Palatal tremor as a presenting symptom of amyotrophic lateral sclerosis

Amir-Hadi Maghzi, MD, Supreet Sahai, MD, Simon Zimnowodzki, MD, and Robert H. Baloh, MD, PhD

Neurology® 2018;90:801-802. doi:10.1212/WNL.0000000000005363

Correspondence
Dr. Maghzi
Amir.maghzi@cshs.org

MORE ONLINE

→ **Video**
links.lww.com/WNL/A398

Palatal tremor, also known as palatal myoclonus, is a sign caused by a lesion to the Guillain-Mollaret triangle. In some cases, imaging may also reveal hypertrophic olivary degeneration, which is due to trans-synaptic degeneration and gliosis of the inferior olivary nucleus. The underlying etiology is commonly due to unilateral involvement of the central tegmental tract due to ischemic, neoplastic, demyelinating, traumatic, inflammatory, and rarely neurodegenerative processes such as progressive supranuclear palsy, multiple system atrophy, and Alexander disease.[1] We describe a patient who presented with palatal tremor as the presenting symptom of amyotrophic lateral sclerosis (ALS).

Case report

A 66-year-old man presented with cognitive difficulty, voice changes, rhythmic palatal movements, and difficulty speaking followed by weakness in the right arm and twitching in the arm and chest. Neurologic examination 4 months after onset showed normal mental status and significant palatal tremor (video, links.lww.com/WNL/A398). The patient denied clicking sounds in the ears, tinnitus, or the ability to suppress the tremors. On motor examination, he had muscle atrophy and weakness (4/5) in the right upper extremity, but preserved strength in other extremities, visible fasciculations in the upper extremities, and brisk 3+ reflexes throughout. There was no evidence of ataxia and the rest of the neurologic examination was unremarkable.

Routine laboratory tests (antinuclear antibodies, vitamin B_{12}, folate, angiotensin-converting enzyme, and paraneoplastic antibodies) were normal or negative. CSF analysis revealed 1 red blood cell, 2 white blood cells, protein of 44 mg/dL, glucose of 66 mg/dL, 1 oligoclonal band, and immunoglobulin G index of 0.53.

Brain MRI with and without gadolinium revealed bilateral olivary hypertrophy as shown in the figure. Cervical and thoracic cord MRIs and CT scan of chest, abdomen, and pelvis were normal.

Whole exome sequencing did not reveal any genetic variants associated with motor neuron disease or other degenerative disorders previously associated with palatal tremor, including polymerase-gamma 1 (POLG1) or glial fibrillary acidic protein (GFAP). Repeat primed PCR was negative for C9orf72 hexanucleotide repeat expansion.

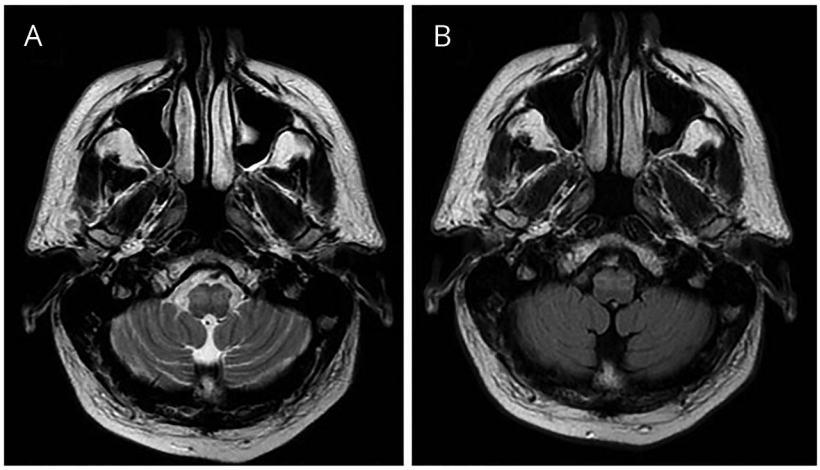
EMG/nerve conduction velocities revealed acute denervation, fasciculations, and unstable polyphasic motor units in right upper limb and thoracic paraspinals, while bulbar muscles were normal. A diagnosis of ALS was made based on clinical and electrodiagnostic findings with no alternative etiology.

After 3 months, the disease had progressed significantly, with worsening spastic dysarthria, bilateral spread of arm weakness and atrophy, and spasticity in the lower extremities. The palatal tremor had spread to involve the patient's tongue and larynx (video, links.lww.com/WNL/

From Cedars-Sinai Medical Center, Los Angeles, CA.

Go to Neurology.org/N for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

Figure Bilateral olivary hypertrophy



Bilateral olivary hypertrophy seen as hyperintensities on T2 (A) and fluid-attenuated inversion recovery (B) sequences. The lesions were isointense on T1 and diffusion-weighted sequences (images not shown).

A398). On examination, the patient had increased muscle wasting and fasciculations throughout the arms and chest and weakness of both arms distally and proximally. Legs were full strength bilaterally but he had slow foot tapping and a spastic gait. Six months later, the patient and family decided to pursue palliative measures given continued severe facial and palatal tremor, difficulty with swallowing and breathing, and severe limb weakness, and he died approximately 14 months after onset of symptoms.

The study was reviewed and approved by the local institutional review board and written consent was obtained from the patient.

Discussion

We present a unique case of simultaneous onset of progressive palatal tremor and motor neuron disease, an association not previously reported to our knowledge. Palatal tremor in conjunction with ataxia is referred to as progressive ataxia palatal tremor syndrome (PAPT).[1] The familial form has most commonly been linked to mutations in *GFAP*. Oculopalatal tremor, characterized by oscillations of the eyes and palate, is also part of the PAPT syndrome and has been reported in patients with adult-onset gangliosidosis type II (Sandhoff disease) resulting from *HEXB* mutations as well as a heterozygous *POLG1* mutations.[2] Other associations with palatal tremor include neuroferritinopathy (an autosomal dominant frameshift mutation in the ferritin light chain gene),[3] mutation in interferon-related developmental regulator-1,[4] and spinocerebellar ataxia type 20.[5]

ALS-plus syndromes describe a subgroup of ALS in which patients meet clinical criteria for ALS and have other features that are not commonly seen with motor neuron diseases, including dementia, extrapyramidal signs, sensory loss, autonomic dysfunction, cerebellar degeneration, or ocular motility disturbance.[6] This is the first description of ALS presenting with palatal tremor. The association of these 2 rare conditions could be coincidental, but the parallel onset and disease course argues they were due to a shared underlying degenerative process. Tongue myoclonus has been reported as the onset symptom of ALS, which could also localize to the Guillain-Mollaret triangle.[7] Assuming further cases are identified, palatal tremor may be added to the growing list of ALS-plus syndromes.[6]

Author contributions

A.-H.M., S.S., S.Z., and R.H.B. were involved in acquisition and interpretation of data. A.-H.M. drafted the manuscript and S.S., S.Z., and R.H.B. provided revisions and edits.

Study funding

R.H.B. is supported by grants RN3-06530 (California Institute for Regenerative Medicine) and NS097545 (NIH).

Disclosure

The authors report no disclosures relevant to the manuscript. Go to Neurology.org/N for full disclosures.

Received November 27, 2017. Accepted in final form January 31, 2018.

References

1. Samuel M, Torun N, Tuite PJ, Sharpe JA, Lang AE. Progressive ataxia and palatal tremor (PAPT): clinical and MRI assessment with review of palatal tremors. Brain 2004;127:1252–1268.
2. Kang S, Shaikh AG. Acquired pendular nystagmus. J Neurol Sci 2017:8–17.
3. Wills AJ, Sawle GV, Guilbert PR, Curtis ARJ. Palatal tremor and cognitive decline in neuroferritinopathy. J Neurol Neurosurg Psychiatry 2002;73:91–92.
4. Echeveste B, Covarrubias E, Cabello JP, Luquin MR. Isolated palatal tremor as unique clinical manifestation of SCA 18 due to a new mutation of IFRD1. Parkinsonism Relat Disord 2017;42:100–101.
5. Storey E. Spinocerebellar Ataxia Type 20. Seattle: GeneReviews; 1993.
6. McCluskey L, Vandriel S, Elman L, et al. ALS-Plus syndrome: non-pyramidal features in a large ALS cohort. J Neurol Sci 2014;345:118–124.
7. Civardi C, Collini A, Mazzini L, Testa L, Monaco F. Isolated continuous lingual myoclonus: unusual presentation of amyotrophic lateral sclerosis. Mov Disord 2010; 25:1309–1310.