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 rhomboencephalic 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 rhomboencephalic 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. Rhomboencephalic syndrome.

Tembor palatal sintomático: un estudio de cohorte descriptivo de 27 casos en un hospital terciario

Resumen

Antecedentes: El temblor palatino sintomático (TPS) es un trastorno hipercinético 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...
Introduction

Symptomatic palatal tremor (SPT) is an uncommon hyperkinetic movement disorder. 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 nucleus. The interruption of the cerebellar inhibitory output to the ION gradually causes hypertrophy, leading to abnormal neuronal discharges and subsequent tremor.

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.

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

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.

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.

Other etiologies included: 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).

Discussion

Since its first report by Oppenheim in 1887, HOD continues to be an uncommon condition with a variety...
of etiologies and clinical manifestations, with palatal tremor as a unifying criterion\textsuperscript{10}.

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\textsuperscript{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/69    | 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                        | Acetzolamide/ 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 / biperidine | 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. 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 encephalitis.

Although most of the patients with HOD and SPT have no symptomatic discomfort, several drugs, including beta-blockers, antiepileptic, benzodiazepines, and neuroleptics, are commonly used. 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 effects.

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 tremor.

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.

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 cause. 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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