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## Extreme volume expansion of a vestibular schwannoma due to intratumoral hemorrhage after gamma knife radiosurgery



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### ABSTRACT

A 48-year-old man with right hemi-facial palsy and cerebellar ataxia was referred to our hospital. Three years and 10 months earlier he had undergone gamma knife radiosurgery (GKRS) at the referring hospital for an 18 mm right vestibular schwannoma. Slight tumor enlargement had been observed on MRI performed at the referring hospital 3 years after the GKRS. On close follow-up after another 6 months an MRI showed an obvious enlargement of the tumor. An MRI on admission revealed an iso-intense mass lesion measuring 36 mm in maximum diameter at the right cerebellopontine angle. A two stage surgery was conducted using a retrosigmoid approach because bleeding from the tumor wall was difficult to control intraoperatively during the first operation. At the second operation, the majority of the tumor capsule had converted to necrotic tissue. A large hematoma cavity was present inside the tumor capsule which explained the rapid increase in size over a short period of time. Near total removal was achieved. Histopathological examination revealed massive intratumoral hemorrhage within a typical vestibular schwannoma with no malignancy. The complication of intratumoral hemorrhage is very rare and the utility of stereotactic radiation surgery/therapy, including GKRS, for vestibular schwannoma is well known. However, we must emphasize that careful follow-up is still required, even after several years.

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### 1. Introduction

The usefulness of stereotactic radiation surgery/therapy (SRS/SRT), including gamma knife radiosurgery (GKRS), for vestibular schwannoma is well known [1]. Rare complications of rapid tumor

expansion due to intratumoral hemorrhage following SRS/SRT have previously been reported [2,3] to have occurred, to our knowledge, in only two of 51 patients (4%) [4]. However, this rare, rapid expansion or regrowth of cerebellopontine angle (CPA) tumors may result in neurological deterioration [1]. Herein, we present a patient with extreme volume expansion of a vestibular schwannoma due to intratumoral hemorrhage over a 10 month period that required two direct surgeries to remove the tumour and occurred 46 months after GKRS.

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## 2. Case report

A 48-year-old man with right hemifacial palsy and cerebellar ataxia was referred to our hospital. Three years and 10 months earlier, he had undergone GKRS at the referring hospital for an  $18 \times 13 \times 11$  mm right vestibular schwannoma with a marginal dose of 12 Gy and a maximum dose of 24 Gy. Slight tumor enlargement was observed on MRI performed in the referring hospital 3 years after GKRS (Fig. 1A–D). On close follow-up at the same institute 6 months later with no additional treatment, MRI showed obvious enlargement of the tumor with irregular enhancement after gadolinium injection (Fig. 1E).

On arrival, the man was well oriented with a full range of eye movements. He exhibited right hemifacial sensory disturbances and palsy (House–Brackmann grade IV), mild right cerebellar ataxia and right-sided deafness. An MRI on admission revealed an iso-intense mass lesion measuring  $36 \times 36 \times 35$  mm in diameter at the right CPA (Fig. 2).

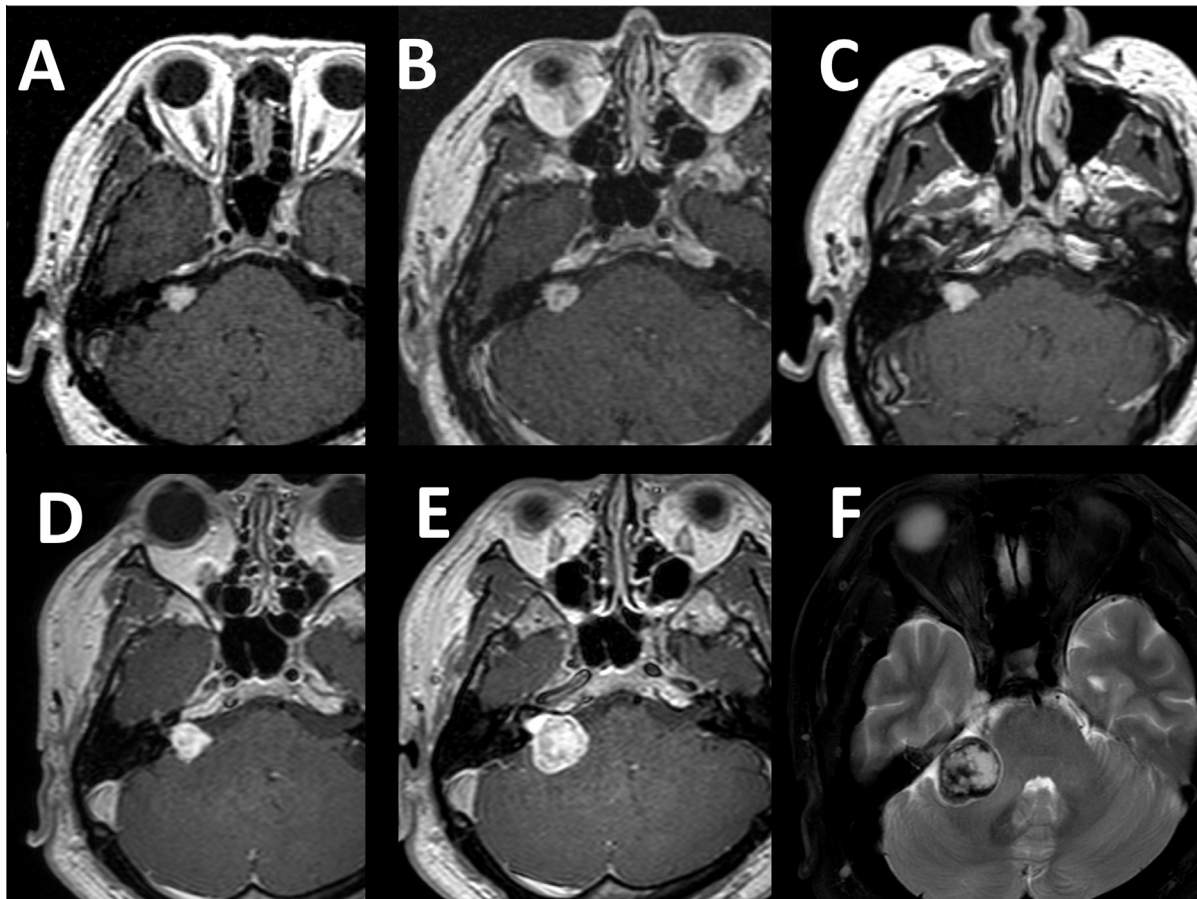
The first operation was conducted using a retrosigmoid approach. After gentle retraction of the cerebellum, a dark red and vascular tumor was observed. Because bleeding from the tumor wall was difficult to control intraoperatively, only partial removal was achieved. A right ventricular drain was placed to control the intracranial pressure. No major neurological deterioration was observed after the operation. No feeding artery that would be occluded by endovascular surgery was identified on a

postoperative angiogram and early phase tumor staining from the anterior cerebellar artery was not confirmed.

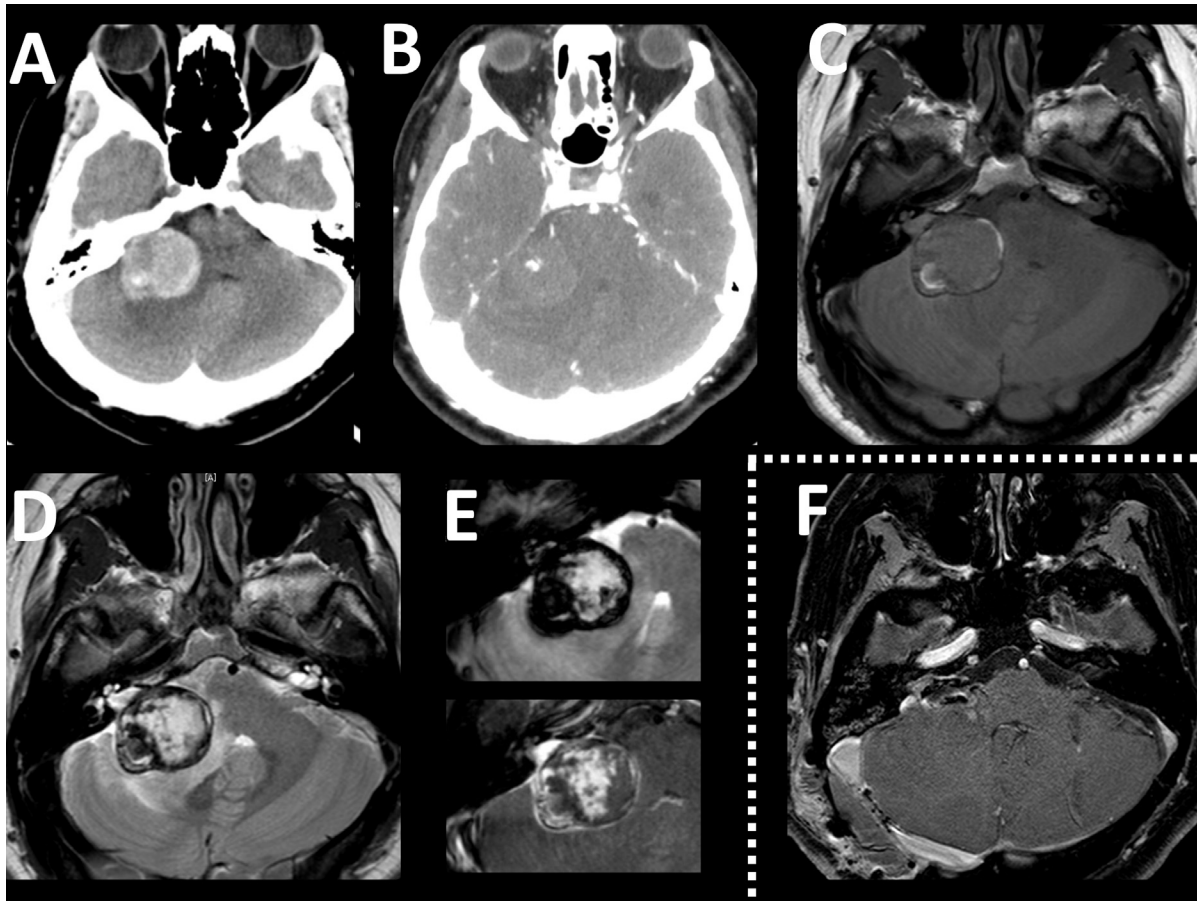
The second operation was performed 1 month after the first surgery and following the reduction of cerebral edema with steroids and osmotherapy. The same approach was used with the exception that the craniotomy was sufficiently enlarged to open the foramen magnum. At that surgery, the majority of the tumor capsule was observed to have changed to necrotic tissue and the hypervascularity of the tumor observed in the first operation was not apparent. A large hematoma cavity explaining the rapid increase in size in a short period of time was present inside the tumor capsule. Near total removal was achieved (Fig. 2F). Histopathological examination revealed massive intratumoral hemorrhage within a typical vestibular schwannoma with no malignancy. The patient exhibited good recovery after a short period of rehabilitation. The facial palsy improved to a House–Brackmann grade III and the Karnofsky Performance Scale score was 90 at 3 months after the second operation.

## 3. Discussion

Spontaneous intratumoral hemorrhage of vestibular schwannoma remains a rare entity [1]. Moreover, tumor expansion due to intratumoral hemorrhage is not the typical type of postradiosurgical tumor expansion. In their study of 254 patients with



**Fig. 1.** MRI showing sequential changes in the right vestibular schwannoma. (A) Axial, T1-weighted image with gadolinium contrast immediately before gamma knife radiosurgery (GKRS) showing a mass lesion in the cerebellopontine region. (B) Axial, T1-weighted image with gadolinium contrast 1 year after GKRS. (C) Axial, T1-weighted image with gadolinium contrast 2 years after GKRS showing no change in tumor diameter. (D) Axial, T1-weighted image with gadolinium contrast 3 years after GKRS showing slight enlargement of the mass. (E) Close follow-up T1-weighted axial with gadolinium contrast imaging at 3 years and 6 months after GKRS showing obvious enlargement of the mass with irregular enhancement. (F) T2-weighted image at the same time as E showing hemosiderin inside the mass lesion indicating intratumoral hemorrhage.



**Fig. 2.** (A–E) Axial MRI and CT scans on admission 3 years and 10 months after GKRS. (A) CT scan showing a relatively hyperdense mass lesion with (B) slight contrast enhancement inside the mass lesion. (C) The mass exhibited mixed intensity on T1-weighted imaging and (D) internal hyperintensity with a surrounding hemosiderin capsule on T2-weighted imaging and (E, upper) T2\*-weighted imaging. (E, lower) Irregular enhancement is evident inside the mass on fat-suppression T1-weighted imaging after gadolinium administration. (F) Axial, T1-weighted image with gadolinium contrast immediately after the second surgery showing near total removal of the mass.

acoustic neuroma treated by GKRS, Hasegawa et al. reported three typical classification patterns [2]. The first pattern involves central necrosis with a loss of central enhancement on MRI that typically occurs 3–6 months after GKRS. The second pattern is characterized by solid expansion that typically develops at the time of re-enhancement after a loss of central enhancement and normally occurs approximately 1 year after GKRS. The final pattern involves cystic enlargement, which can occur at any time. Delayed cyst formation is less likely to be transient or to require craniotomy [2]. In our patient, the mass began to expand rapidly 3 years after GKRS and included irregular enhancement of the tumor and hemosiderin imaging characteristics inside the tumor and in the tumor capsule (Fig. 1). Although central necrosis and solid expansion might be related, our patient differed from these three patterns of expansion. We assume that the causes of the rapid increase in size and the hemorrhage were an intratumoral infarction or venous occlusion that occurred a few years after the low dose radiotherapy. Four similar patients have been reported [3–5] and all of these patients exhibited rapid increases in hematoma size several years after radiotherapy.

A well known surgical risk of vestibular schwannoma removal following previous radiotherapy is a low rate of facial nerve preservation [6]. However, in the present patient, controlling the bleeding was very difficult in the first operation and was the most difficult part of the surgery. Therefore, a two stage surgery was employed and proved effective. Similar operative difficulties have been reported in one previous patient [5]. The hypervascularity

might have been induced by radiation. Cassis et al. reported vascular endothelial growth factor (VEGF) clustering around blood vessels in a vestibular schwannoma after GKRS which suggests that the VEGF-induced angiogenesis can promote tumor survival [7]. We also hypothesize that increased intratumoral pressure following an intratumoral infarction and venous occlusion followed by hemorrhage caused the additional difficulty in controlling the bleeding during the first operation.

The utility of SRS/SRT, including GKRS, for vestibular schwannoma is well known. However, we must emphasize that careful follow-up is still needed even after several years. While rare, a rapid increase in the size of a CPA tumor can easily result in neurological deterioration [2].

#### 4. Conclusion

Volume expansion due to intratumoral hemorrhage of a vestibular schwannoma can occur more than 3 years after GKRS. The degree of tumor hypervascularity that is likely to be encountered during the operation should not be underestimated preoperatively.

#### Conflicts of Interest/Disclosures

The authors declare that they have no financial or other conflicts of interest in relation to this research and its publication.

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# Metronidazole toxicity presenting with acute onset of aphasia and right sided weakness



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## ABSTRACT

We report a 37-year-old man with a history of cirrhosis and methicillin-sensitive staphylococcus aureus (MSSA) bacteremia who presented from a nursing home with 1 week of progressive confusion followed by acute onset of aphasia, forced left eye deviation and right sided weakness. While clinical presentation was concerning for a left middle cerebral artery stroke, MRI was consistent with leukoencephalopathy. The man had been on metronidazole for 2 months for treatment of *Clostridium difficile* infection. This case exemplifies a stroke mimic to be considered when a patient presents with an acute focal neurological deficit.

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## 1. Introduction

We report a 37-year-old man with a history of cirrhosis and methicillin-sensitive staphylococcus aureus (MSSA) bacteremia who presented from a nursing home with 1 week of progressive confusion followed by acute onset of aphasia, forced left eye deviation and right sided weakness. While clinical presentation was concerning for a left middle cerebral artery stroke, MRI was consistent with leukoencephalopathy. The man had been on metronidazole for 2 months for treatment of *Clostridium difficile* infection. This patient exemplifies a stroke mimic to be considered when a patient presents with an acute focal neurological deficit and the importance of maintaining metabolic dysfunction (metronidazole toxicity) in the differential diagnosis.

## 2. Case report

A 37-year-old man with a history of cirrhosis presented with wake up symptoms of aphasia and right sided weakness. The man had recently been treated with a course of antibiotics for MSSA bacteremia complicated by *C. difficile* associated diarrhea. He was completing a 6 week course of metronidazole at a nursing facility. One week prior to admission, he started complaining of dizziness and was noted to be increasingly confused. The patient initially presented to an outside facility for altered mental status. There, a CT scan of the head revealed no acute pathology. The patient was transferred to our facility at that time. At the time of

admission to our center he was able to speak, following commands and had full motor power throughout.

The following morning the stroke team was notified when the patient was found to have a left gaze deviation, right sided hemiplegia and global aphasia upon awakening. Head MRI was notable for confluent areas of restricted diffusion involving the left hemisphere which extended into the corpus callosum (Fig. 1A). This correlated with loss of signal on the apparent diffusion coefficient (ADC) image (Fig. 1B). T2 hyperintensities were seen within the bilateral dentate nuclei (Fig. 1C). Five days after metronidazole was stopped the patient improved clinically with resolution of the radiographic abnormalities (Fig. 1D–F). MRA obtained with the initial MRI (not shown) displayed patent neck and intracranial arteries.

## 3. Discussion

Metronidazole is a well-recognized neurotoxin associated with peripheral neuropathy as well as encephalopathy, cerebellar dysfunction [1–3,5] and seizures [1,2]. Particularly vulnerable neural substructures include the splenium of the corpus callosum, dentate nuclei, as well as the brainstem, with concomitant symptoms of confusion, dysarthria, ataxia and nystagmus [3,4]. Typically, lesions are bilateral and symmetric. Diffusion weighted imaging restricted diffusion associated with decreased ADC map, as was observed in our patient, is rare [4], as are focal symptoms such as gaze deviation, aphasia and hemiplegia. In a recent review of the literature, 64 patients with metronidazole toxicity were identified and only 11 had subcortical white matter tract involvement [2]. Most patients had cerebellar dysfunction (75%) and many had encephalopathy (33%) or seizures (13%).

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