

Tumor control of third ventricular central neurocytoma after gamma knife radiosurgery in an elderly patient

A case report and literature review

Sue-Jee Park, MD^a, Tae-Young Jung, MD^{a,*}, Seul-Kee Kim, MD^b, Kyung-Hwa Lee, MD^c

Abstract

Rationale: Central neurocytoma is rare benign tumor that occurs in high probability in young adults in the lateral ventricle. Herein, we report an unusual case of an elderly woman who was diagnosed with central neurocytoma isolated to the third ventricle. This deeply located tumor was effectively treated using gamma knife radiosurgery (GKR).

Patient concerns: A 79-year-old woman was admitted to hospital with gait disturbance and cognitive dysfunction.

Diagnosis: Brain magnetic resonance imaging (MRI) revealed a homogeneously enhancing multilobulated mass in the posterior third ventricle measuring 1.8 cm in size. The tumor was diagnosed as a central neurocytoma isolated to the third ventricle.

Interventions: Neuronavigation-guided endoscopic third ventriculostomy and biopsy were performed. One week following surgery, GKR was performed using a prescribed dose of 14 Gy with 50% isodose lines, and a target volume of 1.62 cc.

Outcomes: Three months after GKR, brain MRI revealed a decrease in the size (to 1.4 cm) of the multilobulated strong enhancing mass in the posterior third ventricle, and the patient's symptom of confusion was improved.

Lessons: Previous studies have reported that tumors in unusual locations, such as those isolated to the third ventricle, are different according to age, either in young children or elderly individuals. Although complete surgical resection is an effective treatment for central neurocytoma, it is often difficult to approach these tumors through surgery. GKR could, therefore, be an alternative primary treatment option for deeply located central neurocytomas in elderly patients.

Abbreviations: Bx = biopsy, ETV = endoscopic third ventriculostomy, GKR = gamma knife radiosurgery, MRI = magnetic resonance imaging, STR = subtotal resection.

Keywords: central neurocytoma, elderly, stereotactic radiosurgery, ventriculostomy

1. Introduction

Central neurocytomas are rare brain tumors, which represent only 0.25% to 0.5% of all intracranial tumors.^[1] The first case

Editor: N/A.

The authors declare that they have no competing interests, and manuscript is approved by all authors for publication. The author would like to declare on behalf of his co-authors that the work described was original research that has not been published previously, and not under consideration for publication elsewhere, in whole or in part.

This study was supported by the Basic Science Research Program through the National Research Foundation of Korea (NRF), funded by the Ministry of Science, ICT, & Future Planning (2017R1A1A1A05001020).

The authors have no conflicts of interest to disclose.

^a Department of Neurosurgery, ^b Radiology, ^c Pathology, Chonnam National University Medical School, Chonnam National University Hospital and Chonnam National University Hwasun Hospital, Gwangju, Republic of Korea.

* Correspondence: Tae-Young Jung, Department of Neurosurgery, Chonnam National University Hwasun Hospital, 160, IIsim-ri, Hwasun-eup, Hwasun-gun, Jeollanam-do, 519-809, Republic of Korea (e-mail: jung-ty@chonnam.ac.kr).

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Medicine (2018) 97:50(e13657)

Received: 6 July 2018 / Accepted: 20 November 2018

<http://dx.doi.org/10.1097/MD.0000000000013657>

was reported by Hassoun and colleagues in 1982.^[2] With non-aggressive characteristics that generally do not recur after total surgical resection, they are usually considered benign and are classified as grade II tumors by the World Health Organization.

These tumors are typically encountered in young adult patients (average age, 28.5 years), with equal distribution between the sexes.^[3] Moreover, they are found in intraventricular locations along the septum pellucidum. The most common site is the lateral ventricle near the foramen of Monro, with a predilection for the left anterior horn.^[1] These tumors can occur simultaneously in the lateral and third ventricles but are rarely isolated to the third and/or fourth ventricles.^[4] Because these tumors are located in the ventricles and cause obstructive hydrocephalus, most patients exhibit symptoms of increased intracranial pressure such as vomiting, headache, nausea, gait disturbance, and cognitive dysfunction.^[5] The primary treatment is surgical excision. The extent of resection is the most important prognostic factor and, if the tumors are completely resected, survival rates can be as high as 100%.^[6] The local control rate at 5 and 10 years after surgery is 91% and 77%, respectively. Some studies have reported the effectiveness of stereotactic radiosurgery.^[7,8] In particular, recurring cases, deep-seated lesions with difficult surgical access, or high operative risks, such as old age or general weakness, have been treated.

We report a case of an elderly 78-year-old woman who was diagnosed with central neurocytoma isolated to the third ventricle. Previously, there was a published literature which introduced gamma knife radiosurgery (GKR) such as old age or

general weakness have been treated for third ventricle central neurocytoma as the alternative treatment.^[9] This case also supports that this unusually deeply located tumor was effectively treated using GKR.

2. Case report

This study has been approved by our institutional review board, and the need for written informed consent was waived due to retrospective study of medical record.

A 79-year-old woman was admitted to hospital with gait disturbance and cognitive dysfunction. Previously, she had a 4.5 mm aneurysm on the right middle cerebral artery for 1-year, and radiological follow-up was performed without treatment. Her symptoms began to worsen 20 days before the admission. She had a confused mental state without specific motor weakness and was not ambulatory. Brain magnetic resonance imaging (MRI) revealed a multi-lobulated mass, 1.8 cm in size, on the posterior third ventricle, which exhibited low- to iso-signal intensity on T1-weighted images and high signal intensity on T2-weighted images (Fig. 1A and 1B). The mass was homogeneously and strongly enhanced after gadolinium administration (Fig. 1C). Obstructive hydrocephalus developed due to the presence of the mass on the

posterior third ventricle (Fig. 1D). Regional cerebral blood volume was slightly increased on perfusion magnetic resonance images. The provisional diagnosis was meningioma or lymphoma. Neuronavigation-guided endoscopic third ventriculostomy (ETV) was performed on the tuber cinereum between the mammillary bodies. Ventriculostomy was done using a monopolar coagulator and a balloon catheter; the arteries were atherosclerotic (Fig. 2A). Endoscopic biopsy (Bx) of the lesion on the third ventricle was obtained. Intraoperatively, the mass was pinkish in color and friable, with mildly increased vascularity (Fig. 2B). After surgery, her gait disturbance was improved, and she ambulated using a walker. The resected specimen was a cellular tumor that was composed of densely packed, round monomorphic cells exhibiting a solid growth pattern (Fig. 3A). The nuclei were round to oval and exhibited fine granular chromatin (Fig. 2B). Acellular neuropil islands were also observed and were positive on glial fibrillary acidic protein (GFAP) immunohistochemistry (Fig. 3C). Tumor cells were strongly immunopositive for synaptophysin (Fig. 3D) and negative for CD3 and CD20, which are representative T cell and B cell markers. The tumor was diagnosed as central neurocytoma. One week following surgery, GKR was performed using a radiosurgery planning software (Leksell Gamma, Elekta

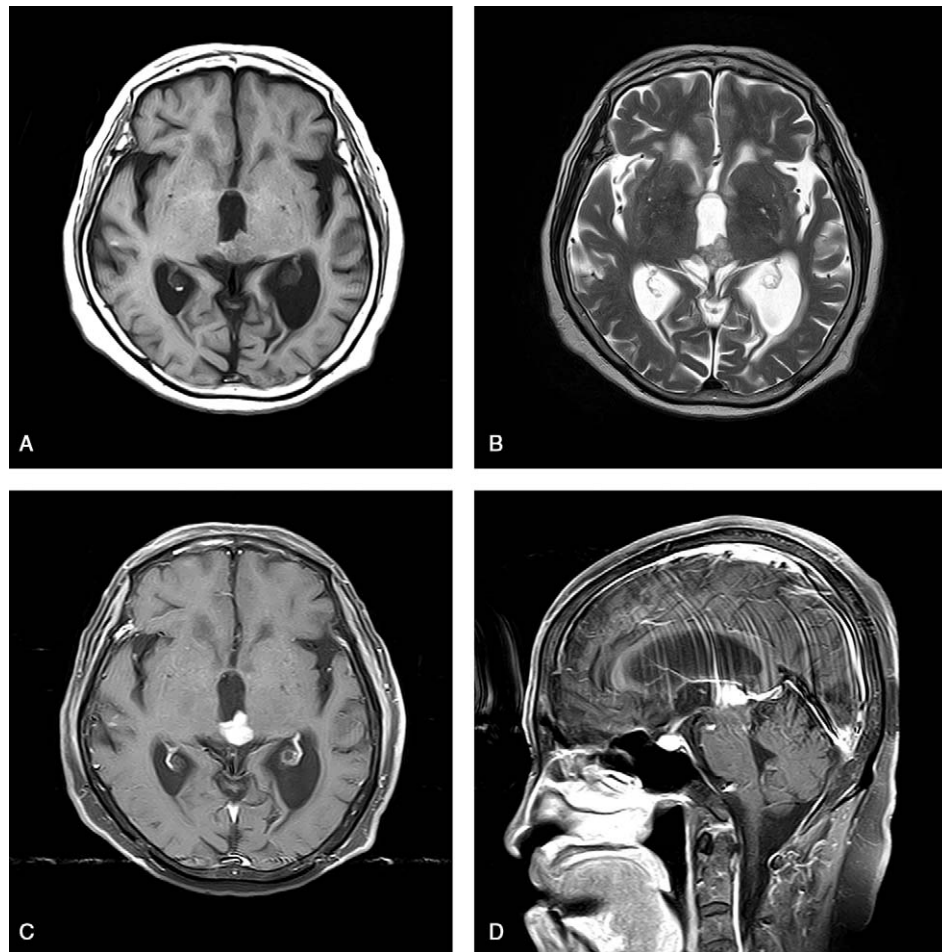


Figure 1. Preoperative radiological findings. A: A 1.8 cm multilobulated mass on the posterior third ventricle exhibiting low- to iso-signal intensity on T1-weighted MRI. B: The mass exhibited high signal intensity on T2-weighted MRI. C: The mass was homogeneously and strongly enhanced after gadolinium enhancement. D: Obstructive hydrocephalus developed due to the presence of the mass on the third ventricle. MRI= magnetic resonance imaging.

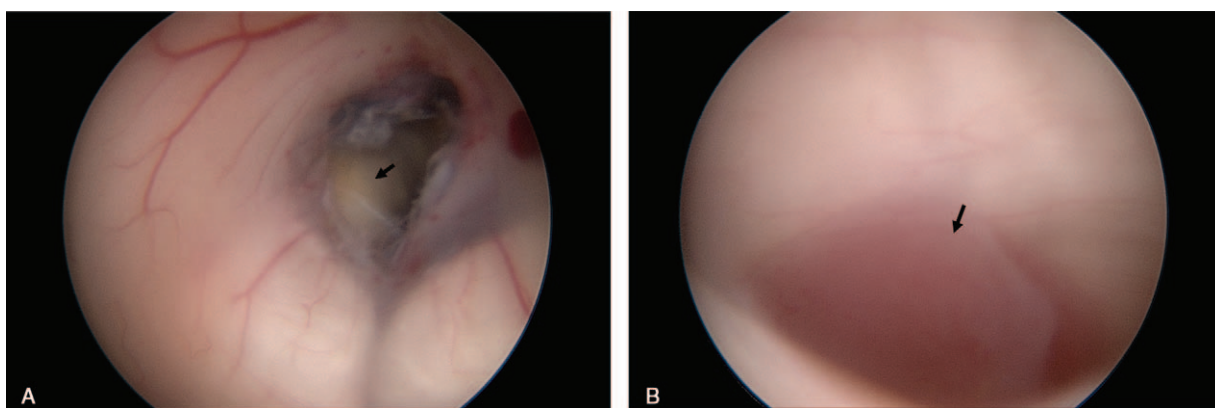


Figure 2. Endoscopic third ventriculostomy and biopsy. A: Endoscopic third ventriculostomy was performed (arrow: atherosclerotic basilar artery). B: The third ventricular lesion was pinkish in color and friable, with mildly increased vascularity (arrow: mass).

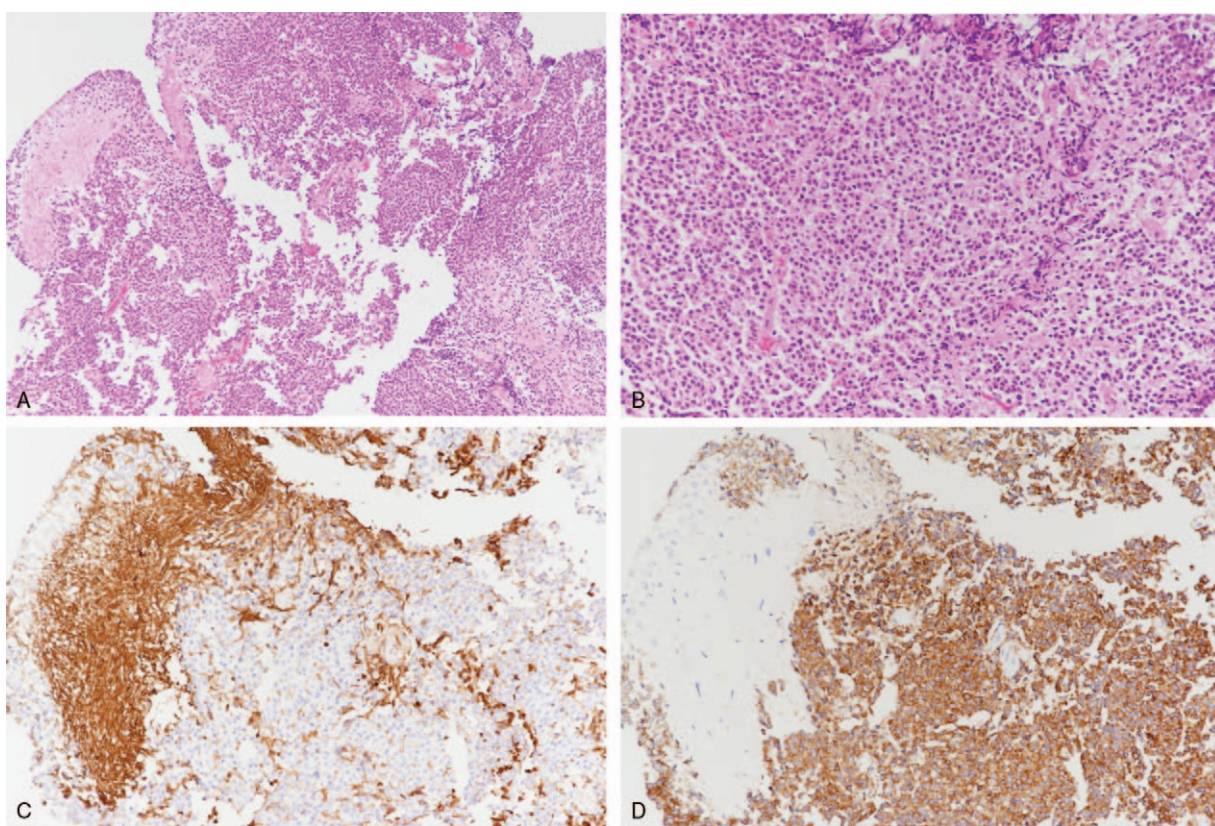


Figure 3. Pathology of the resected tumor. A: The tumor was consisted of densely packed tumor cells and exhibited occasional neuropil islands (hematoxylin and eosin stain, original magnification $\times 100$). B: Tumor cells were small and monotonous, and exhibited round to oval nuclei (hematoxylin and eosin stain, original magnification $\times 200$). C: Only the neuropil islands were positive for glial fibrillary acidic protein immunohistochemistry, revealed by strong positive reaction in the neuropil islands but negative reaction in tumor cells (immunohistochemistry, original magnification $\times 200$). D: Tumor cells were strongly positive for synaptophysin, a diagnostic marker of central neurocytoma (immunohistochemistry, original magnification $\times 200$).

Instruments AB, Stockholm, Sweden). The prescribed dose was 14 Gy with 50% isodose lines, and the target volume was 1.62 cc (Fig. 4A). Three months after GKR, brain MRI revealed a decrease in the size of the multi-lobulated strong enhancing mass in the posterior third ventricle from 1.8 cm to 1.4 cm (Fig. 4B), and her confusion was improved. She did not undergo additional treatment including radiotherapy or chemotherapy. The patient

had been followed-up 8 months with no signs of neurological deterioration.

3. Discussion

For review of articles, the Pubmed database was searched by using terms of “central neurocytoma” and “third ventricle”

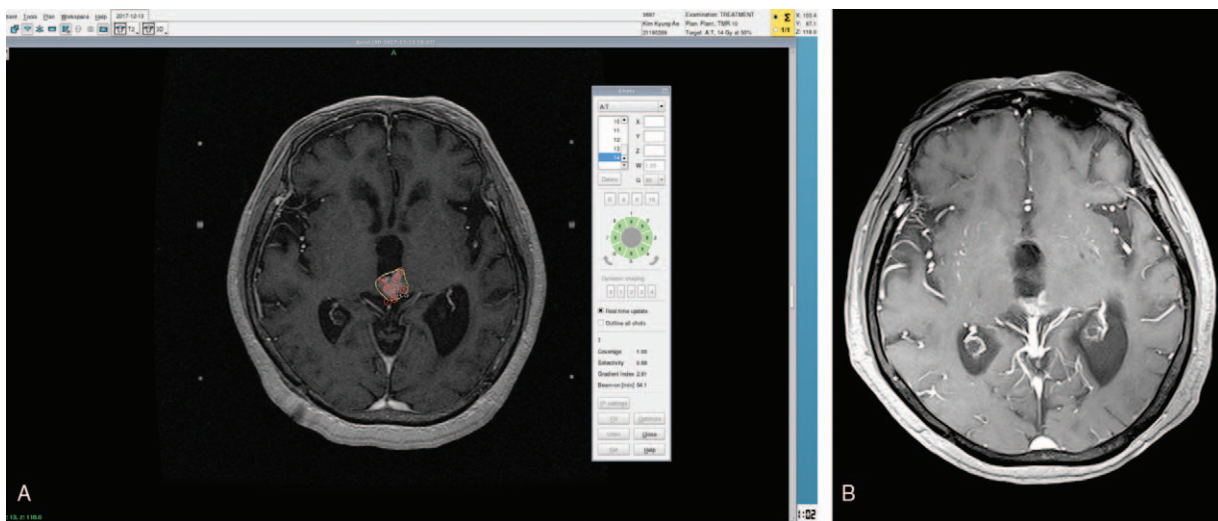


Figure 4. GKR and follow-up radiological findings. A: The prescribed dose was 14 Gy with 50% isodose lines, and the target volume was 1.62 cc. B: Three months after GKR, brain magnetic resonance imaging revealed a decrease in the size of the multilobulated strong enhancing mass (from 1.8 cm to 1.4 cm) in the posterior third ventricle. GKR=gamma knife radiosurgery.

including all the searchable data. The cases were included by these criteria. Inclusion criteria were pathologically diagnosed with central neurocytoma and radiologically located on isolated third ventricle. Exclusion criteria were similar pathology such as atypical central neurocytoma or central neuroblastoma, and tumor coexistence such as in lateral ventricle and third ventricle etc. The reviewed literature including these criteria were searched between 1988 and 2018. The cases of isolated third ventricular central neurocytomas are summarized in Table 1.^[9–14]

Central neurocytoma is rare neuroepithelial tumor that is usually located in intraventricular locations near the foramen of Monro.^[1,15] Central neurocytomas usually occur in the lateral ventricle, with only 3% isolated to the third ventricle.^[4] The previous literature report that these tumors are usually found in young adults, with a median age between 25 and 30 years. Because of the location of central neurocytoma which is usually presented near foramen Monro, the tumors can cause obstructive hydrocephalus and increased intracranial pressure.^[1] Most

patients present with vomiting, headache, nausea, cognitive dysfunction, or gait disturbance without motor weakness, which are consistent with increased intracranial pressure. The typical imaging findings of central neurocytoma are round or lobulated mass that is iso-intense to hyperintense to gray matter in T1- and T2-weighted MRI.^[16] The tumors contain a solitary mass and clusters of cysts of varying sizes, which exhibit a “soap bubble appearance”. The tumors exhibit mild to moderate contrast enhancement after gadolinium administration. Compared to previously published cases, central neurocytomas isolated to the third ventricle exhibit different clinical presentations. The age at which the tumor develops is different. These tumors usually occur in high probability in young or older individuals.

Pathologically, the tumors exhibit varied histological characteristics, despite being from the same specimen.^[1,16] In some areas, findings include less-dense tumor parts, composed of fibrillary matrix area. Alternative findings include dense tumor cells consisting of small-to-medium round monomorphic cells

Table 1
Review of isolated third ventricular central neurocytoma.

First author [ref] (year)	Age (years)/sex	Signs & symptoms	Treatment	Outcome
Majos ^[10] (1997)	40/M	Headache, syncope	Surgery (no data)	Eight-month follow-up, no recurrent tumor
Javedan ^[9] (2003)	54/M	Headache, gait unsteadiness	Endoscopic Bx, ETV, GKR	Two-year follow-up, decreased tumor and neurologically intact
Gome ^[11] (2006)	58/M	Memory loss, gait disturbance, headache	Endoscopic Bx, ETV	One-year follow-up, no growth of tumor, neurologically intact
Romano ^[12] (2009)	37/F	Headache, vomiting, diplopia	Endoscopic tumor removal (TR), ETV	Three-year follow-up, no recurred tumor and no neurological deficit
Shravan Kumar ^[13] (2010)	6/no data	Headache, vomiting	Surgery (STR), radiotherapy	Six weeks after RT, no residual tumor and no clinical data
Baishya ^[14] (2016)	9/F	Headache vomiting	Surgery (TR)	No follow-up data, no neurologic deficit after surgery
Present study	79/F	Gait disturbance, cognitive dysfunction	Endoscopic Bx, ETV, GKR	Eight-month follow-up, decreased tumor and improved neurological symptoms

Bx=biopsy, ETV=endoscopic third ventriculostomy, F=female, GKR=gamma knife radiosurgery, M=male, ref=reference, STR=subtotal resection, Surgery=craniotomy and tumor removal, TR=total resection.

with a perinuclear halo-like “fried egg” appearance, perivascular pseudorosettes, and honeycomb patterns. Given these findings, central neurocytomas had previously been misdiagnosed as ependymomas of the foramen of Monro, or intraventricular oligodendrogliomas.^[17] Presently, a diagnosis can be made using specific antibodies. The tumors are strongly immuno-positive for synaptophysin and neuronal-specific enolase (NSE) in fibrillary and perivascular area as the most reliable diagnostic marker.^[18] These tumor cells are relatively less immuno-positive for GFAP, which is more strongly immuno-positive in cases of astrocytoma and ependymoma.

Until recently, surgical treatment involving gross total resection (GTR) was considered to be the standard treatment for central neurocytoma. Patients who underwent GTR have a 100% 5- and 10-year survival rate, while those who underwent a subtotal resection (STR) have a 5- and 10-year survival rate of 93%.^[6] The local control rate was 91% for 5 years and 77% for 10 years in those who underwent GTR, whereas the rate was 77% for 5 years and 45% for 10 years in those who underwent STR.^[6] Due to the results reported in previous studies, patients who had undergone STR received adjuvant radiotherapy or chemotherapy.^[6] The STR and radiotherapy group demonstrated a significantly good local control rate, even though there was no effect on the survival rate. The local control rate was 92% at 5 years and 86% at 10 years in the group that underwent STR and radiotherapy.^[6] Pathologically, central neurocytomas present atypical features, such as focal necrosis, increased mitotic activity, endothelial proliferation, an elevated MIB-1 labeling index and/or cellular pleomorphism, which are more aggressive and have increased likelihood of recurrence.^[6,19] Tumors exhibiting the above features could be recommended for postoperative radiotherapy.

On the review of isolated third ventricular central neurocytoma, each of the published cases received different treatments.^[9–14] Surgical tumor removal was performed in 4 cases. Three underwent craniotomy and surgical removal, and one had endoscopic tumor removal and third ventriculostomy. One of 4 underwent postoperative radiotherapy after STR. Endoscopic Bx and third ventriculostomy were performed in 3 patients. In 2 of 3 cases, stereotactic radiosurgery was performed after Bx. Regardless of how these tumors were treated, neurological symptoms were all improved and the tumors were well controlled.

Although standard treatment for central neurocytoma is complete surgical resection, it is difficult to remove the tumor completely because of its location.^[15] Recent studies have suggested that stereotactic radiosurgery is an effective treatment modality because radiosurgery has the advantage of preserving normal brain tissues and delivering high doses of radiation to specified lesions compared with other radiotherapies. According to a recent systematic analysis, patients who underwent GKR alone had a survival rate of 98% at a mean follow-up of 62.4 months.^[15] The tumors were treated with a mean marginal dose of 14.7 Gy (range, 9–25 Gy) and had mean tumor volume of 9.3 mL (range, 0.4–36.4 mL). These results are comparable with the 100% 5-year survival rate of patients who underwent surgical total resection. Overall, local control of GKR for central neurocytoma was 92.2%, which supported the efficacy of GKR for central neurocytoma.^[7,15,20] In these studies, stereotactic radiosurgery was usually performed on asymptomatic, relatively small tumors in the absence of hydrocephalus. In addition, even with hydrocephalus symptoms, GKR with ETV can be performed when the tumors are placed deep in a location

where surgical access was difficult. GKR has been performed in cases of deep location as well as high-risk surgery, including our case. GKR could demonstrate potential efficacy as an alternative primary treatment in these patients.

Limitations of this paper were a small number of reviewed cases and follow-up period. Because of the rarity of central neurocytoma, it could be difficult to generalize this hypothesis that central neurocytomas isolated to the third ventricle may occur in high probability at young or older individuals. In this case, the follow-up period was short to claim that GKR could be an effective treatment. Nevertheless, this paper was meaningful in that it first mentioned that central neurocytomas isolated to the third ventricle could exhibit different clinical presentations, and GKR could be an alternative treatment option in elderly patients.

In summary, central neurocytoma is rare benign tumor that usually presented in the lateral ventricle at young ages. Previous studies have reported that tumors in unusual locations, such as those isolated to the third ventricle, are different in terms of onset age, either in young children or elderly. Although complete surgical resection is an effective treatment for central neurocytoma due to the decreased risk for recurrence after surgery, it is often difficult to approach tumors through surgery. GKR could, therefore, be an alternative primary treatment option for deeply located central neurocytomas in elderly patients.

Author contributions

Conceptualization: Tae-Young Jung.

Methodology: Tae-Young Jung, Seul-Ke Kim, Kyung-Hwa Lee.

Project administration: Tae-Young Jung, Sue-Jee Park.

Software: Sue-Jee Park.

Supervision: Tae-Young Jung.

Writing – original draft: Sue-Jee Park, Kyung-Hwa Lee.

Writing – review & editing: Tae-Young Jung, Seul-Ke Kim.

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