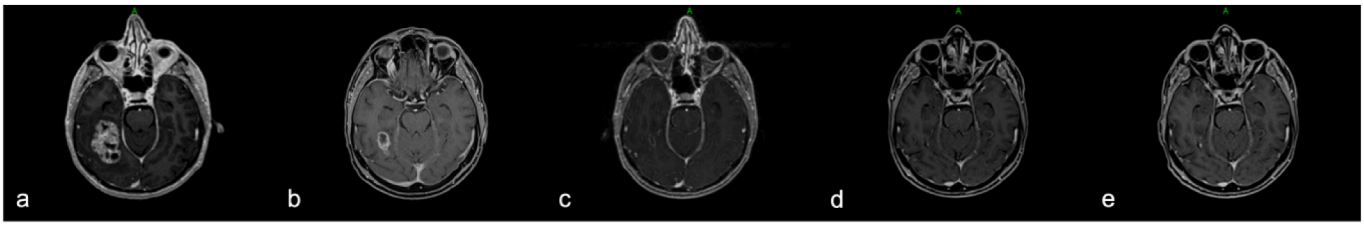


Fig. 3. Serial MRIs showing right temporal metastatic lesion on the day of treatment (a), and treatment response during follow-up at 1 month (b), 4 months (c), 11 months (d), and 17 months (e) post-Gamma Knife hfRS.

definitive role of radiotherapy continues to be debated [5].

A review of the literature identified 43 reported cases of TC brain metastasis, with a predominance among male patients (Table 1). The mean age at diagnosis was 53 years, and the average interval from initial diagnosis to CNS involvement was approximately 19 months. The majority of patients presented with multiple lesions, while only eleven cases involved a solitary metastasis. Three patients were managed conservatively without specific treatment for the brain metastases while 2 of them deceased during follow-up. Surgical resection alone was employed in four cases and only 1 patient was alive at the 12-month follow-up, whereas two patients received WBRT as monotherapy and both died at 2 and 7 months. The remaining cases in the literature underwent various combinations of surgery, radiotherapy, chemotherapy and SRS. Regarding remission outcomes, seven cases achieved complete remission, four showed progression, seven studies did not define remission status, and one study reported a median progression-free survival of 14 months. The present case is unique in being treated exclusively with hfRS and achieving complete remission with an overall survival for 17 months to date, representing one of the longest reported survival durations. However, due to the distinct treatment approach and favorable outcome in our case, as well as the variability among previously reported cases in terms of therapeutic strategies and metastatic burden, direct comparison remains limited.

The efficacy of SRS in managing brain metastases from TC has not been conclusively established yet [5]. To date, only five cases in which SRS was employed, generally alongside surgical resection, to achieve intracranial disease control have been reported (Table 2). In the first case, a 55-year-old male underwent cyst evacuation followed by Gamma Knife radiosurgery (GKRS) [11]. At the time, hfRS had not yet been developed, and combining resection with SRS represented a reasonable approach. The second case involved a multimodal regimen including surgical resection, WBRT, and SRS, though the follow-up period was limited to nine months, restricting conclusions about long-term efficacy [6]. The third patient underwent GKRS twice but without a durable response and later required surgery. Despite aggressive management, the patient died 14 months after the diagnosis [5]. Notably, hfRS were used in only two cases, both following resections, and failed to achieve sustained disease control [4,12]. Uniquely, in the present case, Gamma Knife hfRS alone resulted in complete remission without the need for surgery. To our knowledge, this is the first reported case using hfRS as monotherapy for TC brain metastasis.

In this patient, the decision to pursue hypofractionated stereotactic radiosurgery (hfRS) as monotherapy was guided by multiple clinical considerations. These included the solitary and relatively large size of the lesion (33.8 cm^3), its eloquent location accompanied by peritumoral edema, the asymptomatic presentation, and the patient's clear preference to avoid invasive procedures. Additionally, the patient had previously undergone multiple lines of systemic therapy, including chemotherapy, immunotherapy, and targeted agents, indicating a potentially reduced physiological reserve and limited tolerance for surgical intervention. Notably, the primary tumor had demonstrated a favorable radiological response to earlier radiotherapy, suggesting a degree of intrinsic radiosensitivity. Collectively, these factors, supported by a multidisciplinary tumor board consensus, justified the selection of hfRS as a noninvasive, yet potentially effective, standalone treatment. While a lesion of this volume would traditionally prompt consideration of surgical resection followed by radiosurgery, surgery was deferred in this case due to the absence of neurological deficits or significant mass effect [13]. Instead, a hypofractionated regimen (5 × 5 Gy) was chosen over single-session SRS to enhance safety, particularly by reducing the risk of radiation necrosis and edema. Hypofractionation also facilitates better preservation of surrounding critical brain structures, especially in larger lesions. The prescribed dose was carefully tailored to the lesion's volume and proximity to eloquent areas, with planning optimized to remain within safe V24 brain tolerance thresholds, minimizing radiation exposure to normal brain parenchyma while ensuring therapeutic

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Table 1
Reported cases of TC brain metastasis.

Study	Number of patients	Age/sex	Symptoms	Time to brain metastasis, months	Number of metastases	Location	Treatment	Outcome	Remission status
Arriagada et al., 1984 [15]	5	NA	NA	NA	5	NA	Primary tumor treated	NA	NA
Dewes et al., 1987 [16]	1	49/M	Left hemiparesis	8	1	Right parietal	Surgery + Radiotherapy	Alive at 2 years	Complete remission
Yamamura et al., 1993 [17]	1	72/M	Left hemiparesis	4	1	Parafalcine	Surgery	Died at 12 months	NA
Nicolato et al., 2001 [11]	1	55/M	Left hemianopsia	18	2	Left temporal and right occipital	Surgery + SRS	Alive at 3 years	Complete remission
Ahn et al., 2002 [18]	1	31/F	Headaches, hemiparesis	10	1	Right temporal dural-based	Surgery + Radiation	Alive at 12 months	Complete remission
Chalabreysse et al., 2002 [3]	4	NA	NA	NA	4	NA	NA	NA	NA
Al-Barbarawi et al., 2004 [19]	1	49/M	Headache, hemiparesis, dysphasia	0	2	Left frontal and parietal	Surgery (left frontal only)	Died at 20 days	Progression at 3 days
Tamura et al., 2004 [20]	1	50/M	Headache and scalp mass	0	1	Right occipital bone with extension to intradural and extracranial spaces	Surgery + Chemotherapy	Alive at 6 months	Complete remission
Kong et al., 2005 [6]	6	Average of 48 years/4 M, 2F	Headache, hemiparesis and vomiting	Average for 51	2 multiple, 4 solitary	Cerebral hemispheres, 1 cerebellar, 1 pons	2 with surgery and WBRT; 1 with surgery, WBRT, and SRS; 2 with WBRT only; 1 conservative treatment only	3 died at 2, 7, and 9 months; 3 alive at 2, 2, and 9 months	NA
Ersahin et al., 2007 [10]	1	38/M	Dysphasia, disequilibrium, memory loss	0	>70	NA	None	Died on day 2	NA
Walid et al., 2008 [21]	1	49/F	Headache, SIADH	NA	NA	Right temporal	Surgery	NA	NA
Tsutsumi et al., 2010 [22]	1	39/M	Ophthalmoplegia and visual field deficit	0	1	Extra-axial left middle cranial fossa	Surgery + Chemotherapy	Died at 16 months	NA
Yang et al., 2010 [9]	1	42/M	Headache, vomiting	62	Multiple	Intracranial	Surgery + Radiotherapy + Chemotherapy	Alive at 8 years	Complete remission
Kosty et al., 2016 [23]	1	47/M	Headache, nausea, ataxia	NA	NA	Left cerebellum	Surgery	Alive at 1 year	Complete remission
Sinclair et al., 2017 [12]	1	50/M	Dysphasia	12	6	4 left temporal, 1 left parietal, 1 cerebellar	Surgery + Chemotherapy + hfRS	Alive at 12 months	Progression at 11 months
Kouitcheu et al., 2019 [5]	1	73/F	Headache, nausea, right hemiplegia	4	5	Insular, frontal, right parafalcine and left temporal (x2)	Surgery + SRS	Died at 14 months	Progression at 4 months
Kropf et al., 2019 [24]	1	69/F	Hip pain	0	1	Corpus callosum	Radiotherapy + Chemotherapy	Alive at 14 months	Complete remission
Benitez et al., 2021 [2]	12	NA	Headache or focal neurologic symptoms, such as vertigo and diplopia	Median 9	NA	NA	SRS ± chemotherapy	Median overall survival 22 months	Median progression free survival 14 months
Mitsui et al., 2022 [4]	1	81/F	Gait disturbance, nausea	114	Multiple	Left cerebellum	Surgery + hfRS	Died at 7 months	Progression at 7 months

F female, *GKRS* gamma knife radiosurgery, *Gy* gray, *hfRS* hypofractionated radiosurgery, *LINAC* linear accelerator, *M* male, *NA* not available, *SIADH* syndrome of inappropriate antidiuretic hormone secretion, *SRS* stereotactic radiosurgery, *WBRT* whole brain radiotherapy.

efficacy [7].

Resource efficiency is another notable advantage of hfRS. As an outpatient procedure, it avoids the costs and complications associated with hospitalization and post-operative recovery, making it a pragmatic option in both high- and low-resource settings [14].

This case and the literature review further emphasize the importance of routine surveillance. In the reviewed cases, the mean interval from initial diagnosis to CNS metastasis detection was 25.84 months. In our case, the brain metastasis emerged nearly four years after diagnosis, underscoring the potential for late intracranial dissemination. Notably, the lesion was detected incidentally during routine follow-up imaging, despite the patient having previously undergone chemotherapy, targeted therapy, and thoracic radiotherapy. These findings align with existing reports suggesting that CNS metastases from TC may occur late in the disease course, often after multiple lines of systemic treatment. Given this pattern, current expert consensus recommends regular brain MRI surveillance, ideally at six-month intervals, in high-risk thymic carcinoma patients with advanced-stage disease. Our case reinforces the

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Table 2
Reported cases of TC brain metastases treated with SRS.

Study	Age/sex	Symptoms	Time to brain metastasis, months	Number of metastases	Location	Treatment	SRS modality	Treatment protocol	Outcome	Remission status
Nicolato et al., 2001 [11]	55/M	Left hemianopsia	18	2	Left temporal and right occipital	Surgery + SRS	GKRS	22–23.2 Gy (55–80 % edge isodose)	Alive at 3 years	Complete remission
Kong et al., 2005 [6]	49/F	Hemiparesis	16	Multiple	NA	Surgery + WBRT + SRS	GKRS	NA	Alive at 9 months	NA
Sinclair et al., 2017 [12]	50/M	Progressive expressive dysphasia	12	6	4 left temporal, 1 left parietal, 1 cerebellar	Surgery + Chemotherapy + hfRS	LINAC and GKRS	LINAC 5 × 6 Gy (4 lesions), GKRS 5 × 6 Gy (2 lesions), 19 Gy (50 % edge isodose) (1 lesion)	Alive at 12 months	Progression at 11 months
Kouitcheu et al., 2019 [5]	73/F	Headache, nausea, right hemiplegia	4	5	Left insular, left frontal, right parafalcine and left temporal	Surgery + SRS (twice)	GKRS	22–23 Gy (twice for 2 lesions and once for the rest)	Died at 14 months	Progression at 4 months
Mitsui et al., 2022 [4]	81/F	Gait disturbance, nausea	114	Multiple	Left cerebellum	Surgery + hfRS	NA	5 × 7 Gy	Died at 7 months	Progression at 7 months

F female, *GKRS* gamma knife radiosurgery, *Gy* gray, *hfRS* hypofractionated radiosurgery, *LINAC* linear accelerator, *M* male, *NA* not available, *SRS* stereotactic radiosurgery, *WBRT* whole brain radiotherapy.
Unfortunately, one relevant cohort study of 12 patients was excluded from this table due to lack of treatment details [2].

necessity of adhering to such surveillance protocols to enable early detection and timely intervention.

A key limitation of this case is the absence of direct histological confirmation of the intracranial lesion. However, the diagnosis was supported by robust clinical and radiological evidence, including a known history of metastatic thymic carcinoma, characteristic imaging findings on advanced MRI sequences (such as perfusion and diffusion-weighted imaging), and a newly identified hypermetabolic lesion on PET-CT. Based on these findings, a multidisciplinary tumor board concluded that invasive biopsy or resection was not warranted, and that a non-invasive therapeutic strategy with hfRS would be both safe and effective. Notably, the favorable clinical outcome achieved in the absence of surgical intervention prompts consideration of the underlying factors that may have contributed to treatment success. First, the tumor likely demonstrated intrinsic radiosensitivity, as indicated by its prior favorable response to mediastinal radiotherapy. Second, the patient's history of extensive systemic therapy, including cytotoxic chemotherapy, immunotherapy, and targeted agents, may have exerted a radiosensitizing effect, enhancing the efficacy of hfRS. Additionally, the metastasis exhibited favorable radiological features: it was solitary, moderately sized, and located in a non-eloquent brain region, factors known to correlate with improved stereotactic radiosurgical outcomes. The radiosurgical plan itself was meticulously executed, achieving high target coverage and conformity with an optimal fractionation scheme that minimized the risk of radiation necrosis. While the literature frequently reports the use of 5 × 6 Gy dosing for large brain metastases, including in cases of thymic carcinoma (Table 2), the clinical and radiological profile of this patient favored a slightly reduced dose of 5 × 5 Gy [13]. This regimen, also well-established in the literature for solitary and sizable lesions, was selected to maintain efficacy while limiting unnecessary radiation exposure, particularly in accordance with V24 brain tolerance thresholds (volume of brain tissue receiving more than 24 Gy) [7]. Lastly, the incidental early detection of the lesion during routine surveillance imaging, prior to the development of neurological symptoms or significant mass effect, enabled timely and targeted intervention. Although these hypotheses remain speculative in the absence of histopathological data, they are consistent with established predictors of radiosurgical success. Collectively, this case underscores the potential of hfRS as an effective and resource-efficient monotherapy for select patients with solitary brain metastasis from thymic carcinoma, particularly when used in the context of a multidisciplinary, individualized treatment strategy.

4. Conclusion

Brain metastasis from TC is rare and aggressive, lacking standardized treatment protocols. This case demonstrates that complete and lasting remission can be achieved with Gamma Knife hfRS alone. Given the unpredictable and delayed metastatic potential of TC, neuroimaging should be integral to long-term follow-up. Further research is needed to optimize management strategies for this uncommon yet clinically significant presentation.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Ethical approval

As this is a case report, it is exempt from ethical approval according to our institutional guidelines.

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Declaration of competing interest

The authors declare no competing interests.

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