ORIGINAL ARTICLE Brain Tumor Res Treat 2025;13(2):45-52 / pISSN 2288-2405 / eISSN 2288-2413
https://doi.org/10.14791/btrt.2024.0045

Check for updates

Treatment Outcomes and Prognostic Factors of Intracranial Germ Cell Tumors: A Single Institution Retrospective Study

Eunjong Lee[1], Kihwan Hwang[2], Kyeong-O Go[3], Jung Ho Han[2], Hyoung Soo Choi[4], Yu Jung Kim[5], Byung Se Choi[6], In Ah Kim[7], Gheeyoung Choe[8], Chae-Yong Kim[2]

[1]Department of Neurosurgery, Seoul National University Bundang Hospital, Seongnam, Korea
Departments of [2]Neurosurgery, [4]Pediatrics, [5]Internal Medicine, [6]Radiology, [7]Radiation Oncology, and [8]Pathology, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seoul, Korea
[3]Department of Neurosurgery, Gyeongsang National University Changwon Hospital, Gyeongsang National University College of Medicine, Changwon, Korea

Received December 15, 2024
Revised February 17, 2025
Accepted March 18, 2025

Correspondence
Chae-Yong Kim
Department of Neurosurgery, Seoul National University Bundang Hospital, Seoul National University College of Medicine, Seongnam, Korea
Tel: +82-31-787-7165
Fax: +82-31-787-4097
E-mail: chaeyong@snu.ac.kr

Background This study analyzed the epidemiology and treatment outcomes of germ cell tumor patients at a single institution.

Methods A retrospective analysis was conducted on intracranial germ cell tumor (iGCT) patients treated at a single tertiary hospital from 2004 to 2019. Patients were categorized based on treatment modality: Korean Society for Pediatric Neuro-Oncology (KSPNO) protocol or bleomycin, etoposide, and cisplatin with radiation therapy.

Results Forty-nine iGCT patients treated with combined chemotherapy and radiotherapy were analyzed. The median age was 19 years (range: 6–40), with a median follow-up duration of 148.0 months (range: 10.5–265.5). Tumors were most common in the pineal gland (51.0%). Although no significant differences in outcomes were observed between treatment modalities, outcomes varied significantly by pathological type. The 10-year progression-free survival rates for germinoma and non-germinomatous germ cell tumors (NGGCTs) were 88.1% and 32.7%, respectively (p=0.003), while the 10-year overall survival rates were 92.9% and 67.5%, respectively (p<0.001). Fourteen patients experienced CTCAE (Common Terminology Criteria for Adverse Events) grade ≥3 adverse events, with one event-related death.

Conclusion Pure germinoma demonstrated higher survival and lower recurrence rates compared to NGGCT. The KSPNO protocol appears to be an acceptable and safe treatment option for iGCT patients. Further multi-institutional studies with larger cohorts are warranted.

Keywords Germ cell tumor; Germinoma; Chemotherapy; Radiotherapy; Outcomes.

INTRODUCTION

Intracranial germ cell tumors (iGCTs) are rare neoplasms, comprising approximately 2%−3% of pediatric brain tumors, with germinomas accounting for roughly two-thirds of all iGCTs [1]. They are generally classified into germinomas and non-germinomatous GCTs (NGGCTs) [2-4]. Germinomas are highly curable with multimodal treatment approaches, whereas NGGCTs typically exhibit less favorable prognoses and survival outcomes [2,4,5]. Notably, the 10-year overall survival (OS) of intracranial and central nervous system (CNS) germinoma is approximately 90% [2,6-8]. Standard treatment for iGCTs includes surgery, chemotherapy, and radiation therapy, all aimed at reducing tumor burden while minimizing long-term toxic effects [2,5,8,9]. The roles of these treatments differ according to tumor classification. In cases of germinoma, radiation therapy has traditionally been considered a cornerstone of treatment. Although craniospinal irradiation (CSI) has been used, efforts have been made to reduce the radiation

field to minimize long-term sequelae [10-13]. Moreover, local radiation therapy alone has been associated with a higher risk of recurrence, which has led to the adoption of whole ventricular irradiation (WVI) as the standard approach. For NGGCTs, the 10-year OS rate remains significantly lower compared with that of germinomas, even when aggressive chemotherapy and high-dose radiotherapy are employed [1,14]. Given that a higher dose of radiation is required for NGGCTs than for germinomas, debate persists as to whether WVI could replace CSI to reduce radiation-related toxicity.

Radiation-induced complications following treatment are often unavoidable, prompting numerous researchers to explore strategies that reduce radiation doses while enhancing the role of chemotherapy to minimize adverse effects [2,9,12,15,16]. The Korean Society of Pediatric Neuro-Oncology (KSPNO) was first launched in 2005 to standardize treatment approaches and improve survival outcomes of iGCTs. The representative clinical trials include the KSPNO G051/G081 protocols for germinoma and the KSPNO G052/G082 protocols for NGGCTs (Table 1) [17]. The G051 protocol was designed to compare the efficacy of low-dose CSI alone versus upfront chemotherapy followed by reduced dose and volume radiation therapy. However, due to poor patient accrual, it was modified in 2008 to the KSPNO G081 protocol, which emphasized upfront chemotherapy followed by reduced-dose radiation therapy (Table 2) [17]. Subsequently, the KSPNO G082 protocol was integrated to refine this approach, ultimately unifying the G081/G082 protocols to optimize outcomes for iGCTs while removing CSI alone as treatment option. The primary objective of the KSPNO protocol was to achieve maximum tumor control while reducing the treatment-related toxicity, thereby maximizing cure rates and improving survivor's quality of life [17]. In 2009, our institute adopted these KSPNO G081/G082 clinical trial protocol for patients with iGCTs.

This study aimed to analyze the OS and progression-free survival (PFS) of patients with iGCTs treated at our institution. Additionally, we sought to identify factors influencing these outcomes. Through this analysis, we have evaluated the efficacy and safety of the new protocol, thereby contributing to the ongoing refinement of treatment strategies for iGCTs.

Table 1. Chemotherapy regimen for KSPNO protocol (A/B/A/B, total 4 courses every 3 weeks, alternating)

	Germinoma	NGGCT
Course A		
Carboplatin	450 mg/m^2 D1	450 mg/m^2 D1−2
Etoposide	150 mg/m^2 D1−3	150 mg/m^2 D1−3
Bleomycin	-	15 mg/m^2 D3
Course B		
Cyclophosphamide	1,000 mg/m^2 D1−2	2,000 mg/m^2 D1−2
Etoposide	150 mg/m^2 D1−3	150 mg/m^2 D1−3
Bleomycin	-	15 mg/m^2 D3

KSPNO, Korean Society for Pediatric Neuro-Oncology; NGGCT, non-germinomatous germ cell tumor. Adpated from Han et al. Clin Pediatr Hematol Oncol 2016;23:17-27 [17], based on Creative Commons License (CC-BY-NC).

MATERIALS AND METHODS

A comprehensive review of electronic medical records was conducted at Seoul National University Bundang Hospital (SNUBH)—a tertiary care center—to identify all histologically and clinically diagnosed GCTs from 2004 through 2019. Among 6,394 patients with intracranial tumors, 61 (0.95%) were diagnosed with iGCTs. After we excluded patients with incomplete medical records (n=2), those lost to follow-up (n=2), and those treated with a single treatment modality (n=8), 49 patients were included in the final analysis.

Most patients (n=38) had histologically confirmed diagnoses. For patients in whom tissue biopsy was challenging due to the tumor location, clinical diagnoses were made based on elevated tumor markers (beta-human chorionic gonadotropin levels in the serum or cerebrospinal fluid >50 mU/mL, serum alpha-fetoprotein levels >10 ng/mL, or cerebrospinal fluid serum alpha-fetoprotein levels >2.0 ng/mL) accompanied by

Table 2. Radiotherapy plan for KSPNO G081 and G082

Classification	Response to chemotherapy	CSRT (Gy)	LFRT (Gy)	Total (Gy)
KSPNO G081				
Solitary	CR	0	30.6	30.6
	<CR	19.5	19.8	39.3
Multiple or disseminated	CR	19.5	10.8	30.3
	<CR	24	16.2	40.2
KSPNO G082				
Localized		36	18−23.4	54−59.4
Disseminated		39	14.4−19.8	53.4−58.5

KSPNO, Korean Society for Pediatric Neuro-Oncology; CR, complete remission; CSRT, craniospinal irradiation; LFRT, local field irradiation. Adpated from Han et al. Clin Pediatr Hematol Oncol 2016;23:17-27 [17], based on Creative Commons License (CC-BY-NC).

characteristic radiological features.

The primary outcome was OS, defined as the interval from the date of diagnosis, whether diagnosed pathologically or clinically, to the date of death or last follow-up. Clinically diagnosed patients were assigned a diagnosis date based on either the date of reported serologic test results or the date of radiologic test. The secondary outcome, PFS, was defined as the period from the date of diagnosis to the date of disease progression, as confirmed by follow-up MRI. For patients with no evidence of progression, OS and PFS were considered equivalent. Significant adverse events during chemotherapy were defined as grade 3 or higher according to the Common Terminology Criteria for Adverse Events (CTCAE) version 5.0 [18]. Statistical analyses were performed using logistic regression and Kaplan−Meier survival analysis. All analyses were conducted using SPSS Statistics for Windows, version 21 (IBM Corp.).

Patients with pure germinoma were treated according to the KSPNO G081 protocol, while those with NGGCTs received treatment based on the KSPNO G082 protocol. For patients with solitary tumors, the treatment regimen consisted of chemotherapy combined with radiation therapy. Local radiation therapy was performed without CSI if a complete response was observed. CSI was applied to all cases of multiple or disseminated tumors, and a lower dose was applied to achieve complete remission (CR).

Prior to the implementation of the KSPNO protocols, the BEP (bleomycin, etoposide, and cisplatin) regimen was used for the treatment of both middle-aged adult and pediatric patients. The BEP regimen administered every 3 weeks (21 days) for a total of 4 cycles, along with pegfilgrastim (filgrastim), with dosages and schedules adjusted based on patient age and risk factors.

Ethics statements

All procedures performed in studies involving human participants were in accordance with the ethical standards of the Seoul National University Bundang Hospital research committee (IRB No. B-1106-129-803) and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. This study was performed retrospectively; consequently, the need for informed consent was waived.

RESULTS

We analyzed 49 consecutive patients with iGCTs; their characteristics are summarized in Table 3. The median follow-up duration was 148.0 months (range: 10.5−265.5). Patients were predominantly male (male-to-female ratio=6:1), with a median age of 19 years (range: 6−40). The pineal region was the most common tumor location (51.0%, n=25). Germinomas were diagnosed in 34 patients (69.4%) and NGGCTs were diagnosed in 15 patients (30.6%). Histological confirmation was obtained in 82.3% (28/34) of germinoma patients and 66.7% (10/15) of NGGCT cases. The detailed distribution of tumor types, including subtypes of NGGCTs, and their allocation between KSPNO and other treatment protocols are presented in Table 4.

Treatment outcomes and survival analysis

Twenty-three patients (46.9%) were treated according to the KSPNO protocol. The median CSI dose with boost was 52.2 Gy, while the median whole-brain or ventricle radiation dose was 39.6 Gy. Within the CSI field, NGGCTs received a significantly higher median radiation dose (33.3 Gy) than germinomas (23.7 Gy; p=0.008). Total radiation doses did not differ significantly between the KSPNO group (median 50.4 Gy) and other protocol groups (median 47.7 Gy; p=0.476).

Kaplan−Meier survival curves for PFS and OS are presented in Figs. 1 and 2. The mean PFS was 140.5 months (range: 1.2−265.5) and the mean OS was 134.6 months (range: 10.5−265.5). Nine patients (18.4%) experienced disease recurrence post-treatment. The KSPNO protocol group demonstrated a lower, albeit not statistically significant, recurrence rate compared to other treatment groups (17.4% vs. 19.2%, p=0.868). Pathological subtype analysis revealed significantly improved PFS in the germinoma group compared to the NGGCT group (10-year PFS: 88.1% vs. 32.7%, p=0.003).

Forty-three patients (87.8%) survived throughout the follow-up period. Although no significant OS differences were observed between treatment protocols, a significant difference was noted between pathological subtypes (10-year OS for germinoma vs. NGGCT: 92.9% vs. 67.5%, p<0.001). Among the 49 patients, six deaths occurred during the observation period; disease progression accounted for five deaths, while one patient died of septic shock.

Morbidity and adverse events

Post-treatment morbidity persisted in 39 patients (79.6%). The most prevalent sequelae were hormonal disturbances requiring replacement therapy (53.8%, n=21), followed by visual disturbances (33.3%, n=13), cognitive dysfunction (15.4%, n=6), and hydrocephalus necessitating shunt operation (10.3%, n=4).

Adverse events of CTCAE grade 3 or higher were observed in 14 patients (28.6%) (Table 5). Blood and lymphatic system disorders, primarily manifesting as neutropenic fever, were the most frequent, occurring in 12 patients. Single cases of musculocutaneous, respiratory, renal, and nervous system complications were also reported. The musculocutaneous and renal

Table 3. Basic characteristics of study participants by treatment protocol

Protocol	Total (n=49)	KSPNO (n=23)	Others (n=26)	*p*-value
Sex, M:F	42:7	21:2	21:5	0.424
Age (yr)	19.0 (6–40)	16.0 (6–24)	20.5 (7–40)	0.005**
Tumor location				
Pineal gland	25 (51.0)	14 (60.1)	11 (42.3)	
Sellar & supra sellar	5 (10.2)	2 (8.7)	3 (11.5)	
Cerebrum	1 (2.0)	0	1 (3.8)	
Intraventricular	2 (4.1)	0	2 (7.7)	
Thalamostriate	1 (2.0)	1 (4.3)	0	
Disseminate	3 (6.1)	2 (8.7)	1 (3.8)	
Multifocal	11 (22.4)	4 (17.4)	7 (26.9)	
Others	1 (2.0)	0	1 (3.8)	
Pathological type				0.224
Germinoma	34 (69.4)	14 (60.9)	20 (76.9)	
NGGCT	15 (30.6)	9 (39.1)	6 (23.1)	
Total radiation dose (Gy)	50.4 (30.3–59.4)	50.4 (30.3–54)	47.7 (35–59.4)	0.476
Radiation therapy (n, median dose)				
CSI+local boost	34 (52.2 Gy)	17 (54.0 Gy)	17 (50.4 Gy)	
WBRT or WVI	9 (39.6 Gy)	3 (30.6 Gy)	6 (45.0 Gy)	
WBRT or WVI+local boost	6 (45.0 Gy)	3 (45.0 Gy)	3 (45.0 Gy)	
Follow-up (month)	148.0 (10.5–265.5)	131.0 (10.5–234.6)	166.4 (14.6–265.5)	
Mean PFS (month)	140.5	128.6	161.8	0.869
Mean OS (month)	134.6	102.1	160.0	0.869
Recurrence	9 (18.4)	4 (17.4)	5 (19.2)	0.868
Mortality	6 (12.2)	2 (8.7)	4 (15.4)	0.476
Comorbidity	39 (79.6)	18 (78.2)	21 (80.8)	0.553
Hormonal disturbance	21	8	13	
Visual disturbance	13	6	7	
Cognitive dysfunction	6	4	2	
Hydrocephalus	4	2	2	
Etc.	9	5	4	

Values are presented as median (range), number (%), or number only, unless otherwise indicated. **p<0.01. KSPNO, The Korean Society of Pediatric Neuro-Oncology; NGGCT, non-germinomatous germ cell tumor; CSI, craniospinal irradiation; WBRT, whole brain radiotherapy; WVI, whole ventricular irradiation

system complications coincided with blood and lymphatic system disorders in the affected patients.

DISCUSSION

CNS GCTs exhibit a bimodal age distribution, with a higher prevalence among children and adolescents (particularly among Eastern population), who account for 2%–3% of all primary intracranial tumors [1,4,19-21]. These tumors are highly radiosensitive and potentially curable, with radiotherapy alone yielding cure rates of 72%–100% [8,22-26]. Management of CNS GCTs may require neurosurgical interventions, such as tumor debulking or biopsy for pathological confirmation, as well as treatment of tumor-related hydrocephalus. The complexity of CNS GCT management necessitates a multidisciplinary approach. However, patients admitted to institutions without an established multidisciplinary team may receive varying treatment protocols depending on the admitting department. This inconsistency highlights the importance of standardized, collaborative care for CNS GCT patients.

The KSPNO introduced the KSPNO-G081/G082 protocol in 2009. Since its implementation, this protocol has been applied to patients diagnosed at Seoul National University Bundang Hospital. The cohort of patients treated under the KSPNO protocol comprises consecutively diagnosed individuals, forming a relatively homogeneous group. The treatment process is coordinated among departments through outpatient clinics and institutional conferences, employing a multidisciplinary approach. In this study, the authors compared and analyzed the KSPNO protocol group with other protocol groups by us-

Table 4. Distribution of tumors by pathological type

	Total (n=49)	KSPNO (n=23)	Others (n=26)
Germinoma	34 (69.4)	14 (60.9)	20 (76.9)
NGGCT	15 (30.6)	9 (39.1)	6 (23.1)
Mature teratoma	2 (4.1)	0 (0)	2 (7.7)
Mixed GCT	6 (12.2)	5 (21.7)	1 (3.8)
Choriocarcinoma	3 (6.1)	1 (4.3)	2 (7.7)
Immature teratoma	1 (2.0)	1 (4.3)	0 (0)
NOS	3 (6.1)	2 (8.7)	1 (3.8)

Values are presented as number (%). KSPNO, The Korean Society of Pediatric Neuro-Oncology; NGGCT, non-germinomatous germ cell tumor; GCT, germ cell tumor; NOS, not otherwise specified

ing shared clinical information across departments. This study was significant for its efforts to validate the effectiveness and safety of the KSPNO protocol.

In recent decades, radiation doses applied to primary sites for CNS germinomas have typically exceeded 50 Gy [14,27]. However, the histological similarities among CNS germinoma, testicular seminoma, and ovarian dysgerminoma suggest that CNS germinoma might be effectively treated with lower doses of 25–30 Gy, which are standard for these related tumors [25]. This hypothesis is further supported by a case report by Sung et al. [28] documenting CR at autopsy of a pure CNS germinoma treated with 16 Gy of radiation. Moreover, some studies have demonstrated that radiation doses can be reduced

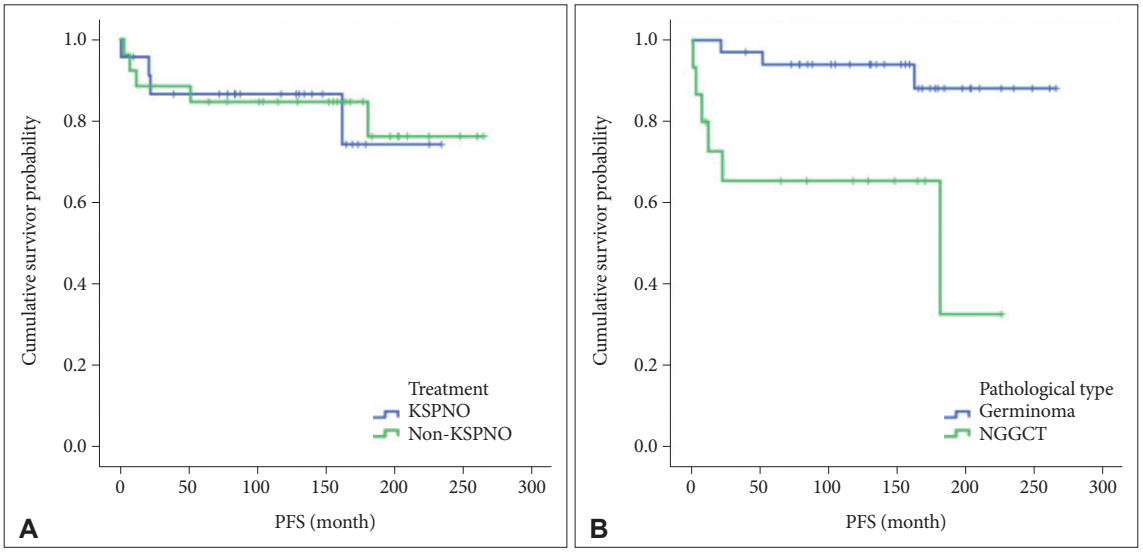

Fig. 1. Kaplan-Meier survival curves for PFS stratified by treatment protocol (A) and pathological type (B). PFS, progression-free survival; KSPNO, Korean Society of Pediatric Neuro-Oncology; NGGCT, non-germinomatous germ cell tumor.

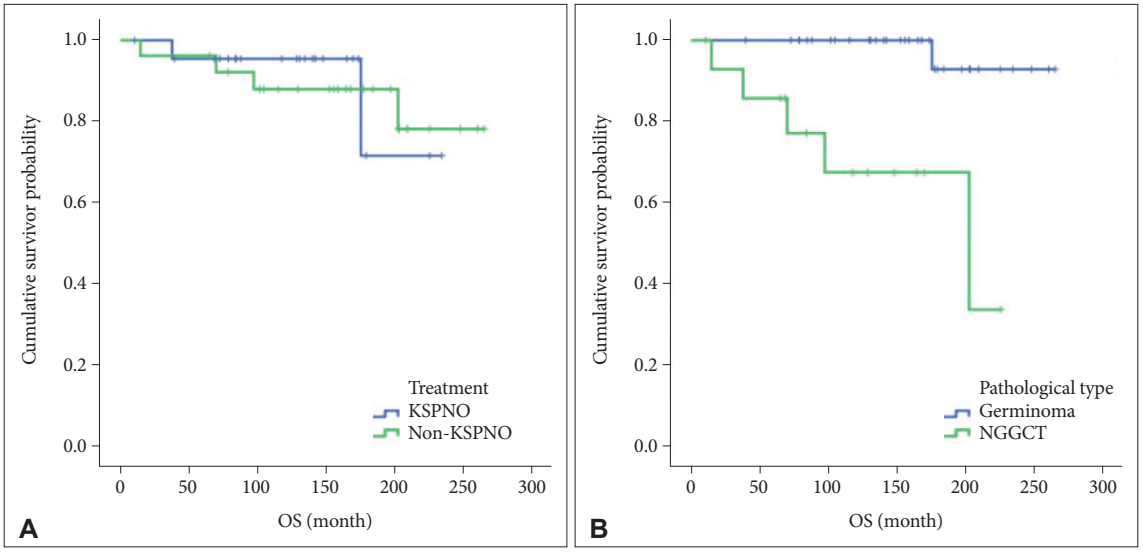

Fig. 2. Kaplan-Meier survival curves for OS stratified by treatment protocol (A) and pathological type (B). OS, overall survival; KSPNO, Korean Society of Pediatric Neuro-Oncology; NGGCT, non-germinomatous germ cell tumor.

Table 5. Adverse events observed during treatment

	CTCAE (v5.0) grade ≥3			
	Total (n=49)	KSPNO (n=23)	Others (n=26)	*p*-value
Total, n (%)	16 (32.7)	12 (52.1)	4 (15.4)	0.124
Blood & lymphatic system	12	9	3	
Musculocutaneous	1	1*	0	
Respiratory	1	1	0	
Renal & Urinary	1	1†	0	
Nervous system	1	0	1	

*†Overlap with blood & lymphatic system, respectively. CTCAE, Common Terminology Criteria for Adverse Events; KSPNO, Korean Society of Pediatric Neuro-Oncology

to below 36 Gy in WVI without pre-irradiation chemotherapy while preserving treatment efficacy [7,29].

A previous study showed that radiotherapy alone is associated with a risk of new CNS relapse [30]. Despite this concern, CNS germinomas generally have a favorable prognosis, with studies reporting a 10-year OS rate of approximately 90%, which aligns with the findings of the present study [2]. While radiation therapy is a cornerstone of treatment for CNS germinomas, it has long-term risks. Radiation-induced secondary brain tumors and subsequent malignant neoplasms, although rare, have been documented in the literature [6,26,31,32]. The cumulative risk of developing brain tumors 15 years following cranial irradiation has been estimated at 2.7% [6].

CNS germinomas are highly sensitive to both radiation and chemotherapy. Platinum-based chemotherapy has been shown to reduce late complications associated with radiation therapy while allowing for a reduction in therapeutic radiation doses to 24−30 Gy without compromising treatment efficacy [2,9,12,15,16]. However, some studies have reported treatment failures when radiation fields were limited to the localized germinoma site rather than encompassing the whole ventricular system [10,33-35].

The KSPNO protocol employs neoadjuvant chemotherapy to maintain therapeutic efficacy while allowing for reduced radiation doses. Recent consensus suggests that radiation fields should encompass at least the whole ventricular system to minimize the risk of local germinoma recurrence [2]. As previously mentioned, several studies have investigated the use of chemotherapy and combination therapy to determine the necessity of CSI based on treatment response. These approaches aim to reduce the final radiation dose and mitigate long-term radiation-related complications [35-39].

A significant proportion of germinomas occur in the pineal, sellar, and suprasellar regions. Therefore, it is crucial to reduce nephrotoxicity, as patients often experience diabetes insipidus prior to treatment. The KSPNO protocol replaces cisplatin used in traditional regimens with carboplatin, potentially reducing nephrotoxicity relative to conventional therapy. However, cyclophosphamide—also included in the protocol—carries a risk of urotoxicity. To mitigate this risk, MESNA (sodium 2-mercaptoethanol sulfonate) is added to the regimen [37,40]. In the KSPNO group, only one instance of a CTCAE grade 3 or higher adverse event affecting the renal system was reported. This patient was hospitalized with gross hematuria—suspected to be hemorrhagic cystitis induced by cyclophosphamide—after completing KSPNO G082 1B. The patient was discharged after 10 days of inpatient treatment. Although patients in the KSPNO group experienced a higher incidence of adverse events, the associated mortality was notably lower. This outcome underscores the overall acceptability of the protocol as a treatment option, balancing efficacy with manageable toxicity.

The therapeutic effect of CSI in germinoma treatment is controversial. The benefit of CSI for patients diagnosed with germinoma has been reported to be approximately 15% [11]. Relapses along the neuroaxis outside the radiation field are uncommon, and the improvements in outcomes with CSI are not substantial [41]. In our study, patients with germinoma who received CSI had a mean PFS of 157.4 months, which was significantly higher than the 146.7 months for those who did not receive CSI (p=0.017). However, the morbidity rate in the CSI group (n=19/22, 86.4%) was higher than that among the patients who underwent irradiation to other sites (n=8/12, 66.7%), although this difference did not reach statistical significance (p=0.221).

These findings highlight the complex risk-benefit profile of CSI in germinoma treatment. While CSI may offer a modest improvement in PFS, it is associated with a trend towards increased morbidity. This underscores the importance of carefully weighing the potential benefits of CSI against its associated risks when determining the optimal treatment strategy for patients with intracranial germinoma. The decision to use CSI should be individualized based on factors such as disease extent, patient age, and potential long-term complications. Further research is needed to identify subgroups of patients who may derive the greatest benefit from CSI while minimizing treatment-related morbidity.

This study did not demonstrate the therapeutic superiority of the KSPNO protocol. Several limitations should be considered when interpreting these results. First, a substantial proportion of patients (47.8%, n=11) in the KSPNO group were classified as high risk, presenting with leptomeningeal seeding or elevated tumor markers. Additionally, the median age at diagnosis in the KSPNO group (16 years) was younger than that in the other group (20.5 years, p=0.005), potentially in-

fluencing the adoption of more aggressive treatment plans. Moreover, due to the rarity of the disease, the group size may not have been sufficient to elucidate statistically significant differences between treatment protocols. These factors collectively impact the interpretation of the study results and highlight the challenges in comparing treatment outcomes for rare diseases like intracranial germinomas.

Pathological type is a significant prognostic factor in CNS GCTs. The comparison of the KSPNO protocol with other treatment protocols for iGCTs at a single tertiary institution did not demonstrate its superiority, likely due to a high proportion of high-risk patients, patients being diagnosed at a young age, and the limited sample size.

Nevertheless, the KSPNO protocol remains significant, as it not only establishes a unified treatment approach for CNS GCTs but also demonstrates an acceptable safety profile. Future studies should be designed with larger cohorts, longer follow-up periods, and enhanced risk stratification to better evaluate the protocol's long-term efficacy and safety.

Availability of Data and Material

Due to privacy and ethical concerns, neither the data nor the source of the data can be made available.

ORCID iDs

Eunjong Lee https://orcid.org/0009-0009-5905-8737
Kihwan Hwang https://orcid.org/0000-0001-7211-729X
Kyeong-O Go https://orcid.org/0000-0003-3515-3771
Jung Ho Han https://orcid.org/0000-0003-1748-6898
Hyoung Soo Choi https://orcid.org/0000-0002-4837-164X
Yu Jung Kim https://orcid.org/0000-0002-5037-0523
Byung Se Choi https://orcid.org/0000-0001-6310-1798
In Ah Kim https://orcid.org/0000-0001-9838-5399
Gheeyoung Choe https://orcid.org/0000-0001-6547-5603
Chae-Yong Kim https://orcid.org/0000-0001-9773-5553

Author Contributions

Conceptualization: Eunjong Lee, Kihwan Hwang, Kyeong-O Go, Chae-Yong Kim. Data curation: Eunjong Lee, Kyeong-O Go, Chae-Yong Kim. Formal analysis: Eunjong Lee, Kyeong-O Go. Funding acquisition: Kihwan Hwang. Investigation: Eunjong Lee, Kyeong-O Go. Methodology: Kihwan Hwang, Hyoung Soo Choi, Yu Jung Kim, Byung Se Choi, In Ah Kim, Gheeyoung Choe. Project administration: Kihwan Hwang. Resources: Eunjong Lee, Kyeong-O Go. Software: Eunjong Lee, Kyeong-O Go. Supervision: Kihwan Hwang, Jung Ho Han, Chae-Yong Kim. Validation: Eunjong Lee, Kyeong-O Go. Visualization: Eunjong Lee, Kyeong-O Go. Writing—original draft: Eunjong Lee, Kyeong-O Go. Writing—review & editing: Kihwan Hwang, Jung Ho Han, Hyoung Soo Choi, Yu Jung Kim, Byung Se Choi, In Ah Kim, Gheeyoung Choe, Chae-Yong Kim.

Conflicts of Interest

Hyoung Soo Choi and Chae-Yong Kim, contributing editors of *Brain Tumor Research and Treatment*, were not involved in the editorial evaluation or decision to publish this article. All remaining authors have declared no conflicts of interest.

Funding Statement

None

Acknowledgments

None

REFERENCES

1. Brain Tumor Registry of Japan. Brain Tumor Registry of Japan (2005-2008). Neurol Med Chir (Tokyo) 2017;57(Suppl 1):9-102.
2. Kamoshima Y, Sawamura Y. Update on current standard treatments in central nervous system germ cell tumors. Curr Opin Neurol 2010;23:571-5.
3. Lee D, Suh YL. Histologically confirmed intracranial germ cell tumors; an analysis of 62 patients in a single institute. Virchows Arch 2010;457:347-57.
4. Matsutani M, Sano K, Takakura K, Fujimaki T, Nakamura O, Funata N, et al. Primary intracranial germ cell tumors: a clinical analysis of 153 histologically verified cases. J Neurosurg 1997;86:446-55.
5. Kellie SJ, Boyce H, Dunkel IJ, Diez B, Rosenblum M, Brualdi L, et al. Primary chemotherapy for intracranial nongerminomatous germ cell tumors: results of the second international CNS germ cell study group protocol. J Clin Oncol 2004;22:846-53.
6. Acharya S, DeWees T, Shinohara ET, Perkins SM. Long-term outcomes and late effects for childhood and young adulthood intracranial germinomas. Neuro Oncol 2015;17:741-6.
7. Chen YW, Huang PI, Ho DM, Hu YW, Chang KP, Chiou SH, et al. Change in treatment strategy for intracranial germinoma: long-term follow-up experience at a single institute. Cancer 2012;118:2752-62.
8. Ogawa K, Shikama N, Toita T, Nakamura K, Uno T, Onishi H, et al. Long-term results of radiotherapy for intracranial germinoma: a multi-institutional retrospective review of 126 patients. Int J Radiat Oncol Biol Phys 2004;58:705-13.
9. Aoyama H, Shirato H, Ikeda J, Fujieda K, Miyasaka K, Sawamura Y. Induction chemotherapy followed by low-dose involved-field radiotherapy for intracranial germ cell tumors. J Clin Oncol 2002;20:857-65.
10. Douglas JG, Rockhill JK, Olson JM, Ellenbogen RG, Geyer JR. Cisplatin-based chemotherapy followed by focal, reduced-dose irradiation for pediatric primary central nervous system germinomas. J Pediatr Hematol Oncol 2006;28:36-9.
11. Linstadt D, Wara WM, Edwards MS, Hudgins RJ, Sheline GE. Radiotherapy of primary intracranial germinomas: the case against routine craniospinal irradiation. Int J Radiat Oncol Biol Phys 1988;15:291-7.
12. Sawamura Y, Shirato H, Ikeda J, Tada M, Ishii N, Kato T, et al. Induction chemotherapy followed by reduced-volume radiation therapy for newly diagnosed central nervous system germinoma. J Neurosurg 1998;88:66-72.
13. Yen SH, Chen YW, Huang PI, Wong TT, Ho DM, Chang KP, et al. Optimal treatment for intracranial germinoma: can we lower radiation dose without chemotherapy? Int J Radiat Oncol Biol Phys 2010;77:980-7.
14. Abay EO 2nd, Laws ER Jr, Grado GL, Bruckman JE, Forbes GS, Gomez MR, et al. Pineal tumors in children and adolescents. Treatment by CSF shunting and radiotherapy. J Neurosurg 1981;55:889-95.
15. Fouladi M, Grant R, Baruchel S, Chan H, Malkin D, Weitzman S, et al. Comparison of survival outcomes in patients with intracranial germinomas treated with radiation alone versus reduced-dose radiation and chemotherapy. Childs Nerv Syst 1998;14:596-601.
16. Sawamura Y, de Tribolet N, Ishii N, Abe H. Management of primary intracranial germinomas: diagnostic surgery or radical resection? J Neurosurg 1997;87:262-6.
17. Han JW, Koh KN, Kim JY, Baek HJ, Lee JW, Shim KY, et al. [Current trends in management for central nervous system germ cell tumor]. Clin Pediatr Hematol Oncol 2016;23:17-27. Korean
18. National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE) v5.0 [Internet]. Bethesda: National Cancer Institute, 2017. (Accessed February 5, 2024, at https://ctep.cancer.gov/protocoldevelopment/electronic_applications/ctc.htm.)
19. Dho YS, Jung KW, Ha J, Seo Y, Park CK, Won YJ, et al. An updated na-

tionwide epidemiology of primary brain tumors in Republic of Korea, 2013. Brain Tumor Res Treat 2017;5:16-23.
20. Ho DM, Liu HC. Primary intracranial germ cell tumor. Pathologic study of 51 patients. Cancer 1992;70:1577-84.
21. Suh YL, Koo H, Kim TS, Chi JG, Park SH, Khang SK, et al. Tumors of the central nervous system in Korea: a multicenter study of 3221 cases. J Neurooncol 2002;56:251-9.
22. Rich TA, Cassady JR, Strand RD, Winston KR. Radiation therapy for pineal and suprasellar germ cell tumors. Cancer 1985;55:932-40.
23. Shibamoto Y, Sasai K, Oya N, Hiraoka M. Intracranial germinoma: radiation therapy with tumor volume-based dose selection. Radiology 2001;218:452-6.
24. Wara WM, Fellows CF, Sheline GE, Wilson CB, Townsend JJ. Radiation therapy for pineal tumors and suprasellar germinomas. Radiology 1977;124:221-3.
25. Wara WM, Jenkin RD, Evans A, Ertel I, Hittle R, Ortega J, et al. Tumors of the pineal and suprasellar region: Childrens Cancer Study Group treatment results 1960--1975: a report from Childrens Cancer Study Group. Cancer 1979;43:698-701.
26. You SH, Lyu CJ, Kim DS, Suh CO. Second primary brain tumors following cranial irradiation for pediatric solid brain tumors. Childs Nerv Syst 2013;29:1865-70.
27. Huh SJ, Shin KH, Kim IH, Ahn YC, Ha SW, Park CI. Radiotherapy of intracranial germinomas. Radiother Oncol 1996;38:19-23.
28. Sung DI, Harisiadis L, Chang CH. Midline pineal tumors and suprasellar germinomas: highly curable by irradiation. Radiology 1978;128:745-51.
29. Lavey RS, Olch AJ. Optimal treatment for intracranial germinoma: can we lower, radiation dose without chemotherapy? In regard to Yen S-H et al. (Int J Radiat Oncol Biol Phys Epub October 27, 2009). Int J Radiat Oncol Biol Phys 2010;77:638-9.
30. Aoyama H, Shirato H, Kakuto Y, Inakoshi H, Nishio M, Yoshida H, et al. Pathologically-proven intracranial germinoma treated with radiation therapy. Radiother Oncol 1998;47:201-5.
31. Hwang K, Lee KS, Choe G, Cho BG, Kim CY. Secondary glioblastoma after treatment of intracranial germinoma - would radiation-only therapy still be safe? Case report. BMC Cancer 2018;18:1119.
32. Nishio S, Morioka T, Inamura T, Takeshita I, Fukui M, Sasaki M, et al. Radiation-induced brain tumours: potential late complications of radiation therapy for brain tumours. Acta Neurochir (Wien) 1998;140:763-70.
33. Nguyen QN, Chang EL, Allen PK, Maor MH, Ater JL, Mahajan A, et al. Focal and craniospinal irradiation for patients with intracranial germinoma and patterns of failure. Cancer 2006;107:2228-36.
34. Shim KW, Kim TG, Suh CO, Cho JH, Yoo CJ, Choi JU, et al. Treatment failure in intracranial primary germinomas. Childs Nerv Syst 2007;23:1155-61.
35. Finlay J, da Silva NS, Lavey R, Bouffet E, Kellie SJ, Shaw E, et al. The management of patients with primary central nervous system (CNS) germinoma: current controversies requiring resolution. Pediatr Blood Cancer 2008;51:313-6.
36. Jensen AW, Laack NN, Buckner JC, Schomberg PJ, Wetmore CJ, Brown PD. Long-term follow-up of dose-adapted and reduced-field radiotherapy with or without chemotherapy for central nervous system germinoma. Int J Radiat Oncol Biol Phys 2010;77:1449-56.
37. Lee DS, Lim DH, Kim IH, Kim JY, Han JW, Yoo KH, et al. Upfront chemotherapy followed by response adaptive radiotherapy for intracranial germinoma: prospective multicenter cohort study. Radiother Oncol 2019;138:180-6.
38. Raggi E, Mosleh-Shirazi MA, Saran FH. An evaluation of conformal and intensity-modulated radiotherapy in whole ventricular radiotherapy for localised primary intracranial germinomas. Clin Oncol (R Coll Radiol) 2008;20:253-60.
39. Rogers SJ, Mosleh-Shirazi MA, Saran FH. Radiotherapy of localised intracranial germinoma: time to sever historical ties? Lancet Oncol 2005;6:509-19.
40. Shim KW, Park EK, Lee YH, Suh CO, Cho J, Choi JU, et al. Treatment strategy for intracranial primary pure germinoma. Childs Nerv Syst 2013;29:239-48.
41. Fuller BG, Kapp DS, Cox R. Radiation therapy of pineal region tumors: 25 new cases and a review of 208 previously reported cases. Int J Radiat Oncol Biol Phys 1994;28:229-45.