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Case Report

Palliative Gamma Knife Radiosurgery for a Small Part of a Large Vestibular Schwannoma in an Elderly Patient

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We report a case of a large vestibular schwannoma in an 80-year-old female patient that shrank after palliative Gamma Knife radiosurgery (GKS). Neurological symptoms included hearing deterioration and facial palsy. The tumor volume was 21.9 mL. Craniotomy was considered high-risk, and conventional GKS was risky, owing to the risk of transient enlargement. Therefore, GKS was performed on only a portion of the tumor. The marginal dose (12 Gy) volume was 3.8 mL (17.4%). The tumor began to shrink after transient enlargement. Sixty months later, the tumor volume was only 3.1 mL, and the patient was able to maintain independent activities of daily living without salvage treatment.

Key words: vestibular schwannoma, Gamma Knife radiosurgery, large volume, palliative, elderly patient

In the treatment of vestibular schwannomas, Gamma Knife radiosurgery (GKS) is suggested for small lesions, while craniotomy is considered the first choice for larger lesions because of the lower local control rate of GKS [1, 2]. However, the risks from craniotomy make the development of a treatment plan difficult for patients who are elderly or in poor general condition. As with linear accelerators, fractionated irradiation is now possible using the Gamma Knife; however, there is a risk of transient enlargement and hydrocephalus in vestibular schwannoma cases [3-6]. As the tumor volume increases, the effects of transient enlargement can be more pronounced, and several studies have reported that larger volumes were associated with incidence of hydrocephalus [3-5]. Herein, we report the management of a case in which activities of daily living (ADL) could be maintained without craniotomy by applying palliative GKS to a portion of the tumor volume.

Case Report

The patient was an 80-year-old woman. Prior to presentation, the patient visited a health care facility where she underwent magnetic resonance imaging (MRI) of the brain as part of a health check-up. A lesion of >3 cm was incidentally observed at the cerebellopontine angle on MRI. The patient was informed that the lesion was difficult to treat because of its large size and that follow-up observation was unnecessary. Thereafter, she was referred to our clinic. Her medical history included post-arthroplasty bilateral knee arthropathy, hypertension, and diabetes mellitus. The patient was 146 cm tall and weighed 52 kg. Neurological findings included House Brackmann class 2 facial paralysis, right (66.25 dB) and left (23.75 dB) hearing deterioration, Bruns nystagmus, and cane walking due to a deteriorated gait. Her Mini-Mental State Examination (MMSE) score was low, at 22/30, with no other obvious neurological findings.

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The lesion was a 35-mm tumor in the major axis located at the right cerebellopontine angle. It had a heterogeneous contrast enhancement effect (Fig. 1A) and a multicystic nature indicated by T2-weighted imaging (Fig. 2B). No cerebral edema was observed. The brainstem and fourth ventricle were compressed and deviated towards the left. Hydrocephalus had not occurred, and a gap was observed between the tumor and the adjacent cerebral cisterns on the right (Fig. 2A and 3).

Craniotomy, considered as the first option, was refused by the patient. Additionally, as the patient was aged >80 years, craniotomy was considered to have a high complication risk. As for GKS, an estimated 4-10-mL volume increase could be expected following irradiation of the entire tumor, representing a 20-50% change; maintaining ADL independence under these conditions would be difficult. Moreover, irradiation of the entire tumor might increase the difficulty of salvage surgery. Therefore, we considered partial irradiation as it is difficult to predict the severity of transient increase for tumors even with a low GKS dose. A 0.5-mL space was observed in the cerebellopontine angle lateral to the tumor, which was expected to allow some space for transient enlargement. We assumed that this lateral space in the cerebellopontine angle could tolerate pressure from transient enlargement, and we decided upon a volume of 3.8 mL using the marginal dose. Limited irradiation to the right side of the tumor to avoid high-dose irradiation to the brain stem could be considered if necessary. Therefore, we proposed partial GKS for a portion of the tumor volume. The patient and her family agreed with this treatment plan.

The total tumor volume was 21.9 mL, of which only the outer 3.8 mL was planned for irradiation with a marginal isodose at 60% 12 Gy (Fig. 3). Overall, 18.1% of the entire tumor was within the marginal dose. The dose distribution was designed to avoid high-dose irradiation to the brainstem and the area adjacent to the

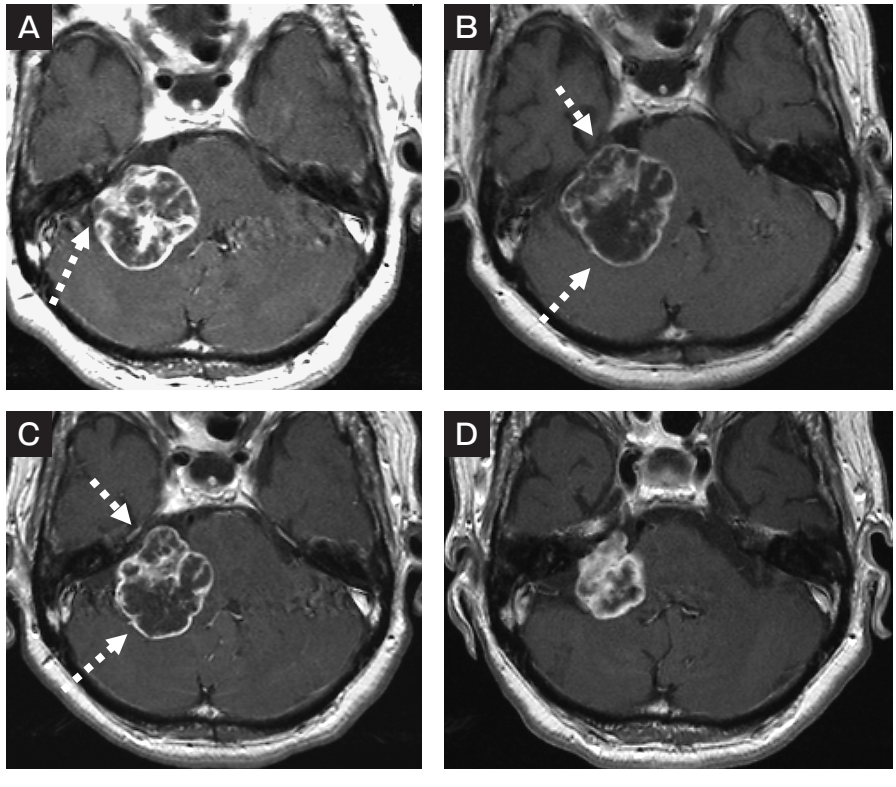

Fig. 1 Axial views of gadolinium-enhanced MRI: **A**, prior to Gamma Knife radiosurgery (GKS). The arrowheads demonstrate a small space in the cerebellopontine cistern; **B**, Six months after GKS. The anterior (upper arrowhead) and posterior part (lower arrowhead) of the tumor show enlargement; **C**, Twelve months after GKS. Protrusion of the anterior part (upper arrowhead) remained; however, the right lateral part (lower arrowhead) of the tumor had shrunk; **D**, Thirty-seven months after GKS. The volume of the tumor had completely shrunk.

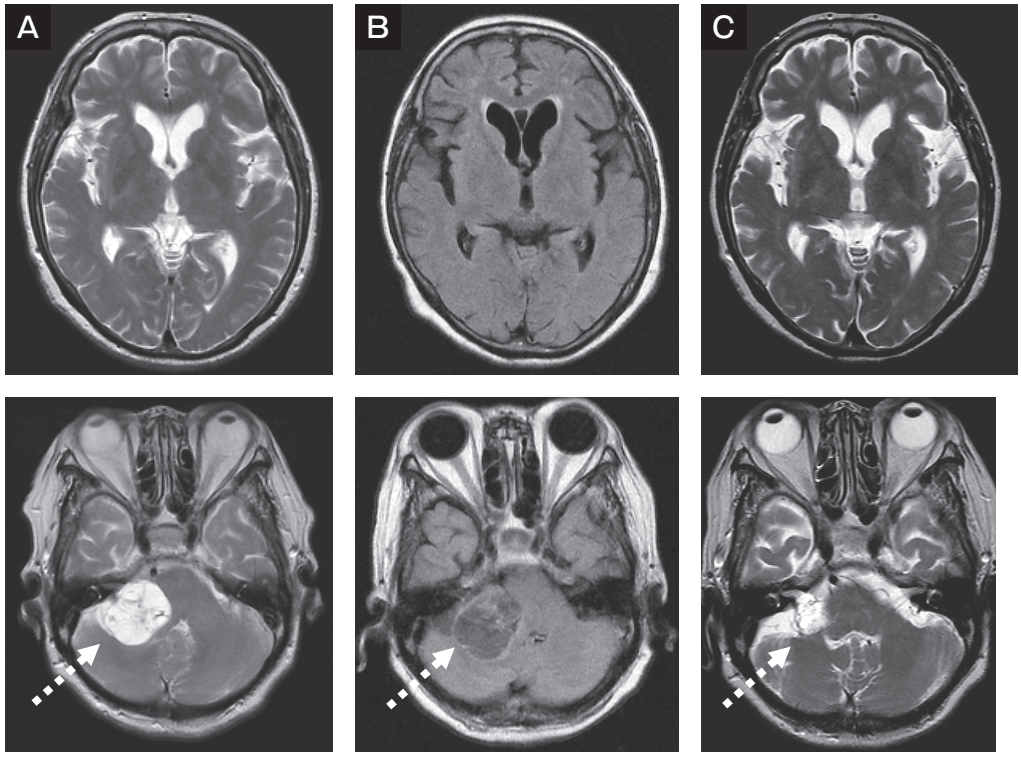

Fig. 2 Axial views of T2-weighted images and fluid attenuated inversion recovery (FLAIR) images. The arrowhead demonstrates the tumor. **A**, T2-weighted images taken prior to Gamma Knife radiosurgery (GKS); **B**, FLAIR images taken 6 months after GKS. Hydrocephalus had not developed; **C**, T2-weighted images 60 months after GKS. Shrinkage of the tumor was obvious.

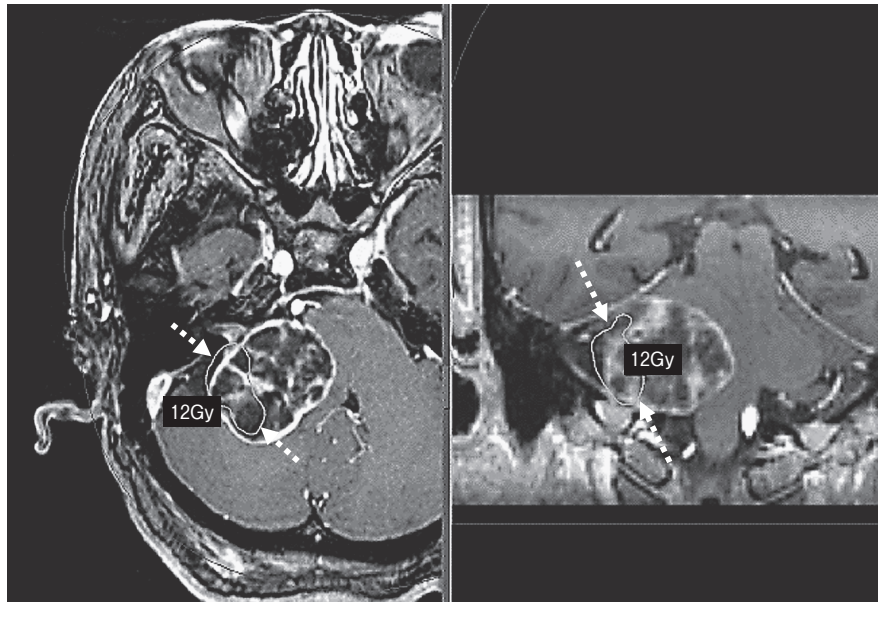

Fig. 3 Images of the radiation dose distribution. Large ellipses indicate the entire tumor and small ellipses indicate the region of the 12-Gy marginal dose. Only the right lateral part of the tumor was irradiated. The arrowheads reveal a small space in the cerebellopontine cistern.

facial nerve, in order to avoid difficulty during a potential craniotomy.

One month after GKS, no neurological deterioration was observed. Six months after GKS, MRI revealed tumor enlargement, as well as increased compression of the brain stem and the right cerebellar peduncle (Fig. 1B). Cerebral edema and hydrocephalus were not observed (Fig. 2B). The MMSE score deteriorated to 19/30, and the patient experienced increased falls while walking. However, the patient's ADL was almost maintained. Twelve months after GKS, although the irradiated area had shrunk, the non-irradiated medial cerebellar region had remained unchanged, and the area adjacent to the brainstem had expanded (Fig. 1C). At 18 months after GKS, facial paralysis disappeared, gait function was restored, and MMSE scores recovered to 22/30. Thirty-seven months after GKS, the tumor volume had shrunk to 9.2 mL (Fig. 1D), and pure-tone audiometry was 70 dB on the affected side. The final MRI performed 60 months after GKS revealed further tumor shrinkage to 3.1 mL (Fig. 2C). At this stage, the patient had lost her hearing on the affected side, and her MMSE score had decreased to 19/30. The ADL had been maintained until then; however, 67 months after GKS, the patient lost the ability to walk owing to declining strength. The patient remains alive 12 years after GKS.

Discussion

Craniotomy is the primary treatment option for patients with large vestibular schwannomas because of the lower control rate with GKS [2]. Performing craniotomy becomes more challenging after GKS due to fibrosis and scarring from the radiation [7]. However, lengthy craniotomies are a problem for elderly patients and individuals with comorbidities. In elderly patients, the rate of gross total tumor resection was reported to be only 33.3-35.6% [8-9].

Several studies have been conducted on conventional GKS for large vestibular schwannomas. Table 1 shows the local control rate in GKS studies for large vestibular schwannomas [10-15]. Williams *et al.* reported an 81% 5-year local control rate [14]. Given the low control rate after conventional GKS, fractionated irradiation with a linear accelerator (*e.g.* CyberKnife) [16], or bi-phasic irradiation (in which the entire tumor is divided into two parts that receive separate irradiation with a several-month interval) — *i.e.*, volume-staged GKS — is an option [11]. However, both fractionated radiation and bi-phasic irradiation involve irradiation of the entire tumor, and transient enlargement therefore remains a problem.

Transient enlargement has been reported in 77% of vestibular schwannoma cases [6]. This condition often

Table 1 summary of the past studies of GKS for large vestibular schwannoma (>3 cm or >10 mL)

Author, year	Numbers of cases	Ages	Volume (mL)	Past surgery (%)	The prescription dose (Gy)	Follow-up time (months)	Local control rate (%)	Salvage treatment (%)
Chung, 2010	21	49.5 (mean)	17.3 (median)	66.7	12 (median)	53 (median)	85.7	23.8 (2 cases resections, 2 cases shunt surgery)
Yang, 2011	65	51 (mean)	9 (median)	26	12 (median)	36 (median)	91	11 (resections), 5 (shunt surgery)
Williams, 2013	24	61.5 (mean)	9.52 (median)	38	11 (median)	48.5 (median)	81.8 (at 5 years)	33.3 (6 cases resections, 3 cases GKS, 2 cases shunt surgery)
Zeiler, 2013	28	56 (mean)	9.71 (mean)	48	12.5 (mean)	20.4 (mean)	92	14.3 (1 cases: resections, 3 cases shunt surgery)
Huang, 2018	35	49.7 (mean)	14.8 (median)	25.7	11 (median)	48 (median)	85.7	20 (4 cases: resections, no shunt surgery for hydrocephalus)
Yeole, 2022	34	45.5 (mean)	10.9 (mean)	23.5	12 (median)	34.7 (mean)	94.2	14.7 (4 cases: resections, 1 cases shunt surgery)

peaks six months after GKS, but may persist thereafter [6]. If patients' ADL scores deteriorate due to transient enlargement or occlusive hydrocephalus, craniotomy or shunt surgery should be considered. As in the present case, when the tumor volume is already large, the risk of losing ADL independence due to transient enlargement may be high. Even in the present case, when the marginal dose volume was limited to 18.1% of the entire tumor, transient enlargement still occurred. The tumor components outside the marginal dose area also increased in volume, suggesting that transient enlargement may occur in the low dose range. However, the patient's independence of ADL was well-maintained during this transient expansion. Cerebral edema in the high-dose irradiated area should be considered an adverse effect of radiation.

Shunt surgery for post-GKS hydrocephalus has been reported to be required in 5.0% of patients at a median of 15.5 months after GKS [5]. Zeiler *et al.* reported that symptomatic hydrocephalus occurred in 16.0% of patients after GKS for large vestibular schwannomas [15]. As shown in Table 1, the shunt operation rate after GKS for large vestibular schwannoma was 6.3% in all six prior studies [10-15]. A possible mechanism for hydrocephalus development after GKS is the release of proteins and tumor fragments due to irradiation [5]. By limiting the irradiated area, as in the present case, hydrocephalus may be avoided.

The growth rate of vestibular schwannoma is low; in fact, it can shrink during its natural course [17]. Two cases who experienced definite shrinkage of tumors in the natural course have previously been reported [18, 19]. Past studies have also evaluated tumor control rates in patients treated with a relatively low marginal dose (7.5-11 Gy) [20, 21]. It is difficult to determine whether the significant tumor shrinkage in this study resulted from the low dose irradiation or natural disease progression. Transient enlargement occurred at 6 months, but ADLs were maintained, and facial palsy improved. After that, the tumor continued shrinking, reaching a volume of 14.1% after 60 months. It should be noted that in younger patients, the component outside the marginal dose can expand over a longer follow-up period. Our modified treatment strategy involved monitoring of transient enlargement and ensuring that the subsequent shrinkage exceeded or equaled the enlargement outside of the irradiated area. Actually, we consider that a volume reduction after a partial GKS, as encountered in this case, is rare.

Conclusion

Herein, we report the use of partial GKS for a large vestibular schwannoma in an elderly patient. Transient enlargement occurred; however, following this, the tumor shrank noticeably. Additionally, hydrocephalus was avoided, prolonging the duration of ADL independence. From the management and prognosis of this case, we can infer that palliative GKS for a portion of the tumor may effectively prolong ADL maintenance in elderly patients with large vestibular schwannomas; further studies are warranted to verify this.

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