

Symptomatic palatal tremor: A descriptive cohort study of 27 cases in a tertiary hospital

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Abstract

Background: Symptomatic palatal tremor (SPT) is an uncommon hyperkinetic movement disorder caused by the interruption of the dentato-rubro-olivary pathway due to a lesion in the brainstem or cerebellum. **Methods:** We describe a cohort of consecutive patients with SPT who were assessed by a single neurologist in a tertiary reference center. **Results:** A total of 27 patients were included in this cohort from 1998 to 2016; 16 males and 11 females, with a mean age of 47 years (range 19-89). The average time from initial insult to a diagnosis of SPT was 14.5 months (range 2-48 months). The most common etiology of SPT was cerebrovascular disease (CVD) in 21 (78%) patients. Other etiologies included infectious and demyelinating diseases of the central nervous system. The remaining unclassified case was accompanied by progressive ataxia pointing toward a neurodegenerative etiology. Twenty-six patients had a history of posterior fossa injury, and all patients had rhombencephalic signs with severe dysarthria. None of them responded significantly to pharmacological treatment. **Conclusion:** SPT is a more common finding than expected, especially in patients with posterior fossa injury secondary to CVD. The main clinical syndrome was the rhombencephalic phenotype, with a predominance of dysarthria. There was no effective treatment in any of the patients.

Key words: Dysarthria. Guillain–Mollaret triangle. Hyperkinetic movement disorders. Palatal tremor. Rhombencephalic syndrome.

Temblores palatales sintomáticos: un estudio de cohorte descriptivo de 27 casos en un hospital terciario

Resumen

Antecedentes: El temblor palatino sintomático (TPS) es un trastorno hiperkinético del movimiento poco frecuente secundario a la interrupción de la vía dentato-rubro-olivar por una lesión en el tronco encefálico o el cerebelo. **Métodos:** Describimos una cohorte de pacientes consecutivos con TPS que fueron evaluados por un mismo neurólogo en un centro de tercer nivel. **Resultados:** Se incluyeron un total de 27 pacientes entre 1998 y 2016; 16 hombres y 11 mujeres, con una edad media de

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47 años (rango 19-89 años). El tiempo promedio desde la lesión inicial hasta el diagnóstico de MPS fue de 14.5 meses (rango 2-48 meses). La etiología principal del TPS fue la enfermedad cerebrovascular (EVC) con 21 (78%) pacientes. Otras etiologías incluyeron: enfermedades infecciosas y desmielinizantes del sistema nervioso central. El caso restante presentó ataxia progresiva de probable etiología neurodegenerativa. Veintiséis pacientes tenían antecedentes de lesión en fosa posterior. Todos los pacientes tenían signos romboencefálicos con disartria severa y ninguno de los pacientes respondió significativamente al tratamiento farmacológico. **Conclusión:** El TPS es un hallazgo más común de lo esperado, principalmente en pacientes con lesión de fosa posterior secundaria a EVC. El principal síndrome clínico fue el romboencefálico con predominio de disartria. No hubo tratamiento efectivo en ninguno de los pacientes.

Palabras clave: Disartria. Triangulo de Guillain-Mollaret. Trastorno hipercinético del movimiento. Temblor palatino. Síndrome romboencefálico.

Introduction

Symptomatic palatal tremor (SPT) is an uncommon hyperkinetic movement disorder¹. The pathophysiological basis of SPT is hypertrophic olivary degeneration (HOD), causing interruption of the dentato-rubro-olivary pathway due to lesions in the olivary body at the medulla oblongata. These lesions usually affect the Guillain–Mollaret triangle (GMT) formed by the red nucleus, the inferior olivary nucleus (ION), and the dentate nucleus². The interruption of the cerebellar inhibitory output to the ION gradually causes hypertrophy, leading to abnormal neuronal discharges and subsequent tremor³. In SPT, the *levator veli palatini* is the main affected muscle, causing a 1-2 Hz palatal tremor that usually persists during sleep; other signs such as ocular, pharyngeal or rubral tremor, ataxia, and pendular nystagmus can also be present^{4,5}.

Although sometimes considered myoclonus, its rhythmic nature and bilateral, symmetrical affection of the soft palate and pharynx is consistent with a tremor. Rhythmic myoclonus is often slower than tremor, is present at rest, is not modified significantly by voluntary movements, and often persists during sleep^{6,7}.

The average reported time between an initial GMT lesion and SPT development is 10-11 months⁸.

SPT reports in the past have described it as a medical curiosity, but this could be due to a low level of diagnostic suspicion and late-onset appearance^{8,9}.

Methods

We describe a large cohort of consecutive patients with SPT who were assessed by the same neurologist in a tertiary referral center, including clinical findings, diagnostic workup, and treatment. Subsequent patients > 18 years with an oscillatory palatal tremor of 1-2 Hz and history of posterior fossa disease were included. All patients included were evaluated for treatment response with a mean follow-up of 11 months.

The study was approved by the local ethical committee and classified as a non-risk study with no intervention. Clinical, images, or video film records were obtained from corresponding patient authorization by written consent in all cases.

Results

A total of 27 patients were included in this cohort from 1998 to 2016; 16 males and 11 females, with a mean age of 47 (range 19-89 years). The average time from presentation to the diagnosis of SPT was 14.5 months (range 2-48 months). The main etiology of SPT was cerebrovascular disease (CVD) with 21 (78%) patients, of which 14 (66%) were classified as ischemic. There were 3 (11%) cases related to infectious diseases: one case due to neurocysticercosis of the fourth ventricle and two others secondary to cerebral toxoplasmosis (in the context of HIV infection) of the posterior fossa. Two females (7%) had brainstem lesions due to neuromyelitis optica spectrum disorder (NMOSD). The remaining case was a young man with progressive ataxia with a probable neurodegenerative disease. Inferior olivary degeneration (T2 sequence hyperintensity on magnetic resonance imaging [MRI]) with or without hypertrophy was observed in 13 of 14 (93%) patients who had available MRI performed at follow-up (Figs 1-3). Except for the patient with progressive ataxia, all other 26 patients had a history of injury to the posterior fossa, in addition to rhombencephalic signs, including severe spastic or ataxic dysarthria. None of the patients responded significantly to pharmacological treatment during the follow-up (specific treatment is described in Table 1).

Discussion

Since its first report by Oppenheim in 1887, HOD continues to be an uncommon condition with a variety

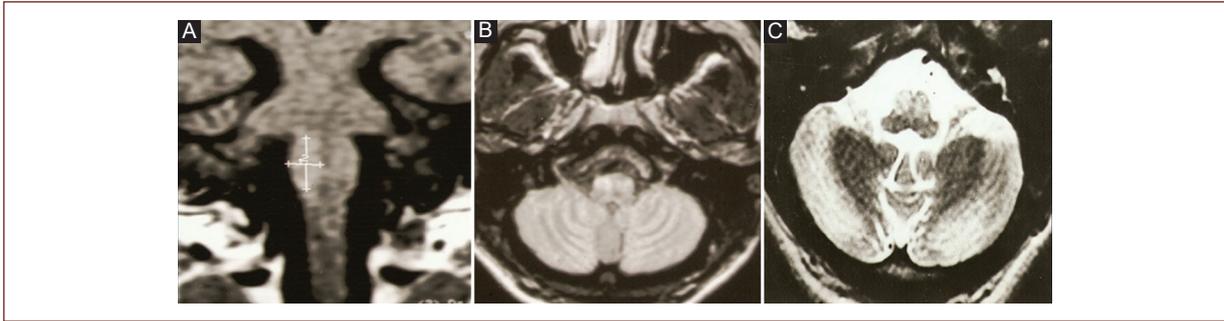


Figure 1. (Patient 2) Magnetic resonance imaging. Coronal T1 **A**: axial FLAIR **B**: and axial T2 **C**: weighted imaging showing olivary hypertrophy degeneration in a patient with progressive ataxia.

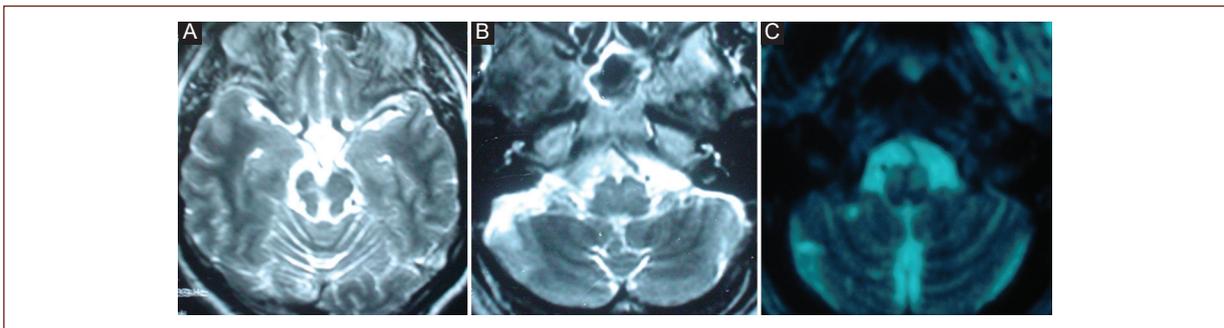


Figure 2. (Patient 18) Magnetic resonance imaging. Axial T2-weighted imaging **A-C**: showing multiple, chronic infarctions in the vertebrobasilar territory (cerebellum and mesencephalon), and olivary hypertrophy.

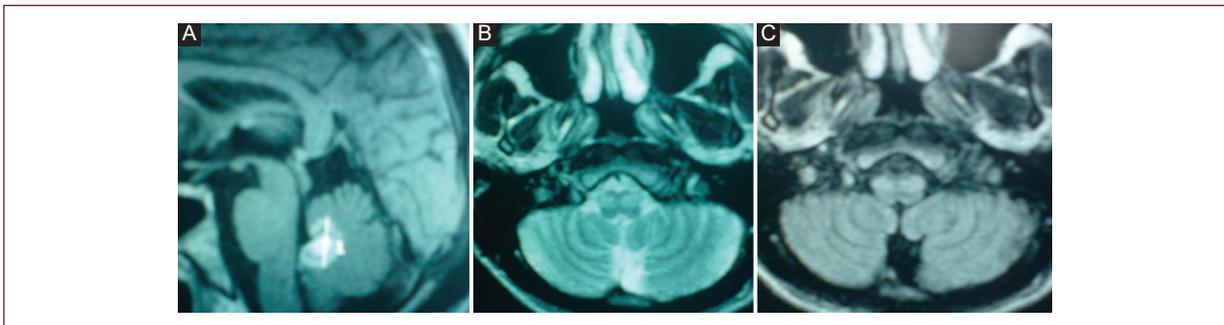


Figure 3. (Patient 20) Magnetic resonance imaging (MRI). Ring enhancement on sagittal T1 contrast-enhanced weighted imaging in the fourth ventricle **A**: consistent with toxoplasmosis in a patient with HIV, axial T2 **B**: and FLAIR **C**: with olivary hypertrophy 11 months after follow-up.

of etiologies and clinical manifestations, with palatal tremor as a unifying criterion¹⁰.

In this study spanning almost two decades, our neurology staff was able to identify approximately 1.5 new cases of SPT per year using the following approach: a history of posterior fossa disease, a careful physical examination, and ordering appropriate neuroimaging

studies; making SPT a more common condition than previously reported^{6,7}. Patients with a history of posterior fossa surgery were not included in our registry, making this condition probably more frequent in neurosurgery departments. Clinically, the HOD can also cause dentato-rubral tremor (Holmes tremor) and ocular myoclonus as late-onset manifestations; however,

Table 1. Symptomatic palatal tremor etiologies, time to diagnosis, treatment, outcome, and MRI findings

No.	Sex/age	Etiology (initial neurological insult)	Time to diagnosis (months)	Treatment	Follow-up (months)	Palatal tremor outcome	MRI inferior olivary hyperintensity/ hypertrophy
1	M/48	Cerebellar infarct	24	Propranolol	4	Unsuccessful	Yes
2	M/34	Progressive ataxia	11	Clonazepam/ botulinum toxin	6	Decrease in frequency	Yes
3	M/25	Multiple infarcts in vertebrobasilar territory	9	None	8	Unsuccessful	Yes
4	F/25	Multiple infarcts in vertebrobasilar territory	12	Clonazepam	10	Unsuccessful	Yes
5	F/47	Right cerebellar hypertensive hemorrhage	36	None	36	Unsuccessful	Yes
6	M/41	Cerebellar peduncular hemorrhage	13	Propranolol	4	Unsuccessful	Unknown
7	F/75	Mesencephalic infarct	8	Propranolol/ levetiracetam	14	Unsuccessful	Unknown
8	M/89	Cerebellar infarct	9	Propranolol/ levetiracetam	2	Unsuccessful	Unknown
9	M/24	Multiple infarcts in vertebrobasilar territory	10	None	3	Unsuccessful	Unknown
10	M/64	Cerebellar hypertensive hemorrhage	24	Propranolol/ levetiracetam	13	Unsuccessful	Yes
11	M/28	Multiple infarcts in vertebrobasilar territory	12	Acetazolamide/ levetiracetam	25	Decrease in frequency	Yes
12	F/20	Cerebellar hemorrhage	11	Propranolol	8	Unsuccessful	Unknown
13	F/34	Fourth ventricle neurocysticercosis	48	Propranolol	1	Unsuccessful	Unknown
14	M/46	Multiple infarcts in vertebrobasilar territory	17	None	4	Unsuccessful	Unknown
15	F/19	Thalamomesencephalic hemorrhage	29	Propranolol	8	Speech improvement	No
16	M/78	Cerebellar infarct	8	Propranolol	9	Unsuccessful	Unknown
17	M/70	Pontine hypertensive hemorrhage	5	Propranolol	5	Unsuccessful	Unknown
18	M/43	Multiple infarcts in vertebrobasilar territory	12	Propranolol	19	Unsuccessful	Yes
19	F/61	Multiple infarcts in vertebrobasilar territory	2	Propranolol	9	Unsuccessful	Unknown
20	M/35	Toxoplasmosis of cerebellum and roof of fourth ventricle	11	Propranolol	7	Unsuccessful	Yes
21	M/56	Multiple infarcts in vertebrobasilar territory	6	None	5	Unsuccessful	Unknown
22	F/68	Multiple infarcts in vertebrobasilar territory	10	Propranolol / levodopa / biperidene	8	Unsuccessful	Unknown
23	M/56	Multiple infarcts in vertebrobasilar territory	18	Nifedipine	3	Unsuccessful	Unknown
24	F/56	Brainstem and diencephalic hemorrhage	16	Propranolol Levetiracetam	16	Unsuccessful	Yes

(Continues...)

Table 1. (Continued)

No.	Sex/age	Etiology (initial neurological insult)	Time to diagnosis (months)	Treatment	Follow-up (months)	Palatal tremor outcome	MRI inferior olivary hyperintensity/ hypertrophy
25	F/48	Neuromyelitis optica spectrum disorder	12	None	38	Unsuccessful	Yes
26	F/63	Neuromyelitis optica spectrum disorder	9	Carbamazepine	16	Unsuccessful	Yes
27	M/40	Toxoplasmosis in posterior fossa (HIV +)	12	None	8	Unsuccessful	Yes

M: male; F: female.

these symptoms did not occur in any of our patients during follow-up^{2,11}.

In our study, the most common cause of SPT was brainstem or cerebellar CVD, representing almost 80% of reported cases. These data are consistent with results from other studies, in which the main causes of SPT were CVD, trauma, metastatic, and astrocytic tumors, multiple sclerosis, surgical interventions, syringobulbia, Behçet's disease, and encephalitis¹²⁻¹⁴.

Although most of the patients with HOD and SPT have no symptomatic discomfort, several drugs, including beta-blockers, antiepileptic, benzodiazepines, and neuroleptics, are commonly used¹². They usually offer partial and non-sustained symptom control in most cases, as reported in this study. Some recent models have demonstrated the influence of cerebellar Purkinje-cell modulation to the hypertrophic ION in SPT, suggesting drug combination therapy for a "double" inhibition with more satisfactory results. These therapies include the use of drugs with GABA-enhancing inhibitory and glutamatergic-coupling effects¹⁵.

Other non-pharmacological options include the administration of botulinum toxin, a safe and effective therapy in selected patients with SPT, and marginal benefits using special dental devices that have been used by some authors in patients with lingual-palatal tremor¹⁶⁻¹⁸.

Deep brain stimulation has not been studied in SPT but is a secure and beneficial procedure in other movement disorders such as essential tremor and Parkinson's disease. It could provide some benefit for SPT in the future^{19,20}.

Patients with a history of brainstem or cerebellar injury with no palatal tremor at diagnosis should be kept under vigilance since SPT can appear during follow-up, up to 30 months after initial presentation. Patients with an incidental finding of palatal tremor should be evaluated to rule out lesions in the posterior fossa since over 75% of

cases reveal an underlying symptomatic cause²¹. This could be a typical scenario of patients with undiagnosed multiple sclerosis or NMOSDs who initially present with posterior fossa symptoms and visit another specialist (such as an otorhinolaryngologist) for medical advice.

During the study, we have been able to identify three clinical characteristics that may facilitate and increase a diagnosis of SPT: (1) history of posterior fossa disease; (2) persistence of severe rhombencephalic signs during the 1st year of symptom onset; and (3) predominance of severe spastic or ataxic dysarthria. More prospective studies with consecutive clinical evaluations should be done to determine the predictive factors involved in these reported findings.

Conclusion

In conclusion, SPT is not as rare as previously reported, and physicians should be aware of associated signs and symptoms for adequate diagnosis, especially in patients with a history of posterior fossa disease.

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Conflicts of interest

None to report.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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