Oculopalatal Tremor

58-year-old male presenting with oscillopsia and voice changes for 5 months following left medullary stroke

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INITIAL PRESENTATION

Chief Complaint: “Shaking eyes”

History of Present Illness

A 58-year-old male with PMH of atrial fibrillation, hypertension, hyperlipidemia, and obstructive sleep apnea presented to the eye clinic with bilateral “shaking eyes” and voice changes for the past 5 months. The patient started experiencing neurological symptoms approximately 1 year prior, when he had an episode of right-sided numbness lasting 5-10 minutes. Workup determined this was a TIA and he was started on aspirin and Plavix. Approximately one month later, he had a similar episode of right-sided numbness/weakness which did not resolve. MRI showed a brainstem stroke in the left side of the medulla. The stroke was ultimately determined to be related to paroxysmal atrial fibrillation, and he is being treated with anticoagulation.

About 5 months after the initial stroke, he developed involuntary movement of the eyes and a voice change. He reported oscillopsia, described as feeling his vision bouncing. An MRI brain completed 2 months later showed hypertrophy of the left inferior olivary nucleus in the ventral medulla. Since the onset of his nystagmus, the oscillopsia has persisted although it is reportedly more tolerable in the mornings. According to his wife, the voice changes appeared around the same time as the vision changes. He denies vision loss but endorses intermittent binocular double vision for the past 1-2 weeks.

Past Ocular History

- None

Past Medical History

- Atrial fibrillation
- Hypertension
- Hyperlipidemia
- Obstructive sleep apnea

Medications

- Apixaban 5 mg BID
- Atorvastatin 80 mg
- Valsartan- hydrochlorothiazide 80-12.5 mg
- Baclofen 10 mg TID
- Diclofenac 1% topical gel 2g PRN
- Fluticasone 50 mcg/actuation nasal spray PRN

Allergies

- Environmental

Family History

- Glaucoma - mother
- Macular Degeneration - father

Social History

- Prior smoker, 2-pack-years, quit 34 years ago
- Used chewing tobacco frequently, but quit in 2023 after stroke
- Prior daily drinker, now 1 drink per weekend

Review of Systems

- Negative, unless discussed in HPI

OCULAR EXAMINATION

- **Snellen**
  - Right eye (OD): 20/50-1
  - Left eye (OS): 20/25-2
- **Other Visual Acuity Tests**
  - OD: 20/30 ph
  - OS: NI ph
- **Ocular Motility/Alignment**
  - OD: Full, Ortho, Nystagmus
  - OS: Full, Ortho, Nystagmus
  - Nystagmus: Conjugate torsional pendular nystagmus with moderate amplitude and ~2 Hz frequency in all gaze positions. Ocular oscillations were synchronous with palatal tremor
- **Intraocular Pressure (IOP) (*Tonopen***
  - OD: Patient deferred IOP measurement with Tonopen, soft to palpation
  - OS: Patient deferred IOP measurement with Tonopen, soft to palpation
- **Pupils**
  - OD: 5 mm in dark, 3 mm in light, no relative afferent pupillary defect (RAPD)
  - OS: 5 mm in dark, 3 mm in light, no RAPD
  - Mild light-near-dissociation bilaterally
- **Confrontation visual fields (*Counting fingers***
  - Full OU
- **External**
  - Normal
- **Slit lamp examination**

Lids/lashes	Normal OU
Conjunctiva/sclera	Clear and quiet OU
Cornea	Clear OU
Anterior Chamber	Deep and quiet OU
Iris	Normal architecture OU
Lens	1-2+ NS OU

- **Dilated fundus examination (DFE)**

Vitreous	Normal

Disc	Normal
Cup-to-disc ratio	0.25 OU
Macula	Normal
Vessels	Normal
Periphery	Normal

- **Additional Testing**

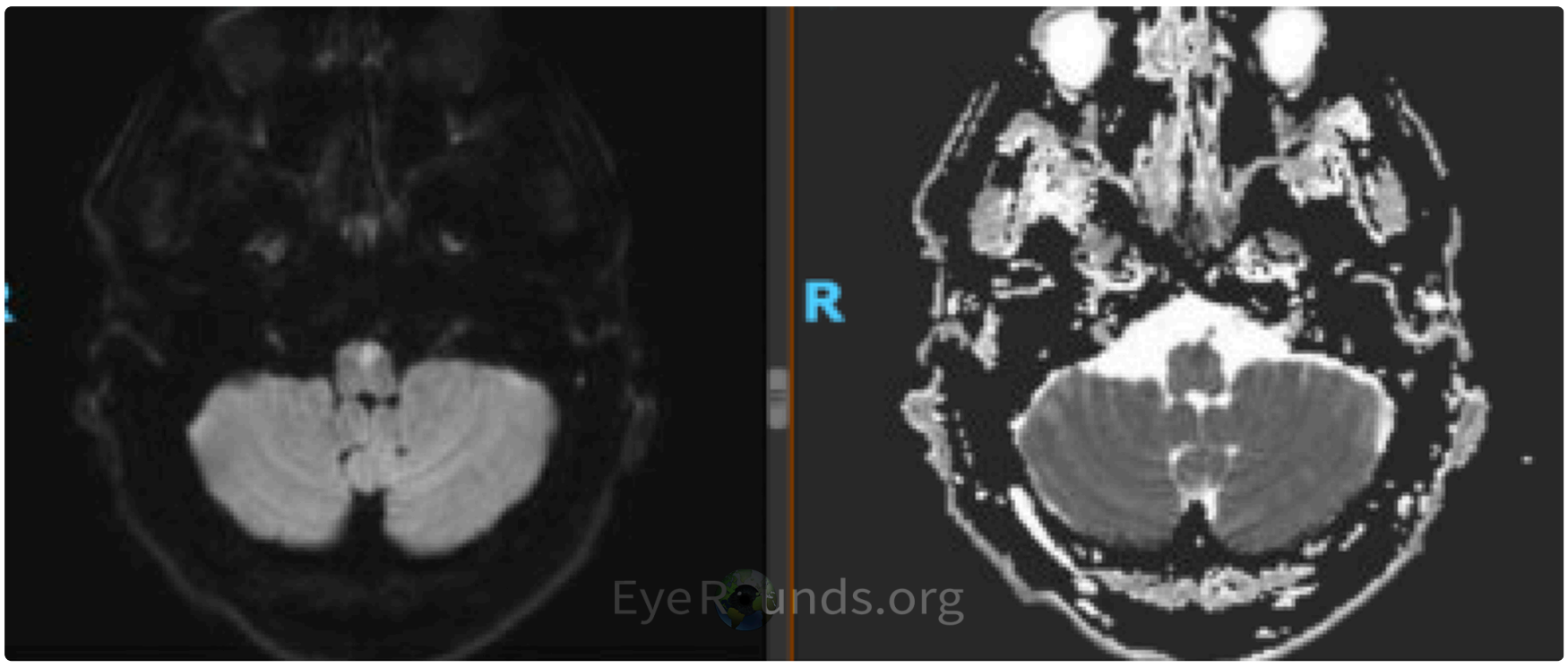

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Figure 1. Initial MRI after acute stroke: Diffusion restriction in the left medulla

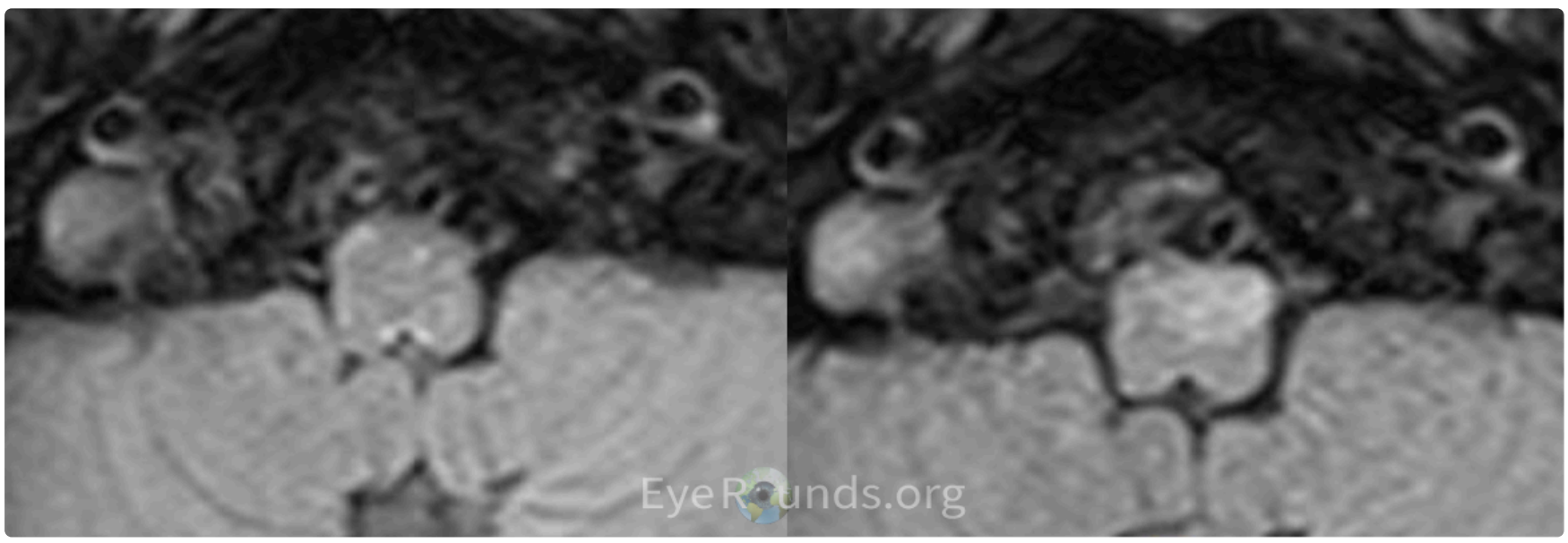

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Figure 2. Follow up MRI 7 months later: Hypertrophy of left inferior olivary nucleus. Baseline (left) and follow-up (right) T2 axial FLAIR images demonstrating interval hypertrophy of the inferior olivary nucleus. The above-pictured infarct was located just superior to this level.

- **Other Physical Exam Findings:**
  - HEENT
    - Soft palate tremor – rhythmic elevations, ~2 Hz
    - **insert palatal tremor video**
  - Neuro:
    - Holds right hand in flexed position
    - Does not have full active extension at right elbow and wrist
    - Drift of RUE
    - Circumducts RLE during gait examination

DIFFERENTIAL DIAGNOSIS:

- Palatal myoclonus
- Acquired pendular nystagmus secondary to multiple sclerosis
- See-saw nystagmus
- Oculo-masticatory myorhythmia/ Oculo-facio-skeletal myorhythmia
- Holmes tremor
- Pendular nystagmus from vision loss
- Congenital pendular nystagmus
- Pendular pseudo-nystagmus

CLINICAL COURSE

Based on the synchronous ocular oscillations and palatal tremor that developed months after a medullary infarct in the path of the Guillan-Mollaret triangle, coinciding with hypertrophy of the inferior olivary nucleus, a diagnosis of oculopalatal tremor was made.

His corticospinal tract lesion has led to spastic weakness in the right upper and lower extremities, for which he is undergoing physical therapy.

For his OPT, he was initially treated with memantine 5 mg BID, which led to a mild improvement in his oscillopsia. His dose was escalated to 10mg to try to provide further benefit.

DIAGNOSIS: Oculopalatal Tremor

DISCUSSION

Etiology/Epidemiology

Oculopalatal tremor (OPT) is a rare, acquired syndrome of continuous and rhythmic movements of the soft palate in conjunction with pendular nystagmus. The disease most commonly arises from a posterior circulation cerebrovascular accident disrupting the dentato-rubro-thalamic tract also known as the Guillain-Mollaret triangle (1,2). A retrospective review by Jang et al. showed that the average age at diagnosis was 54 with a male predilection (3). The most common etiology was vascular in nature although other causes include demyelination, infection, CNS inflammation, brainstem tumors, iatrogenic trauma to the brainstem or cerebellum, and diffuse axonal injury (1,4, 5). Among vascular etiologies, hemorrhagic lesions are more common than ischemic lesions (6).

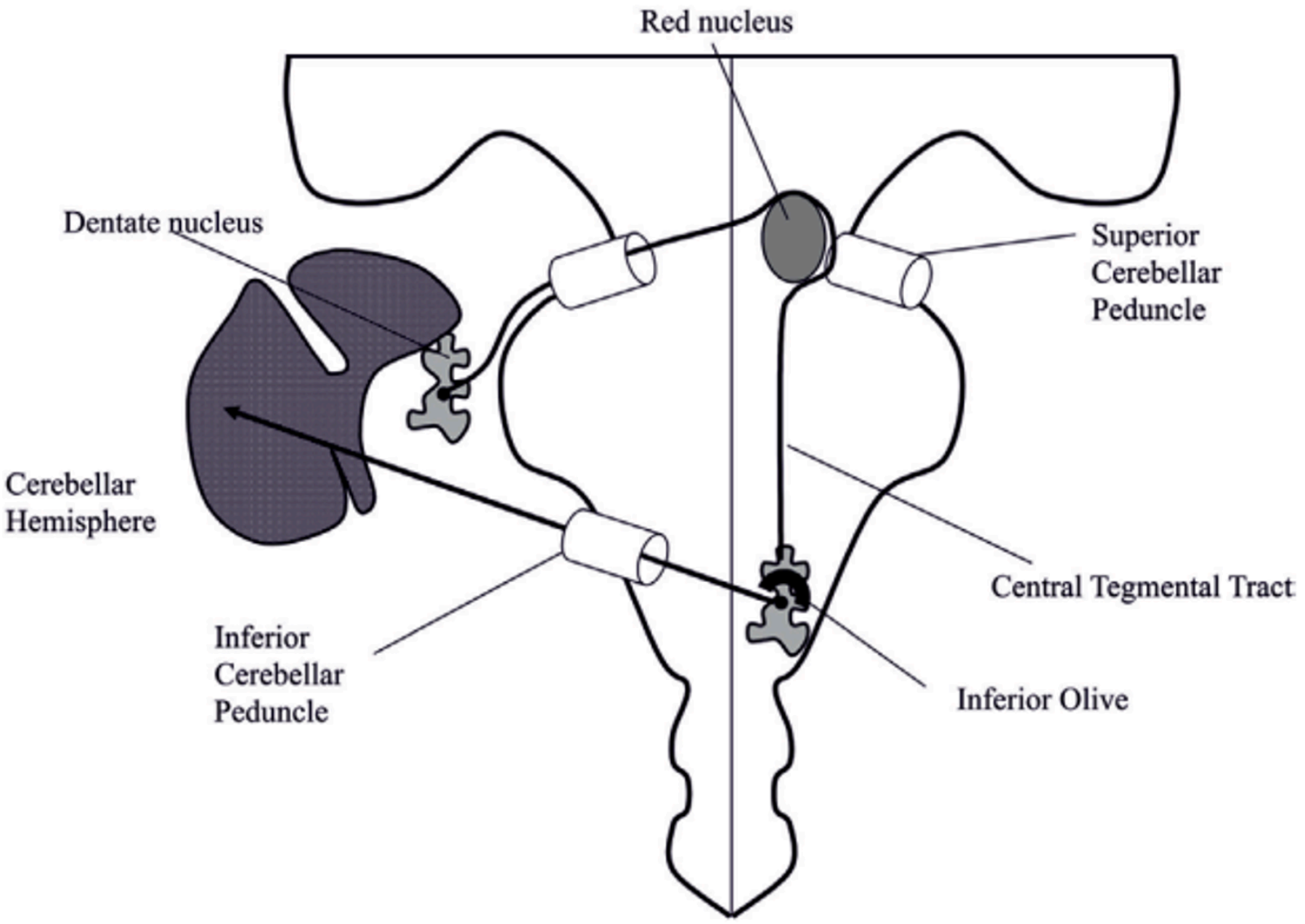

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Figure 3. Tilikete C, Desestret V. Hypertrophic Olivary Degeneration and Palatal or Oculopalatal Tremor. Front Neurol. 2017 Jun 29;8:302.

Pathophysiology

OPT can develop weeks to years after initial insult to the Guillain-Mollaret triangle (GMT), although the complication most typically presents within the first 6-8 months (1). The GMT is a pathway from the dentate nucleus in the cerebellum to the contralateral red nucleus, then to the inferior olive in the superior medulla through the superior cerebellar peduncle via the central tegmental tract, and finally back to the deep cerebellar nuclei (2,4,7). Normally, the deep cerebellar nuclei inhibit conduction through dendro-dendritic gap junctions between adjacent inferior olivary neurons. Lesions to the Guillain-Mollaret triangle result in pseudohypertrophy of inferior olivary neurons, which leads to abnormal soma-somatic gap junctions in which the inhibitory effect is removed (1, 2). These pathologic changes lead to synchronous discharge from the hypertrophied inferior olive, which is the most commonly proposed mechanism of the development of binocular oscillations in the horizontal, vertical, and/or torsional axes in a conjugate or disconjugate manner (2). More recent evidence suggests that lesions involving the central tegmental tract (CTT) are more specifically associated with OPT (2,7).

Shaikh et al. suggest a dual-mechanism hypothesis that involves the hypertrophic inferior olive as the generator of regular, jerky, and pulsatile oscillations while the subsequent maladaptive plasticity of the cerebellum acts as an amplifier and also contributes to smoothing of the waveforms produced by the inferior olive in OPT (2). The inferior olive transmits its signal to the cerebellum via two distinct pathways: directly on large climbing fibers, and indirectly via climbing fiber collaterals that go to the vestibular nuclei, which are pathologically coupled in OPT (1,2). This coupled oscillator output is smoothed by the cerebellum, which learns to pause at the time of the next inferior olive neuronal pulse. Thus, multiple cerebellar neurons pause together to create a smooth output, resulting in a larger, smoother, and less periodic waveform than what would be expected from the inferior olive alone (2). It is also thought that the hyperactive olivo-cerebellar circuit creates an abnormal perception of self-motion, which may contribute to the disabling perceptual function most OPT patients experience (7, 8).

The rhythmic pharyngeal movements are due to contraction of the levator veli palatini muscle (1). Other muscles derived from the branchial arches may more rarely additionally be involved (3).

Signs/Symptoms

Patients with OPT often complain of oscillopsia, or the perception of an unstable visual environment. Oscillopsia is associated with impaired visual acuity and depth perception and is often significantly distressing and disabling for patients (7). The rhythmic palatal movements involving tensor veli palatini may present with voice changes and/or symptoms of ear clicking (9).

Oscillations of the eyes, palate, and occasionally other muscles such as facial muscles, pharynx, tongue, larynx, diaphragm, mouth of Eustachian tube, and less commonly neck, trunk, or extremity involvement are low frequency (1-3 Hz), aperiodic, and smooth in OPT (2). Although more commonly synchronous, the nystagmus may also be asynchronous with the palatal tremor (1). The nystagmus is typically vertical and pendular but may also be horizontal and torsional (4). “Pendular” nystagmus refers to smooth and eye movements that are equal in speed in both directions. This contrasts with jerk nystagmus, in which there is a slow deviation phase and a fast corrective phase (9). Convergent-divergent nystagmus has also been described in OPT. Abnormal eye movements may be unilateral, bilateral, symmetric, or asymmetric. Eye movements are usually nystagmoid but may even be saccadic. Movements may also be dissociative between the two eyes (4). Dissociated pendular nystagmus may be caused by asymmetric ophthalmoplegia and concomitant INO, although many unknown factors may also be at play (10). If the vestibular ocular pathway is involved, vertical binocular diplopia may also be present secondary to skew deviation due to its proximity to the Guillain-Mollaret triangle (1). Patients also frequently have a deficit in horizontal eye movement (4). Eye movement waveforms have been shown to vary between patients; a previous study has shown that OPT patients have distinct patterns of waveforms (2,11).

If an ocular component is absent, the entity is known as palatal myoclonus (1).

Patients frequently present with contralateral hemiplegia, contralateral hemi-hypoesthesia, and/or ipsilateral cerebellar syndrome (4). Additional palsies of cranial nerves V- XII or damage to spinothalamic and pyramidal tracts may be present (9). If unilateral cerebellar signs are present, pendular nystagmus tends to be more prominent on the affected side (4). Delayed tardive ataxia may be present in patients with large bilateral acute lesions (12).

Testing/Laboratory work-up

- Evaluation of the character of nystagmus
    - i.e. pendular, torsional, vertical/horizontal components, conjugate, disconjugate
- Evaluation of soft palate for rhythmic movement of pharynx
    - Typically synchronous with ocular oscillations
- Evaluation of other neurologic deficits including stroke-like symptoms, ear clicks secondary to tremors of tensor veli palatini, movements of facial muscles, pharynx, tongue, larynx, diaphragm, nasopharyngeal end of the Eustachian tube, and possible involvement of neck, trunk, and extremities (1).
- EMG may be used to evaluate oscillations involving limbs (9)
- Video head impulse test, ocular vestibular–evoked myogenic potential to evaluate for vestibular system dysfunction
- Histopathology reveals neuronal swelling with vacuolation, unusual nerve cell shape, fibrillary gliosis, and demyelination of inferior olive white matter (4)

Imaging

- MRI revealing T2 hyperintensity of unilateral or bilateral inferior olivary nuclei, although not required for diagnosis (1)
- Dissociated nystagmus is mostly associated with unilateral involvement of the inferior olivary nucleus on MRI (13, 14).
- Mixed torsional-vertical pendular symmetric nystagmus, as seen in this patient, may show unilateral or bilateral inferior olivary nuclei (14).

Treatment/Management/Guidelines

Acquired pendular nystagmus in patients with oculopalatal tremor can respond to gabapentin (alpha-2-delta calcium channel blocker), memantine (NMDA receptor antagonist), or trihexyphenidyl (15, 16). Gabapentin and memantine are thought to act within the cerebellum, and possibly have effects on the inferior olive pacemaker (16). Both have been shown to reduce the amplitude and velocity of eye movements; however, there is a proportionate increase waveform randomness, which may explain why a patient’s subjective visual quality does not significantly improve with these therapies (11). None of these treatments act directly at the level of misfiring gap junctions within the olivary nucleus. If this maladaptive response is targeted specifically, treatment may be more effective (17). Gabapentin has been shown to be better tolerated than memantine, so it may be favored as a first-line therapy (18). A study evaluating long-term use (6 months) of memantine in OPT patients showed only a small and temporary improvement in nystagmus. Although visual acuity was improved, there was a lack of corresponding vision-related quality of life (19).

There is no definitive surgical intervention to improve oscillopsia, which is the more debilitating component of the disease. Rectus muscle tenotomy or disinsertion has shown limited success in reducing the amplitude of nystagmus. If there is concomitant skew deviation with a vertical component, patients may benefit from prisms (1). The palatal tremor may be directly treated with botulinum toxin although efficacy is limited (20).

EPIDEMIOLOGY OR ETIOLOGY	SIGNS
• Most commonly vascular (hemorrhagic> ischemic) • Brainstem tumor • Iatrogenic brainstem or cerebellar injury • Brain trauma • Demyelinating disease • Infectious disease • Inflammatory disorders affecting the CNS	• OPT is characterized by a low frequency pendular nystagmus (1-3 Hz) in conjunction with a palatal tremor. • The associated nystagmus is most commonly vertical and pendular in nature with possible torsional and horizontal components. Convergent nystagmus has also been described. • The associated palatal tremor is most commonly synchronous with the nystagmus. • ***Links to videos***
SYMPTOMS	**TREATMENT/MANAGEMENT**
• Oscillopsia • Pendular nystagmus synchronous or asynchronous with palatal tremor • Ear clicks • Movements of facial muscles, pharynx, tongue, larynx, diaphragm, mouth of Eustachian tube • Rare neck, trunk, or extremity involvement • Other neurological deficits	• Memantine • Gabapentin • Trihexyphenidyl Titrated up according to beneficial response and side effects

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