A 68-year-old male underwent surgical resection of a right cerebellar metastasis from non-small-cell lung carcinoma. Twelve weeks later, he presented with worsening difficulties in swallowing, verbal and written expression, word retrieval, and gait instability. Neurological examination demonstrated left facial droop, right arm weakness, and slurred speech. Extremity strength was 5/5 and extremity sensation was intact to light touch. Finger–nose–finger testing was dysynergic bilaterally, but slightly worse on the right.

Magnetic resonance imaging (MRI) of the brain revealed non-enhancing T2 hyperintense signal in an enlarged left inferior olivary nucleus (Fig. 1A and B). Prior surgical resection of the right cerebellum involved the region of the dentate nucleus and there was nodular enhancement along the margin of the surgical cavity (Fig. 1C). Imaging findings were compatible with recurrent right cerebellar metastasis and hypertrophic left olivary degeneration.

**Diagnosis**
Hypertrophic olivary degeneration.

**Discussion**
Hypertrophic olivary degeneration (HOD) is a form of transynaptic degeneration. Any lesion interrupting the neuronal pathways connecting the Guillain–Mollaret triangle (also known as the dentatorubral-olivary pathway) can result in hypertrophic olivary degeneration. The Guillain–Mollaret triangle is composed of the ipsilateral red and inferior olivary nuclei and contralateral dentate nucleus of the cerebellum (Fig. 1D). The red nucleus communicates with the ipsilateral inferior olivary nucleus via the central tegmental tract; the inferior olivary nucleus communicates with the contralateral dentate nucleus via the inferior cerebellar peduncle, and the dentate nucleus communicates with the contralateral red nucleus via the superior cerebellar peduncle. The inferior olivary nucleus also communicates with the contralateral cerebellum via the inferior cerebellar peduncle. Consequently, lesions leading to HOD of the left inferior olivary nucleus would involve the left central tegmental tract or right dentate nucleus and/or superior cerebellar peduncle. In our case, the right cerebellar resection involved the dentate nucleus, resulting in loss of transynaptic input on the left inferior olivary nucleus with subsequent degeneration.

Commonly described lesions interrupting the dentatorubral-olivary pathway include ischemic insult, hemorrhage (hypertensive, cavernous malformation, trauma), neoplasm, and demyelination. HOD is almost always unilateral and is ipsilateral to the lesion if it involves the brain stem or contralateral if the lesion involves the cerebellum. Cases of bilateral HOD are rare but have been reported. The inciting lesions in these cases were close to or at the midline at the level of the brachium conjunctivum, where they could conceivably interrupt the decussation of the bilateral dentato-olivary fibers.

Typically, CNS degeneration leads to atrophy characterized by neuronal loss and proliferation of glial elements. Transneuronal degeneration leading to hypertrophy is a distinctive finding localized to the inferior olivary nucleus. Pathological changes of HOD include vacuolar degeneration, neuronal enlargement, astrocyte hypertrophy, and gliosis. These changes lead to macroscopic enlargement of the olive with corresponding nonenhancing focus of T2 hyperintensity on MRI, which is characteristic for HOD. These imaging findings are not immediate but can be observed from approximately 3 weeks to 6 months post ictus. Differential considerations for a T2 hyperintense lesion in the olivary region include infarct, neoplasm, demyelinating process, and infection. However, the lack of enhancement excludes the majority of neoplastic and infectious entities and enlargement of the olive would be atypical in the setting of infarction or chronic demyelination. The most important clue is the association with the inciting lesion of the contralateral cerebellum or ipsilateral brain stem.

There is a spectrum and predictable temporal sequence of microscopic pathological findings in HOD that are well documented. Acutely, no olivary changes are observed within 24 hours of onset, but degeneration of the peripheral white matter of the olive begins between 2 to 7 days. There are three pathological stages of olivary hypertrophy ranging from mild olivary hypertrophy without glial reaction (approximately 3 weeks), culminating olivary hypertrophy with hypertrophy of both neu-
rons and astrocytes (approximately 8.5 months), and olivary pseudohypertrophy with neuronal dissolution with gemistocytic astrocytes (approximately 9.5 months and later). Olivary atrophy is the last stage with neuronal disappearance seen after several years. Corresponding to the pathological changes of HOD, there are three distinct phases seen on MRI. The first stage shows increased T2 signal in the inferior olivary nucleus without hypertrophy and usually occurs within 6 months of the ictus. The second stage shows increased T2 signal and hypertrophy of the inferior olivary nucleus and usually resolves by 3 to 4 years after the ictus. Ultimately, in the third stage, atrophy ensues after several years and olivary shrinkage becomes apparent on MRI, although increased T2 signal can persist.

Common clinical manifestations of HOD include palatal myoclonus and other involuntary movements. Palatal myoclonus is characterized by rhythmic involuntary movements of the oropharynx and usually develops within 10 to 11 months after the inciting lesion but does not always accompany olivary hypertrophy. Anatomically, this correlates with lesions involving the central tegmental tract, which has several connections to the nucleus ambiguous of the vagus nerve involved in control of palatal movement. HOD may also lead to loss of inhibitory control via the dentato-rubral pathway. Clinically this manifests as dentato-rubral tremor characterized by involuntary delayed onset of muscle contraction at 1 to 3 cycles per second. Synchronous contractions of the cervical muscles and diaphragm may also be present. Although the imaging findings of HOD resolve over time, the clinical symptoms typically persist. Our patient had none of these symptoms and gait disturbance was the predominate complaint. However, this may reflect an early stage of HOD where MRI findings are apparent, but without obvious clinical symptoms.

HOD is an interesting imaging entity with characteristic clinical and imaging manifestations. This process should be recognized when there is nonenhancing enlargement of the inferior olivary nucleus with corresponding T2 hyperintensity. Although the differential for a nonenhancing T2 hyperintense lesion is extensive, an inciting lesion in the contralateral cerebellum or ipsilateral brainstem strongly favors the diagnosis of HOD.

References