

# Symptomatic palatal tremor of cortical origin due to stroke

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## ABSTRACT

Palatal tremor (PT) is usually considered a movement disorder that presents with recurring rhythmic contractions of the soft palate. The inferior olive shows a characteristic pseudohypertrophy secondary to brainstem lesions in the triangle of Mollaret and Guillain that interrupt dentato-olivary and tegmental pathways. We report a 35-year-old man with a history of uncontrolled hypertension who presented to the emergency department with PT after a left middle cerebral artery ischemic stroke. The diagnostic work-up consisted of brain MRI, which revealed restricted diffusion over the left frontoparietal lobes without involvement of the brainstem. During hospitalization, the patient reported two brief episodes of soft palate and base-of-the-tongue high-frequency, low-amplitude and rhythmic tremor that resolved after intravenous administration of lorazepam. A 2-hour video electroencephalogram showed no abnormalities. After initiation of levetiracetam therapy, no further spells were reported by the patient. At the 2-month follow-up, the patient had had no episodes of stereotypical PT or upper limb tremors since discharge. This report provides further evidence of the central role of the cortex in the generation of PT. The cortical origin of symptomatic palatal tremor (SPT) should be considered in patients presenting after an acute ischemic insult, particularly if there is no evidence of a brainstem lesion. Potential causes of SPT of cortical origin include focal epilepsy and diaschisis.

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## 1. Introduction

Palatal tremor (PT) is usually considered a movement disorder that presents with recurring rhythmic contractions of the soft palate and sometimes synchronous twitching of the lower facial muscles, pharynx, larynx, trunk, and extremities. Recently the term “palatal tremor” was recommended in preference to “palatal myoclonus”. The inferior olive, which is considered the pacemaker for PT, shows a characteristic pseudohypertrophy secondary to brainstem lesions in the triangle of Mollaret and Guillain interrupting dentato-olivary and tegmental pathways. Reports of PT of cortical origin are rare.<sup>1,2</sup>

## 2. Case report

We report a 35-year-old man with history of uncontrolled hypertension who presented to the emergency department after sudden development of right hemiparesis, hemihypoesthesia, and expressive aphasia. One week earlier, he had experienced similar symptoms and had been diagnosed with a small left frontoparietal ischemic stroke due to symptomatic distal left middle cerebral artery stenosis and had experienced an episode of right arm twitching believed to be epileptic.

Initial diagnostic work-up included MRI of the brain and MRA of the head/neck. This confirmed a new acute ischemic infarct within the territory of the superior division of the left middle cerebral artery (MCA) and did not involve the basal ganglia or brainstem (Fig. 1). During day 1 of admission, the patient had intermittent and rhythmic right face and arm twitching without impairment of consciousness. Empiric therapy with levetiracetam (500 mg twice daily) was initiated without electrographic confirmation as the patient refused to be tested at that time.

During hospitalization, the patient reported two brief episodes of complete inability to speak and tremor of the floor of the mouth. Examination during the first episode revealed soft palate and base-of-the-tongue high-frequency, low-amplitude and rhythmic tre-

mor with subtle right eyebrow twitching and inability to speak (Supplementary Video 1). Intravenous administration of 2 mg of lorazepam stopped the involuntary movements. A 2-hour video electroencephalogram showed broad left fronto-temporal and centro-parietal delta slow waves without epileptogenic activity. However, no clinical spells were captured during the recording.

After administration of lorazepam for the acute event, and increasing the dose of levetiracetam to twice daily 1500 mg, no further episodes of palatal tremor or unilateral face and arm twitching occurred. In the meantime, review of the two prior MRI showed no evidence of lesions within Mollaret's triangle or hypertrophy of the inferior olives. A repeat brain MRI excluded new lesions (Fig. 1D, E). A brain CT perfusion study demonstrated decreased cerebral blood flow, decreased cerebral blood volume with increased mean transit time restricted to the left frontoparietal lobes consistent with his known infarct. On discharge, the patient continued to show signs of clinical recovery without recurrence of the PT. At the 2-month follow-up, the patient had had no episodes of stereotypical PT or upper limb tremors since discharge. Thus, the dose of levetiracetam remained unchanged; however, a slow tapering schedule will be considered after a short period of sustained remission.

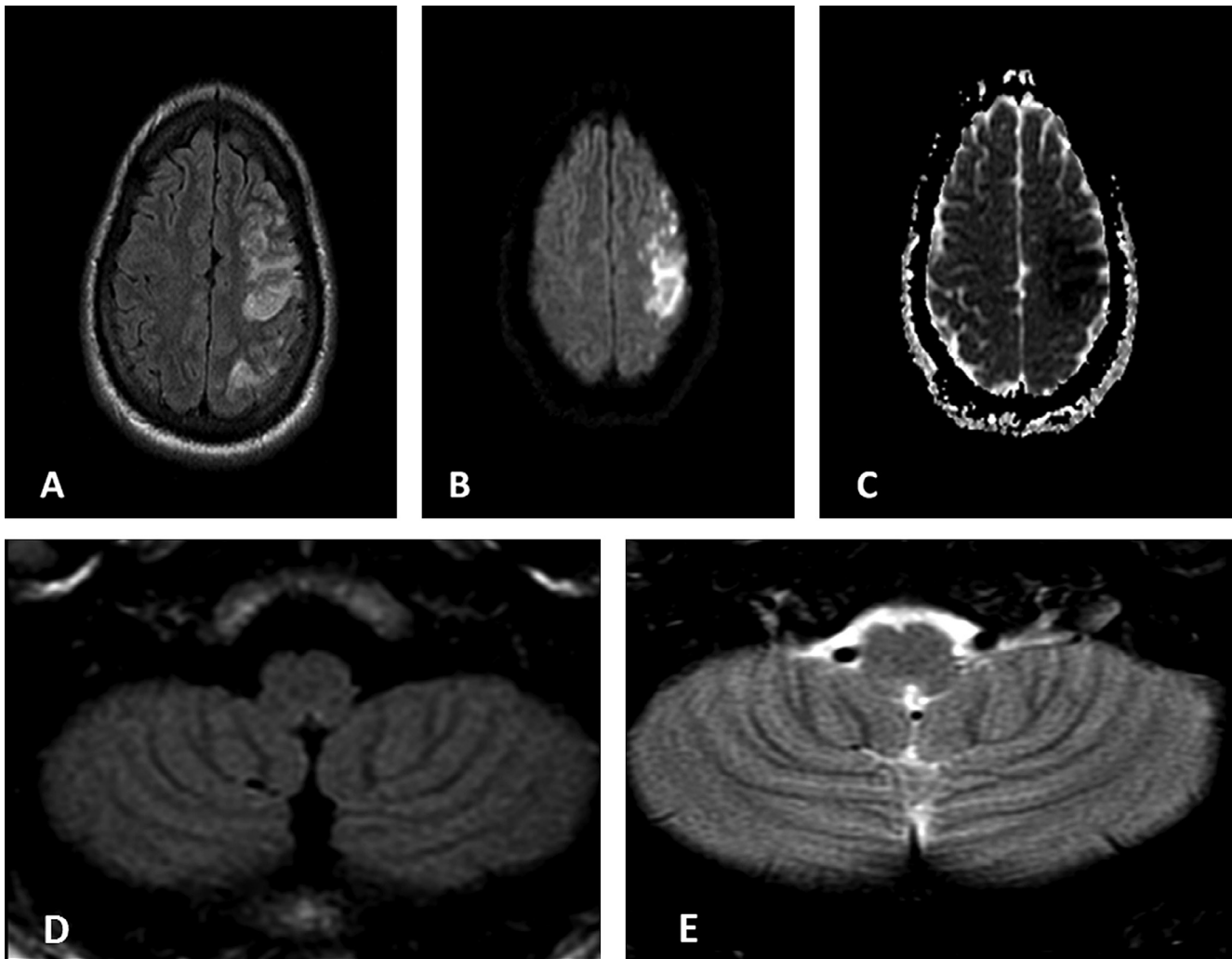
## 3. Discussion

Palatal tremor (PT), earlier known as palatal myoclonus, is a rhythmic contraction of the palatal muscles. Differentiation between essential PT (EPT) and symptomatic PT (SPT) is based on the clinical and radiological findings.<sup>3</sup> The palatal movements consist of activation of the tensor veli palatini muscle in EPT and of the levator veli palatini muscle in SPT. The common causes of PT include cerebrovascular disease, multiple sclerosis, tumors, trauma, Behcet's disease and encephalitis.<sup>3</sup> PT after infarction of the brainstem or cerebellum is due to denervation supersensitivity of the inferior olive from lesions of the dentato-rubro-olivary pathway. Lesions due to cerebrovascular diseases are the most common cause of SPT.<sup>3</sup>

SPT develops between 2 months and 49 months from the onset of the initial lesion, with most reporting development at

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**Fig. 1.** (A–C) Axial (A) T2-weighted fluid-attenuated inversion recovery (FLAIR), (B) diffusion weighted image, and (C) apparent diffusion coefficient map showing patchy areas of diffusion restriction within the white matter and the cortex of the posterior and superior left frontal lobe and the posterior left parietal lobe near the vertex. Axial (D) T2-weighted FLAIR and (E) T2-weighted MRI showing no enlargement or signal changes in the inferior olive.

10–11 months. The involuntary movement of the soft palate is evoked only after the development of further changes in neural circuitry involving pseudohypertrophy of the inferior olivary nucleus as a long-term sequela of the former lesions, possibly resulting from transsynaptic degeneration. There are two noteworthy characteristics in this patient: (i) the rapid development of PT after an ischemic brain insult; and (ii) the absence of brainstem, cerebellar, or basal ganglia lesions, and the presence of cortical lesions only, resulting in PT.

We hypothesize that in our patient, the onset of PT is the result of either epileptiform activity arising from the left frontal motor cortex or diaschisis, where the cortical infarction temporarily produced dysfunction of its subcortical connections within the dentato-rubro-olivary pathway. The preceding seizure-like activity of the arm and face, the associated expressive aphasia, the effective abolition of PT after administration of lorazepam and complete remission of symptoms after introduction of levetiracetam, suggest an epileptogenic etiology as the most likely explanation.

The postulated pathways for the cortex to produce PT are attributed to corticobulbar fibers that may arise from the frontal cortex.<sup>4</sup> These fibers descend bilaterally to innervate the reticular nuclei, which in turn send efferents to the nucleus ambiguus, which supplies motor fibers to the vagus nerve that innervates the palatal

musculature. The plausibility of this pathway was shown by Tatum et al.,<sup>1</sup> who reported a patient with PT of cortical origin diagnosed on the basis of an electroencephalogram and single-photon emission CT scan. These tests showed an area of increased cerebral perfusion in the centrotemporal region.

Additional evidence to support that cortical pathways are involved in the development of PT arise from Haller et al.<sup>5</sup> Blood oxygenation level-dependent functional MRI performed in a patient with PT was associated with peak neuronal activation in the putamen bilaterally. Further neuronal activation was present bilaterally in the precentral gyrus, as well as the right superior temporal and angular gyrus.<sup>5</sup>

The pharmacotherapy of PT with clonazepam, valproate, sumatriptan and trihexyphenidyl has had variable success. Chemodenervation with botulinum toxin injection to palatal muscles using electromyographic guidance has been useful in the treatment of PT. The PT in this patient appeared to respond to lorazepam and did not recur while on levetiracetam, which is likely a result of its presumed epileptic nature.

#### 4. Conclusions

This report provides further evidence of the central role of the cortex in the generation of PT. A cortical origin of SPT should be

considered in patients presenting after an acute ischemic insult, particularly if there is no evidence of a brainstem lesion. Potential causes of SPT of cortical origin include focal epilepsy and diaschisis.

### Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.jocn.2012.05.049>.

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## Tropical spastic paraparesis treated with Combivir (lamivudine–zidovudine)

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### ABSTRACT

Tropical spastic paraparesis (TSP) or human T-cell leukemia virus–type 1 (HTLV-1)-associated myelopathy is caused by human T-lymphotropic virus type 1. It is a slow, progressive spastic paraparesis with significant morbidity and causing profound repercussions on quality of life. No therapies have been found to persistently improve the outcome in these patients. We present a patient with HTLV-1-associated myelopathy/TSP (HAM/TSP) who was treated with Combivir® (lamivudine–zidovudine, GlaxoSmithKline, London, UK). She was walker-dependent for several years but, soon after treatment with lamivudine–zidovudine, was able to walk using only a cane. The role of lamivudine–zidovudine should be investigated further in this patient population.

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### 1. Case report

We present a 72-year-old woman with a past medical history of hypothyroidism, hyperparathyroidism, depression and anxiety who was diagnosed 15 years ago with human T-cell leukemia virus–type 1 (HTLV-1) associated myelopathy/TSP (HAM/TSP) with a positive serum antibody to HTLV-1 (the diagnostic study for HAM/TSP at that time). Her presentation started with increasing falls and a peculiar sensation in her legs. This evolved into an unsteady, clumsy gait with spasticity, neuropathic pain, paraparesis and bladder and bowel incontinence. A brain MRI revealed abnormal fluid attenuated inversion recovery (FLAIR) signal in the subcortical, deep, and periventricular white matter of both frontal lobes and patchy FLAIR abnormality of the pons suggestive of an inflammatory process (Fig. 1). She was not offered treatment at the time as there was no treatment available. Her condition continued to deteriorate and she eventually became walker-dependent. This disability resulted in a major depression episode. She scored a 7.0 on the Expanded Disability Status Scale (EDSS), which is a scale used to measure mobility and is typically used for patients with multiple sclerosis. Her frustration began to grow and she became desperate for any treatment option. Fifteen years after diagnosis, and after much consideration and discussion with her, she was started on Combivir® (lamivudine–zidovudine; GlaxoSmithKline, London, UK) 150/300 mg tablet twice per day. Initially, she experienced some abdominal discomfort; however, within 1 month after the initiation of treatment, she noticed that the spasticity in her legs had decreased although her lower

extremity weakness was unchanged. After 3 months of continued treatment, her spasticity had significantly decreased; she was able to ambulate using a cane. Her lower extremity weakness had much improved. She stopped falling after 5 months of treatment. After 7 months of follow-up after starting lamivudine–zidovudine, her EDSS score improved to 3.0. To the date of writing, she has been on treatment for 9 months and continues to improve. Thus, lamivudine–zidovudine appeared to provide symptomatic relief in this patient who suffers from HAM/TSP and greatly improved her quality of life.

### 2. Discussion

HTLV-1 is the etiological agent of HAM/TSP. It affects fewer than 2% of carriers of HTLV-1.<sup>1</sup> Women are affected more frequently than men due to the higher prevalence of HTLV-1 infection in women. Disease onset occurs at an average age of 40 years. It is a chronic meningoencephalitis of the spinal cord grey and white matter with perivascular demyelination and axonal degeneration caused by HTLV-1. Patients typically develop a slow progressive spastic paraparesis with significant impairment of gait together with hyperreflexia, ankle clonus and extensor plantar responses, autonomic dysfunction of the bladder/bowel, back pain and sensory changes.<sup>2–4</sup> All these symptoms have profound repercussion on quality of life. The disease is progressive and without remission. Diagnosis is made in the setting of chronic spastic paraparesis with elevated HTLV proviral load. The individual's immune response and proviral load correlates with prognosis. There is no curative treatment, although corticosteroids,<sup>4</sup> IFN- $\beta$ 1a<sup>5</sup> and danazol<sup>6</sup> have shown limited benefit. One randomized study evaluated the use

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