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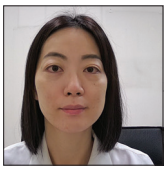
Case Report

Intratumoral hemorrhage in jugular foramen schwannoma after stereotactic radiosurgery: A case report

Mariko Kawashima, Hirotaka Hasegawa, Masahiro Shin, Yuki Shinya, Nobuhito Saito

Department of Neurosurgery, the University of Tokyo Hospital, Tokyo, Japan.

E-mail: *Mariko Kawashima - mariko.furi@gmail.com; Hirotaka Hasegawa - ayhi_hase_dani@yahoo.co.jp; Masahiro Shin - shin-nsu@h.u-tokyo.ac.jp; Yuki Shinya - yukishinya6155@gmail.com; Nobuhito Saito - nsaito-nsu@m.u-tokyo.ac.jp



***Corresponding author:**
Mariko Kawashima,
Department of Neurosurgery,
the University of Tokyo
Hospital, Tokyo, Japan.

mariko.furi@gmail.com

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ABSTRACT

Background: Clinically significant intratumoral hemorrhage is a rare complication of stereotactic radiosurgery (SRS) for benign tumors.

Case Description: Here, we present the case of a 64-year-old man who underwent SRS for a relatively large dumbbell-shaped left jugular foramen schwannoma (JFS) and thereafter developed intratumoral hemorrhage. On post-SRS day 3, he developed lower cranial nerve palsies with radiographically evident tumor expansion. His neurological conditions had gradually improved thereafter; however, he suddenly developed headache, dizziness, and mild hearing deterioration at 7 months due to intratumoral hemorrhage. We managed the patient conservatively, and eventually, his symptoms improved except for slight ataxia and hearing deterioration. Follow-up images at 4 years from SRS demonstrated significant tumor shrinkage. This is the first report describing intratumoral hemorrhage after SRS for JFS.

Conclusion: Transient expansion of the tumor and subsequent venous stasis around the tumor may have played a role in the hemorrhage. Intratumoral hemorrhage should be considered as a rare, but potential complication of SRS for JFSs.

Keywords: Intratumoral hemorrhage, Jugular foramen schwannoma, Radiation-induced adverse event, Stereotactic radiosurgery

INTRODUCTION

Jugular foramen schwannoma (JFS) is a rare intracranial tumor arising from cranial nerves IX, X, or XI, accounting for 2.9–4% of all intracranial schwannomas, which in turn accounts for 8% of all primary intracranial tumors.[25,30] While JFS typically causes dysphagia, hoarseness, hearing loss, and tinnitus, asymptomatic, incidentally found JFS cases have also been increasing because of improved access to non-invasive high-resolution imaging studies, such as magnetic resonance imaging (MRI). As for the treatment, surgical resection is a standard modality of treatment but is associated with considerable invasiveness, as well as a 10–48% risk of permanent lower cranial nerve deficits.[1,3,26-28] In contrast, stereotactic radiosurgery (SRS) is generally accepted as a minimally-invasive treatment option for intracranial schwannomas, with the 5- and 10-year

cumulative tumor control rates being 78–97% and 79–94%, respectively, and the rates of persistent adverse radiation being 3–15%.[4,7,8,10,14,18,22-24,35] To the best of our knowledge, there are no reports on hemorrhagic complications subsequent to SRS for JFS. Here, we present a detailed case report of JFS complicated with subacute tumor expansion and an intratumoral hemorrhage after SRS.

CASE PRESENTATION

A 64-year-old man without known significant medical history was referred to our hospital for the treatment of an incidentally found left JFS. He was found to be completely intact on examination and no family history of neurofibromatosis type 2. MRI revealed a dumbbell-shaped solid mass at the left cerebellopontine angle with marked enlargement of the affected jugular foramen and no sign of dural tail, which was 25 × 27 × 18 mm and 22 × 25 × 19 mm for the intradural and extradural portions, respectively, and 8.4 ml in total volume. The mass mildly compressed brainstem and had no evident sign of hemorrhage [Figure 1a and 1b]. There was no other intracranial tumor. MR venography demonstrated that the left jugular bulb was obliterated because of tumor compression [Figure 1c]. The tumor showed no signs of calcification or hypervascularity, and positron emission tomography with fluorodeoxyglucose did not exhibit increased uptake consistent with malignancy [Figure 1d] or any evidence of other tumors throughout the body. T1-weighted MRI at the level of the internal auditory canal indicated minimal brainstem compression before treatment [Figure 1e]. Based on observations from the aforementioned examinations, two independent radiologists made a diagnosis of sporadic JFS. After thorough discussion, SRS using Gamma Knife (Elekta AB, Stockholm, Sweden) was performed with a marginal and maximal dose of 13 and 26 Gy, respectively.

Post-radiosurgical course

Three days after SRS, the patient developed dysphagia, hoarseness, and leftward deviation of the tongue that were confirmed by otorhinolaryngologic examinations, suggesting injuries of the left vagal and hypoglossal nerves. MRI on post-SRS day 5 showed tumor expansion without peritumoral edema [Figure 1f]. Administration of dexamethasone gradually relieved the symptoms except for vocal cord palsy that later required additional laryngological interventions.

Although his symptoms improved, follow-up MRI at 5 months from SRS showed further tumor expansion with central necrosis and peritumoral edema, albeit asymptomatic [Figure 1g]. This was considered as a slightly more aggressive change than transient tumor expansion typically seen in vestibular schwannomas (VSs), and thus prompted further close follow-ups.

At 7 months, he suddenly developed headache, dizziness, mild hearing deterioration (20 dB decrease in pure tone audiometry), nausea, and vomiting. Imaging studies revealed intratumoral hemorrhage with exacerbation of peritumoral edema [Figure 1h]. At that time, he was not on any blood thinners, and coagulation tests demonstrated normal function. Since he showed no further progression after re-starting the administration of dexamethasone and osmotic diuretics, we continued the conservative management without surgical intervention. He finally recovered almost completely within 2 months after the hemorrhage, and follow-up images at 4 years from SRS demonstrated significant tumor shrinkage [Figure 1i].

DISCUSSION

We experienced a JFS case which was accompanied with acute tumor expansion after SRS and subsequent clinically significant intratumoral hemorrhage. Intratumoral hemorrhage of intracranial schwannoma, particularly histologically detected microhemorrhage, has been recently considered to be more common than previously believed owing to advances in imaging studies and larger analyses.[2,19,21,32] The etiology of intratumoral hemorrhage in intracranial schwannoma has not been completely defined and is likely to be multifactorial. Anticoagulation therapy, high tumor vascularization, hypertension, and large tumor have been recognized as a risk factor.[2,5,9,12,33,34] Especially, rapid tumor growth causes relative shortage of blood supply and tumor necrosis, resulting in increased intratumoral pressure and hemorrhage. This repeated microhemorrhage can also lead to cystic changes and further expansion.[21] Although microhemorrhage alone is asymptomatic in most cases, some patients infrequently present with the abrupt symptom progression.[15] Regarding VS, about 50 cases have been reported in the literature.[15,31] Carlson *et al.* estimated that the rate of intratumoral hemorrhage in untreated VS was 0.4%, which decreased to only 0.2% after excluding patients on anticoagulation.[2] The symptoms are headache, nausea and vomiting, cranial neuropathy, ataxia, and so on. Special care is needed for them because these symptoms can occasionally be life-threatening due to the vicinity of the brainstem.

The influence of radiation on the intratumoral hemorrhage of intracranial schwannoma has not been fully elucidated. In particular, limited to clinically significant hemorrhage, there are eight reported cases in literature [Table 1].[5,9,11,13,16,20,31] A few patients developed symptomatic hemorrhage within 1 month after SRS, while others developed it several months or years later. Some mechanisms could be assumed from previous studies. First, radiation induces microhemorrhage as

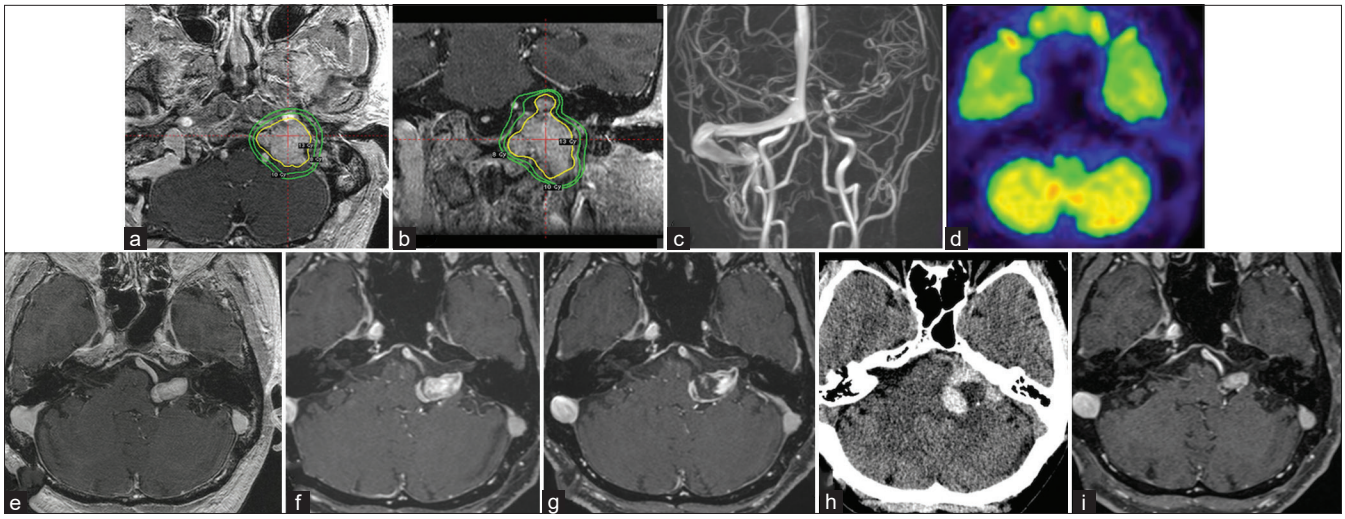

Figure 1: (a-d) Pre-SRS images of the left jugular foramen schwannoma: (a) pre-SRS axial enhanced T1-weighted MRI used in radiosurgery; (b) pre-SRS coronal enhanced T1-weighted MRI used in radiosurgery; (c) MR venography showing the obstructed left jugular bulb; (d) positron emission tomography with fluorodeoxyglucose. These images revealed a well-enhanced, dumbbell-shaped, solid mass extending to the intracranial- and extracranial space, causing expansion of the jugular foramen and invading the hypoglossal canal. (e-i) Chronological changes on axial enhanced T1-weighted MRI at the level of the internal auditory canal where brainstem compression was evident, and computed tomography at the time of the intratumoral hemorrhage; (e) pre-SRS; (f) tumor expansion was observed 5 days after SRS; (g) further expansion 5 months after SRS; (h) computed tomography indicating intratumoral hemorrhage 7 months after SRS; (i) evident tumor shrinkage at the last follow-up 4 years after SRS. SRS: stereotactic radiosurgery, MR: Magnetic resonance, MRI: Magnetic resonance image.

Table 1: Literature review of cases of symptomatic intratumoral hemorrhage after SRS for sporadic intracranial schwannoma.

Author, year	Age, sex	Disease	Modality	Dose (%isodose)	Interval from SRS to hemorrhage	Main symptom	Treatment
Iwai *et al*., 2003[9]	70, F	VS	GK	12 Gy (NR)	60 months	Ataxia	Resection
	NR	VS	GK	NR	80 months	Pain	Conservative
Karampelas *et al*., 2007[11]	53, M	VS	GK	13 Gy (46%)	27 months	Headache, facial spasm	Conservative
Dehdashti *et al*., 2009[5]	47, F	VS	GK	NR	18 months	Headache, ataxia	Resection
Mandl *et al*., 2009[13]	59, F	VS	NR	25 Gy/5Fr (80%)	75 months	Headache, ataxia, papilledema	Resection
Miki *et al*., 2015[16]	48, M	VS	GK	12 Gy (50%)	46 months	Facial palsy	Resection
Thombre *et al*., 2019[31]	63, M	VS	GK	12 Gy (50%)	10 days	Vertigo, facial palsy	Resection
Noureldine *et al*., 2020[20]	71, F	FS	CK	21 Gy/3Fr* (NR)	3 days	Headache, facial palsy	Resection
Present case	64, M	JFS	GK	13 Gy (50%)	7 months	Headache	Conservative

CK: CyberKnife, FS: Facial schwannoma, GK: Gamma Knife, JFS: Jugular foramen schwannoma, NR: Not reported, SRS: Stereotactic radiosurgery, VS: Vestibular schwannoma. *Hemorrhage occurred 3 days after the first fraction, and 7 Gy had been irradiated to tumor

well as other estimated factors, leading to necrotic expansion and rarely massive hemorrhage.[17] Second, radiation would also trigger thrombosis of irradiated endothelial cells, with increase in intravascular outflow resistance and progress in venous congestion, contributing spontaneous intratumoral hemorrhage.[29] It is noteworthy that our case provided sequential MRIs before hemorrhage, which showed relatively rapid tumor expansion with peritumoral edema, finally resulted in symptomatic hemorrhage. Considering venous compromise which had already existed prior to SRS, it is possible that exacerbated venous congestion promoted subsequent hemorrhage in this case.

The optimal treatment for the intratumoral hemorrhage with brainstem compression is basically resection. The previously reported post-SRS cases were managed surgically in six cases and conservatively in two other cases, largely ending up in a good recovery [Table 1].[5,9,11,13,16,20,31] The anti-angiogenic agent, bevacizumab, could be effective for tumor expansion with brain edema after SRS based on the findings of related studies.[6,36] Practically, however, this agent is not covered for schwannomas by the health insurance in our country at present. Although our patient experienced headache, nausea, and mild cranial neuropathy due to intratumoral hemorrhage, he quickly improved and the tumor demonstrated remarkable shrinkage without further intervention, suggesting that necrotic changes mainly caused intratumoral hemorrhage and did not necessarily suggest failed tumor control, similar to transient tumor expansion which is common in VS. Based on our experience, conservative treatment with osmotic diuretics and corticosteroids would be also reasonable unless progressive neurological deterioration is evident. Nevertheless, this is just a case report; thus, accumulation of additional cases and further research is needed to validate these findings.

CONCLUSION

This is the first case reported to demonstrate intratumoral hemorrhage after SRS for JFS. With conservative treatment, subsequent tumor shrinkage was observed in this case. While the etiology is not completely understood, radiation-induced tumor expansion and possible venous compromise are likely to cause the intratumoral hemorrhage. Although surgical resection is needed to be considered at first, conservative management could control the condition unless the hemorrhage is devastating or results in remarkable brainstem compression. Intratumoral hemorrhage should therefore be recognized as one of the potential sequelae after SRS for JFSs.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

There are no conflicts of interest.

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