CASE REPORT

Hypertrophic Olivary Degeneration after Gamma-knife Radiosurgery for Pontine Metastasis

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We present a case of a 57-year-old woman who underwent gamma-knife radiosurgery (GKRS) for pontine metastasis. Magnetic resonance (MR) imaging 2.8 months after GKRS showed T2 hyperintensity and hypertrophy of the left inferior olivary nucleus (ION) without gadolinium enhancement and smaller pontine metastasis. We diagnosed the signal change in the left ION as hypertrophic olivary degeneration (HOD) resulting from damage to the left central tegmental tract. We believe this is the first report to describe HOD after GKRS for pontine metastasis.

Keywords: gamma-knife radiosurgery, Guillain-Mollaret triangle, hypertrophic olivary degeneration, inferior olivary nucleus, magnetic resonance image

Introduction

Hypertrophic olivary degeneration (HOD) is a unique transsynaptic degeneration caused by lesions in the Guillain-Mollaret triangle, which comprises the dentate-rubro-thalamic, central tegmental, and olivocerebellar tracts.1 On magnetic resonance (MR) imaging, HOD can be seen as enlargement of the inferior olivary nucleus (ION) with T2 prolongation.2,3

We present a case of HOD after gamma-knife radiosurgery (GKRS) for pontine metastasis. Although HOD is a well known phenomenon after cerebrovascular diseases, such as hemorrhage or infarction involving the Guillain-Mollaret triangle, little is known about HOD occurring after GKRS for brain tumors.

Case Report

A 57-year-old woman underwent MR imaging of the brain one month after presenting with symptoms of walking disturbance and dysarthria. She had a history of surgery for right breast tumor 19 months earlier and postoperative adjuvant chemotherapy. The pathological diagnosis of the excised breast tumor was invasive ductal carcinoma, scirrhous type. On initial MR imaging, T2-weighted imaging showed hyperintense, well circumscribed tumors on the left side of the pontine tegmentum and subcortical region of the right inferior temporal gyrus (Fig. 1A). Mild peritumoral edema was evident in each tumor. No abnormal intensity was found in the medulla oblongata on the initial T2-weighted image (Fig. 1B). These tumors showed uniform enhancement, and no abnormal contrast enhancement was observed in the left ION. In images obtained 2.8 months after GKRS, the metastases displayed further decreases in size, and enlargement of the left ION with high intensity was found on T2-weighted image (Fig. 3A–C). Gd-enhanced...
**Fig. 1.** Initial magnetic resonance images from a 57-year-old woman with a history of right breast cancer. (A) T2-weighted image shows well circumscribed, hyperintense tumors on the left side of the pontine tegmentum and subcortical region of the right inferior temporal gyrus. (B) No abnormal intensity is apparent in the medulla oblongata on T2-weighted image. (C) These 2 tumors reveal uniform enhancement on gadolinium-enhanced T1-weighted image.

**Fig. 2.** T2-weighted images from 1.4 months after Gamma-knife radiosurgery (GKRS) for 2 metastases on the left side of the pontine tegmentum and right temporal lobe. (A) T2-weighted image shows reductions in the tumor size of each metastasis. (B) T2-weighted image also shows increased T2 signal intensity in the left inferior olivary nucleus (arrow).

T1-weighted images showed no contrast enhancement in the enlarged left ION (Fig. 3D). T2-weighted images 5 months after GKRS showed enlargement of the left ION with high intensity. Enlargement of the left ION was decreased at 18 and 29 months after GKRS on T2-weighted images, but the
Fig. 3. Magnetic resonance images from 2.8 months after gamma-knife radiosurgery. (A) Metastases have further decreased in size on T2-weighted image. (B) Enlargement of the left inferior olivary nucleus with high intensity is found on T2-weighted image (arrow). (C) The metastases that have decreased in size show slight enhancement on gadolinium (Gd)-enhanced T1-weighted image. (D) No contrast enhancement is apparent in the enlarged left inferior olivary nucleus on Gd-enhanced T1-weighted image.

Discussion

HOD is a pathological phenomenon that occurs after injury to the Guillain-Mollaret triangle, primarily as a result of hemorrhage or infarction. Several authors have reported typical MR imaging findings of HOD and its temporal evolution; T2 prolongation in the ION occurs about 3 weeks after cerebrovascular disease affecting the Guillain-Mollaret triangle. Hypertrophic ION with T2 prolongation appears about 5 months later, and MR imaging after a few years demonstrates atrophic ION. These MR imaging findings appear to correlate with the pathologic descriptions by Goto’s group. The initial MR imaging change of T2 prolongation at the ION may relate to an initial phase of neuronal hypertrophy, in which gliosis and increased water content are associated with demyelination and vacuolization. ION hypertrophy is likely the result of neuronal and astrocytic hypertrophic precursors to cell death. Finally, the ION undergoes atrophy. Clinical presentations associated with HOD include palatal tremor and ocular myoclonus. However, the incidence of these symptoms varies.

Some reports describe HOD occurring after surgical resection of a brain tumor, but HOD is rarely caused simply by a tumor in the Guillain-Mollaret triangle. We believe this case report represents the first published description of HOD following GKRS for a brain tumor.
GKRS is a stereotactic radiotherapy that targets only the position in the tumor bed where the radiologist or neurosurgeon directs the high dose, single-fraction irradiation, thereby avoiding radiation of healthy tissue. GKRS is available for various neurological diseases, such as arteriovenous malformations, acoustic neurinomas, meningiomas, and metastatic brain tumors. A few reports have shown histopathological changes at the site of irradiation following GKRS,\textsuperscript{10,11} Hirato and colleagues\textsuperscript{11} reported destructive changes, such as the disappearance of viable cells, coagulation necrosis, and fibrinoid degeneration of the vascular wall in the center of the target of GKRS. It is difficult to clarify whether MR imaging findings in our case indicate such histopathological changes. However, we suppose that invaded fibers within the left central tegmental tract had sufficient destructive histopathological damage by GKRS to cause secondary degeneration in the left ION. Though there are few reports of HOD presenting as enlargement of the ION at MR imaging within 4 months after onset in patients with cerebrovascular disease,\textsuperscript{2–4} we observed ION enlargement with T\textsubscript{2} prolongation 2.8 months after GKRS for pontine metastasis in our patient. We speculate that secondary degeneration of the ION after GKRS for brain tumor occurs more rapidly than secondary degeneration of the ION after cerebrovascular disease because of the difference in the degree and extent of histological damage involving the Guillain-Mollaret triangle.

In cases showing changes in ION signal after GKRS for tumors within the Guillain-Mollaret triangle, it is crucial that the neuroradiologist does not interpret such changes as tumor recurrence. In addition to the location of the irradiated field, a significant clue to diagnosis will be a lack of contrast enhancement within the enlarged ION.\textsuperscript{12} Because many kinds of malignant brain tumors demonstrate good contrast enhancement, Gd-enhanced T\textsubscript{1}-weighted imaging may be useful for distinguishing recurrent tumors from HOD.

In conclusion, damage involving the Guillain-Mollaret triangle after GKRS for brain tumors can cause ION enlargement with T\textsubscript{2} prolongation. This finding on MR imaging represents HOD and should be distinguished from tumor recurrence.

References