

Hypertrophic olivary degeneration and palatal myoclonus from a *Streptococcus intermedius* infection of the brain: illustrative case

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BACKGROUND Hypertrophic olivary degeneration (HOD) is a rare condition that can occur after disruption of the Guillain-Mollaret triangle. Clinically, HOD can present with palatal myoclonus with or without oculopalatal tremor, which sometimes results in symptomatic dysphagia and/or speech abnormalities. This condition is commonly associated with vascular lesions, with only three prior reported cases of HOD resulting from intracranial abscess.

OBSERVATIONS An otherwise healthy patient developed multiple intracranial abscesses. Biopsy showed gram-positive cocci; however, culture findings were negative. Polymerase chain reaction (PCR) identified *Streptococcus intermedius*. The patient demonstrated palatal myoclonus and vertical nystagmus, which resulted in persistent mild dysphagia and altered speech intonation. After appropriate antimicrobial therapy with resolution of the enhancing lesions, symptoms persisted. Follow-up imaging demonstrated progressive hypertrophy of the right olive with persistent disruption of the right-sided rubro-olivary fiber pathways.

LESSONS Although HOD classically occurs after vascular insult, it can also be seen as a postinfectious sequela. Despite eradication of the infection, palatal myoclonus and oculopalatal tremor may have a persistent impact on quality of life due to impaired speech and swallowing. This case emphasizes the utility of universal PCR in detecting fastidious organisms as well as diffusion tensor imaging for characterization of disrupted fiber pathways.

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KEYWORDS brainstem; diffusion tensor imaging; Guillain-Mollaret triangle; hypertrophic olivary degeneration; palatal myoclonus; *Streptococcus intermedius*

Hypertrophic olivary degeneration (HOD) is a rare neurological phenomenon and is thought to occur due to the disruption of the dento-rubro-olivary pathway, also known as the Guillain-Mollaret triangle (GMT).¹ The GMT consists of the red nucleus in the midbrain, inferior olive in the medulla, and contralateral dentate nucleus in the cerebellum. The underlying pathology of the disruptive lesions can be varied, and the literature has reported diverse causes, including autoimmune, neoplastic, infarction, hemorrhage, trauma, surgical, vascular malformations, and infectious.² The most common lesions are cavernous malformations, ischemic and hemorrhagic, with infectious being the least common.² Here we present the first

reported case of HOD in the setting of *Streptococcus intermedius* abscess.

Patients with HOD typically present with palatal tremor (PT) with or without an ocular component consisting of an oculopalatal tremor (OPT). PT is often described as a rhythmic contraction of the levator veli palatine unilaterally or bilaterally raising the soft palate posteriorly and superiorly in a synchronous fashion. Patients with PT usually do not have difficulties with swallowing or speech and continue to experience tremors while sleeping.³ When present, the ocular component of the tremor is in sync with the palatal tremor occurring at a 1–3-Hz frequency.³ OPT is routinely described as

ABBREVIATIONS CTT = central tegmental tract; GMT = Guillain-Mollaret triangle; HOD = hypertrophic olivary degeneration; MRI = magnetic resonance imaging; OPT = oculopalatal tremor; PCR = polymerase chain reaction; PT = palatal tremor; SCP = superior cerebellar peduncle.

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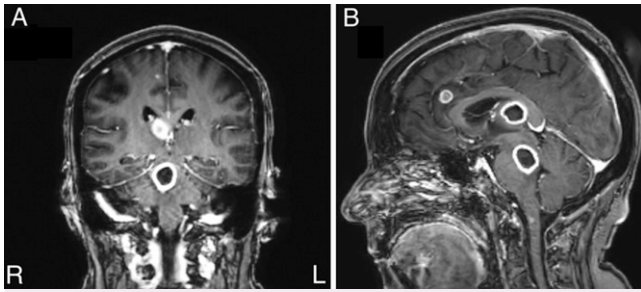


FIG. 1. Coronal (A) and sagittal (B) contrast MRI showing multiple ring-enhancing lesions consistent with intracranial abscesses. Note the largest lesion located dorsally near the junction of the pons and midbrain.

pendular nystagmus and is present in 30% of cases.^{1,4} PT or OPT usually presents 2 to 48 months after initial insult, with a median of 10 months.^{1,5,6} However, delayed presentation of up to 8 years has been reported in the literature.^{1,5} Tremors usually progressively worsen from 5 to 24 months after initial presentation and rarely improve or completely resolve.^{1,7} Treatment is supportive with botulinum toxin injections for the PT.³ OPT is more difficult to treat, and gabapentin and memantine are used with some success.³

Most lesions of neuronal tracts lead to subsequent atrophy. HOD paradoxically presents with olivary hypertrophy. The exact mechanism of this hypertrophy is not fully understood. One explanation states that the denervation of the dento-olivary pathway releases tonic inhibition of olivary neurons that under normal circumstances may develop sustained synchronized oscillations.¹ Histopathological and radiological studies have demonstrated neuronal enlargement in the setting of vacuolization of neurons with associated astrocytic hypertrophy and gliosis with astrocytic mitochondrial proliferation in the setting of hyperperfusion.^{1,8,9} The natural history of the HOD includes initial degeneration of the olivary amiculum at 7 days

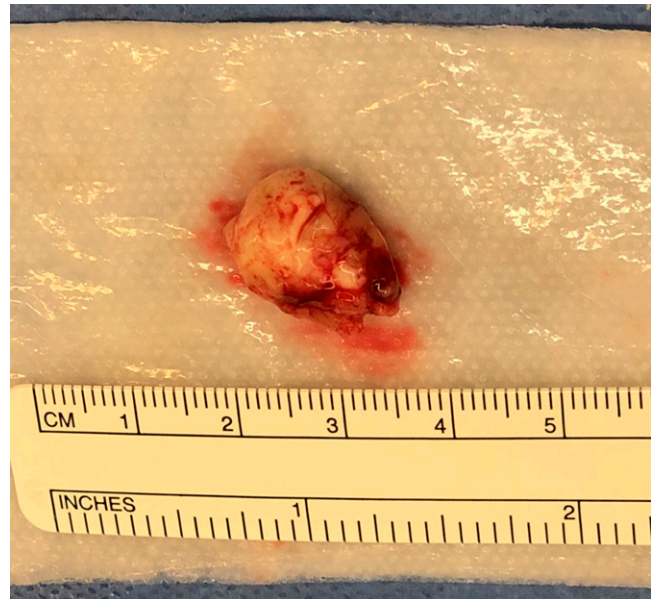


FIG. 2. A superficial intracerebral encapsulated abscess taken from the patient after a left frontal craniotomy.

followed by mild olivary enlargement, with neuronal hypertrophy at 3 weeks without glial reaction and subsequent hypertrophy of neurons and astrocytes at 8 months.¹ These neuropathological findings are concordant with radiological findings wherein the initial presentation of HOD was 1 month after the inciting lesion with T2 fluid-attenuated inversion recovery hyperintensity observed in the inferior olivary nucleus, followed by olivary hypertrophy at 6 months and resolution between 3 and 4 years.^{9,10}

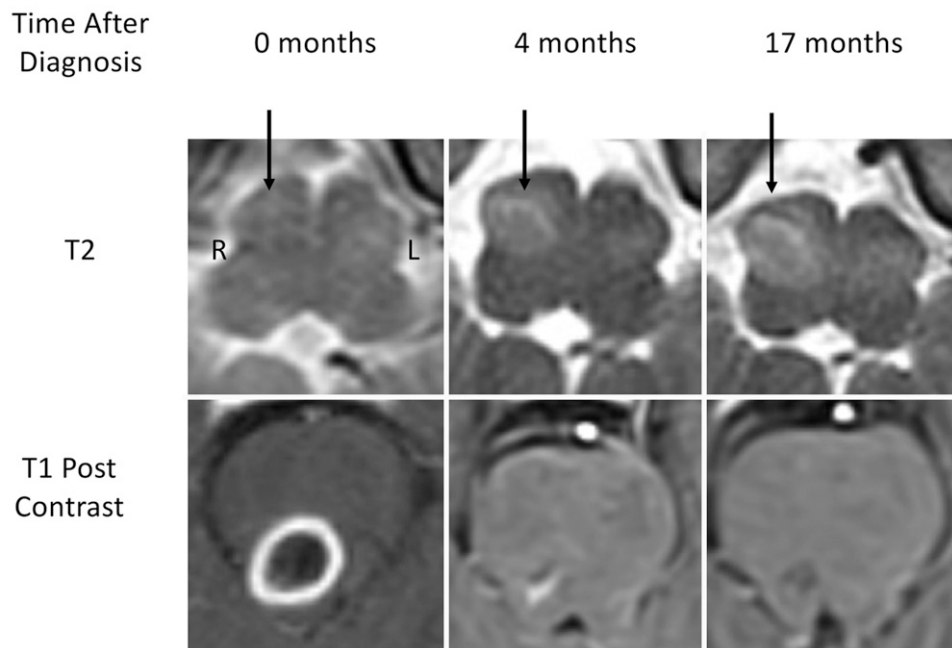


FIG. 3. Serial axial T2-weighted MRI at the level of the medulla (*upper*) and T1-weighted contrast MRI at the level of the rostral pons (*lower*) obtained on diagnosis and up to 17 months after treatment.

Illustrative Case

A 58-year-old female patient presented with dysarthria and palatal myoclonus. She also exhibited a mild, left-sided fourth-nerve palsy and vertical nystagmus with a slight rotatory component. She

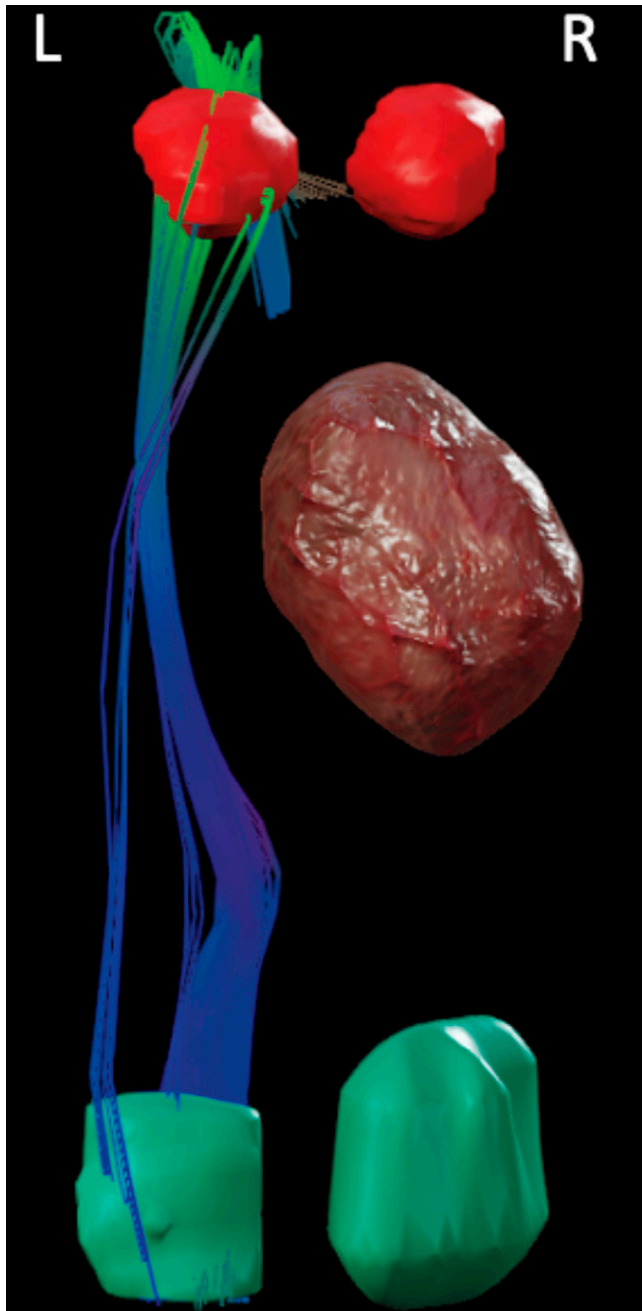


FIG. 4. Three-dimensional reconstruction of magnetic resonance diffusion tensor imaging demonstrating the expected fiber tracts between the unaffected red nucleus in the midbrain and the inferior olive complex of the medulla (*left side*). Note the lack of right-sided fiber tracts on the side ipsilateral to the superimposed site of the abscess. Red nuclei are colored in *red*, medullary olives are shown in *green*, and the pontine cerebral abscess at the time of diagnosis is shown in *brown*. Note the reversal of sidedness as compared with conventional radiographic imaging.

had a spastic gait and difficulty with coordination, as well as a tendency to fall backward if she closed her eyes. Magnetic resonance imaging (MRI) revealed numerous supratentorial and infratentorial ring-enhancing lesions demonstrating diffusion restriction, findings concerning for abscess (Fig. 1). Blood cultures were negative. Transesophageal echocardiography showed aortic valve vegetations. An open biopsy for a cortically based ring-enhancing lesion was performed (Fig. 2). The initial Gram stain demonstrated gram-positive cocci, but cultures showed no growth. Thus, universal polymerase chain reaction (PCR) on the tissue was performed with detection of *S. intermedius*.

In the absence of an alternative source, transient bacteremia from oral/pharyngeal colonization resulting in endocarditis and subsequent septic emboli was presumed. No predisposing immunocompromising conditions were found on work-up. The patient was treated with ceftriaxone, and subsequent MRI revealed resolution of the multifocal intracranial abscesses with progressive hypertrophy of the right olive (Fig. 3). During multiple follow-up visits over the course of nearly 2 years, the patient's symptoms improved as she continued with rehabilitation. However, between years 1 and 2, she plateaued with her treatment, and her swallowing, speech, and walking worsened.

Discussion

In our case, a right-sided abscess within the dorsal midbrain–pontine junction likely caused disruption of the ipsilateral central tegmental tract (CTT), which in turn caused an ipsilateral HOD. The

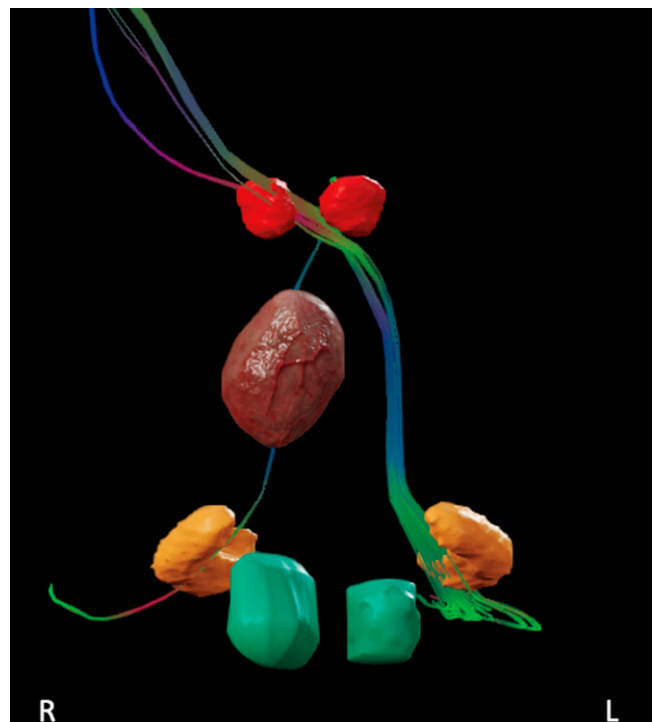


FIG. 5. An alternative view of a three-dimensional reconstruction of magnetic resonance diffusion tensor imaging wherein the fibers directly connecting the red nuclei (*red color*) to the contralateral dentate nucleus within the cerebellum (*tan*) are segmented. Connections with the inferior medullary olives (*green*) are not highlighted in this figure. The abscess (*brown*) involves the right superior cerebellar peduncle disrupting connections between the right dentate nucleus and left red nucleus.

abscess also impacted the superior cerebellar peduncle (SCP), causing a lesser contralateral HOD. The CTT contains axonal fibers from the midbrain that project to the inferior olivary complex, thus playing a role in motor coordination. Magnetic resonance fiber tracking, an imaging technology used to visualize white matter tracts on MRI, showed disruption of the right-sided dento-olivary pathways (Fig. 4), correlating with the right-sided olivary hypertrophy. Lesions of this tract can cause palatal myoclonus. The SCP connects the midbrain with the cerebellum, playing a role in coordination and gait. Atrophy and disruption of the SCP has led to supranuclear palsy and ataxia.¹¹ When fibers passing from the red nucleus to the contralateral nucleus were mapped, there was disruption of the fibers passing through the SCP (Fig. 5).

Observations

Patients with HOD typically present with palatal myoclonus with or without OPTs.³ HOD can be the result of various conditions, including trauma, neoplasm, surgery, or abscess. In this case, HOD was the result of an *S. intermedius* abscess near the dorsal midbrain–pontine junction. *S. intermedius*, also known as *Streptococcus milleri*, is known for its tendency to cause abscesses in the brain and liver. Review of the literature reveals three previously reported cases of infection-related HOD: one case of toxoplasmosis and two cases of listeria. To our knowledge, this is the first reported case of HOD secondary to *S. intermedius*. Lesion location is likely a more significant factor in the development of HOD than causative organism; however, more research into this rare entity is warranted.

The patient in this case developed progressive ataxia and palatal myoclonus secondary to the HOD. Unfortunately, there was no clear treatment for the ataxia or the palatal myoclonus. Therefore, therapies focused on management of ataxia through supportive care, such as physical therapy and speech therapy. Certain medications have been described for management of ataxia, including bupropion, amantadine, riluzole, varenicline, and acetazolamide, but the marginal benefits must be considered in the context of possible side effects.¹² For the palatal myoclonus, botulinum toxin injection can be administered to the palate, and medications can be used, including carbamazepine, lamotrigine, and sodium valproate.³ For the gaze-evoked nystagmus, gabapentin or memantine can be considered.¹³ In our case, the patient deferred medical therapy due to the potential side effects and elected for speech and physical therapy.

Lessons

Lesions within the GMT can result in HOD associated with disabling, chronic palatal myoclonus. Therapies should be discussed with the patient to manage symptoms such as palatal myoclonus, ataxia, and nystagmus—therapies that will ultimately improve the patient's quality of life. Most patients presenting with symptomatic HOD will see their symptoms improve over time. The use of magnetic resonance diffusion tensor imaging has only been reported once, and our hope is that this case may help to further illustrate the pertinent anatomy and aid physician and patient understanding. It may also play a role in further elucidating the complex regional neuroanatomy involved in HOD, and we hope it may lead to more effective treatments, such as with neuromodulation, in the future.

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Disclosures

Dr. Tyrrell is a paid full-time employee of Brainlab, Inc. No other disclosures were reported.

Author Contributions

Conception and design: Robin, Tonnu, Zervos. Acquisition of data: Hunt, Zervos. Analysis and interpretation of data: Robin, Tonnu, Hunt, Tyrrell. Drafting the article: Tonnu, Zervos, Hamilton. Critically revising the article: Robin, Tonnu, Hunt. Reviewed submitted version of manuscript: Robin, Tonnu, Hunt, Zervos, Tyrrell. Approved the final version of the manuscript on behalf of all authors: Robin. Study supervision: Robin, Zervos.

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