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Review

Objective tinnitus secondary to palatal tremor: Two case reports and brief literature review

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ABSTRACT

Objective tinnitus is defined as a type of tinnitus perceived by both the patient and external observer. This paper presents two cases of objective tinnitus related to palatal tremor, along with a literature review. Palatal tremor is a condition characterized by soft palate involuntary contractions. Two types of palatal tremor have been described: symptomatic palatal tremor and essential palatal tremor, with different clinical manifestations. Diagnostic workup is based on medical history and physical examination, including direct oropharynx exploration and cavum visualization through nasopharyngoscopy. Brain MRI is mandatory in all cases. If a secondary origin is suspected, additional lab tests should be performed based on clinical suspicion. First-line treatment is botulinum toxin injection into the *levator veli palatini* and *tensor veli palatini* muscles, with velopharyngeal insufficiency being its main adverse effect. Other medications have not been shown to be effective.

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1. Introduction

Objective tinnitus is defined as a type of tinnitus perceived by the both patient and external observer. This category represents 1.5% of the total number of tinnitus cases evaluated in tertiary healthcare institutions (Kircher et al., 2008). Its main causes are vascular-related disorders such as arterial hypertension, valvulopathies, jugular bulb anomalies, dural arteriovenous fistulas or paragangliomas, manifesting as a pulsatile tinnitus synchronized with the arterial pulse (Sonmez et al., 2007). Less frequently, the underlying cause is related to neuromuscular conditions. In these cases, tinnitus is asynchronous with the arterial pulse (Liyanage et al., 2006; Chan, 2009). This paper presents two cases of objective tinnitus caused by palatal tremor, along with a literature review.

Abbreviations: LVP, *Levator veli palatini*; TVP, *Tensor veli palatini*; SPT, Symptomatic palatal tremor; EPT, Essential palatal tremor; ION, Inferior olivary nucleus.

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2. Case 1

A 31-year-old woman with no relevant medical antecedents was referred to our center with a 2-year history of "clicking" tinnitus in the left ear (video 1). The patient also reported feeling palatal contractions and was diagnosed with palatal tremor in her primary healthcare institution. During follow-up, she reported chronic pelvic pain and suffered a psychotic episode. Oropharynx examination demonstrated soft palate arrhythmic contractions with left side preponderance. This finding was confirmed by flexible nasopharyngoscopy, showing palatal tremor at about 2.2 Hz. Pure-tone audiometry and tympanometry showed no abnormalities. Tinnitus's impact on quality of life was 64 by the Tinnitus Handicap Index (THI) (Newman et al., 1990; Kuk et al., 1990).

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Further tests, including serology, copper metabolism study and brain MRI did not show any alterations. However, during a follow-up MRI a left-sided parietal cavernoma was identified. At her original institution, she had been infiltrated with 6 U of botulinum toxin, causing transient velopharyngeal insufficiency as a side effect. Additionally, medical treatment with propranolol 20 mg every 12 h and clonazepam 0.5 mg every 12 h had been innefective. Due to the impact of tinnitus on patient's quality of life, it was decided to repeat botulinum toxin injections following the descripted procedure as below. Under endoscopic visualization, type A botulinum toxin (Botox 100 U, Allergan Pharmaceuticals, Ireland) was injected with a microlaryngeal surgery syringe in the *Levator veli palatini* (LVP) and *Tensor veli palatini* (TVP) muscles, following reference points described by Conill Tobías et al., 2012. The starting dose was 5 U in a 2.5 U/ml dilution per injection site. Procedures were performed under sedation, except the first injection which was performed under general anesthesia, and local anesthesia (tetracaine 1%- adrenaline 0,01% solution) was administered by surgical patties for 10 min before injection. During a period of 4 years (May 2016 to June 2020), five procedures were performed, obtaining mixed results, with a variable time interval among injections. Outcomes were evaluated 1 month after each infiltration by patient report and THI. The first procedure (10 U total) achieved excellent outcomes: tinnitus totally disappeared and palatal tremor showed a significant frequency reduction for 6 months (THI = 8). Subsequently, both symptoms progressively reappeared, reaching their previous levels 10 months after the procedure. The second procedure (10 U) had a suboptimal outcome, with no change in tinnitus intensity as reported by the patient (THI 56). This is possibly related to inferior turbinate hypertrophy, preventing proper infiltration. The third infiltration (11 U) was preceded by a radiofrequency turbinate reduction and resulted in favorable outcomes, with persistent but reduced tinnitus intensity reported by the patient for 4 months (THI = 28). Despite being carried out correctly, the fourth procedure (12 U) did not achieve satisfactory outcomes, with no modification in symptoms (THI = 58). In the fifth and last intervention (15 U), favorable results were achieved with a reduction in tinnitus intensity reported by the patient for 6 months (THI = 34). Overall, a mean dose of 11.6 U per injection procedure was administered at a mean interval of 10 months between procedures. No side effects were reported for any of these procedures.

3. Case 2

A 9-year-old boy with no relevant past medical history was referred to our center with a 6- month history of moderate bilateral hearing loss, associated with "clicking" type tinnitus in the left ear perceptible by external observers (video 2). The tinnitus had an approximate frequency of 2 Hz, which could be temporarily modified by the patient voluntarily. Flexible nasopharyngoscopy revealed rhythmic soft palate contractions, and pure tone audiometry confirmed hearing loss (Fig. 1). Tympanometry showed type A tympanograms in both ears. Brain MRI showed no pathologic findings. Hearing loss related gene mutations screening was requested, and its results are pending. Currently, the patient uses bilateral Behind-The-Ear hearing aids (BTE) with adequate performance. Since the quality of life is not affected in this patient, an expectant therapeutic approach is chosen.

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4. Discussion

Palatal tremor, previously known as palatal myoclonus, is a condition characterized by soft palate involuntary contractions. Paradoxically it does not meet the conditions of a tremor. It is mainly arrhythmic, and moreover, its frequency has intra and interindividual variability usually ranging between 0.5 and 3 Hz (Zadikoff et al., 2005; Stamelou et al., 2012a). The cases reported here meeting the aforementioned characteristics.

Two types have been described: symptomatic palatal tremor (SPT) and essential palatal tremor (EPT) (Deuschl et al., 1994). SPT is related to Guillain Mollaret triangle injuries, while an underlying cause has not been found in EPT (Zadikoff et al., 2005; Tilikete and Desestret, 2017).

The Guillain Mollaret triangle is a conceptual area of the brainstem with three corners: ipsilateral red nucleus in the midbrain, ipsilateral inferior olivary nucleus (ION) in the medulla and contralateral dentate nucleus in the cerebellum. These nuclei are connected by the dentato-rubro-olivar pathway (Turgut et al., 2021). Injuries in this area, usually ischemic or tumoral, provoke ION alterations (Surisetti et al., 2021; Wang et al., 2019). Hyperintense areas are detectable after 3–4 weeks by MRI, and ION hypertrophy can be seen after 4–6 months. However, the onset of symptoms takes place around 10 months later, and ION atrophy usually takes place after 3 years. There are three patterns of olive degeneration depending on injury location. When the dentate nucleus or superior cerebellar peduncle are injured, contralateral ION is affected. Central tegmental tract injury causes ipsilateral ION alteration. Finally, combined brainstem and cerebellum injury conduces to bilateral ION hypertrophy (Surisetti et al., 2021; Goyal et al., 2000). In addition to those previously mentioned, many other SPT causes have been described such as multiple sclerosis, neurosarcoidosis, infectious diseases or Hashimoto encephalopathy (Nagappa et al., 2018). Furthermore, a condition consisting of progressive ataxia and palatal tremor (PAPT) might have a genetic origin (Nicastro et al., 2016; Gass et al., 2017).

Regarding the causal mechanism of EPT, different hypotheses have been postulated. A central origin is proposed based on functional MRI findings and the response to the central nervous system (CNS) targeting drugs (Nitschke et al., 2001; Fabiani et al., 2000). A peripheral origin is proposed based on case reports which describe related oronasal mucosal inflammation, history of upper respiratory tract infection and clinical improvement after adenotonsillectomy (Wakata et al., 2002; Samuel et al., 2004). However, it is postulated that this peripheral alteration would trigger the disorder, whereas a central mechanism would be necessary for its maintenance. A voluntary behavioral origin has also been theorized, as the capacity of members of a few families to voluntarily trigger palatal tremor and modify its characteristics has been reported (Klein et al., 1998). Finally, a psychogenic origin is postulated; some authors have proposed it as a third etiologic category in addition to EPT and SPT. It is supported by multiple case reports

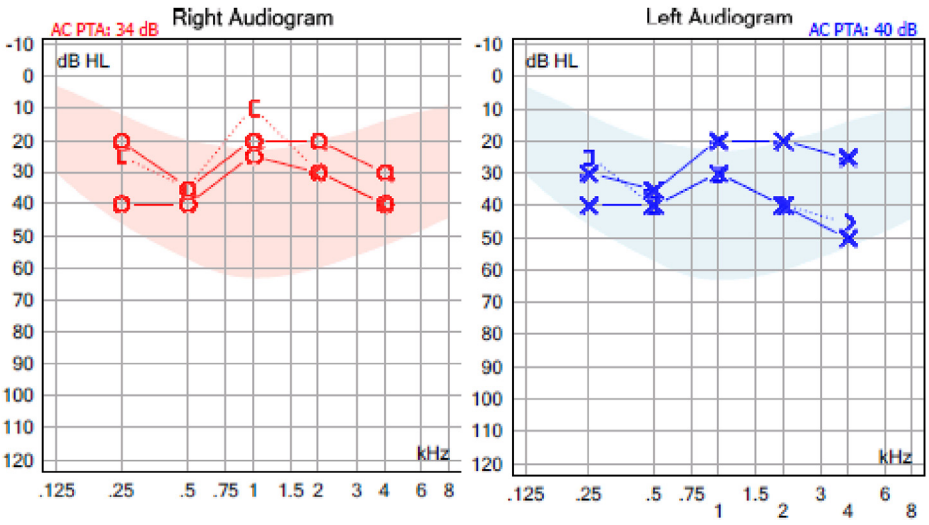

Fig. 1. Pure tone audiometry with and without hearing aids in Case 2.

which describe the presence of psychiatric comorbidity and how a stressful event can trigger the onset of symptoms (Williams, 2004; Stamelou et al., 2012b).

In addition to a diverse etiologic origin, EPT and SPT have different clinical implications (Bhattacharjee, 2020). On the one hand, SPT is caused by LVP contraction, which depends on the vagal nerve, and tinnitus is usually not audible by external observers, does not disappear during sleep, and may be associated with neurological findings including ophthalmoplegia, rubric tremor, dysarthria, dysphagia, ataxia or nystagmus. On the other hand, EPT is caused by TVP contraction, which depends on the trigeminal nerve. Its tinnitus tends to be audible by external observers, usually disappears during sleep and may be associated with oropharyngeal, masseter or temporal muscle tremor. The two cases reported in this article are classified as EPT, since the underlying cause remains unknown after diagnostic workup. Regarding case 1, although a cavernoma is detected during follow-up MRI, its parietal location does not explain the onset of a palatal tremor. Given her psychiatric morbidities and chronic pelvic pain of uncertain cause, a psychogenic origin might be present in this case. Her symptoms match EPT clinical features: i.e. disappearance of tinnitus during sleep and episodic facial tremor reported by the patient during follow-up.

An underlying etiology was not found despite a rather thorough diagnostic workup in case 2 either. This patient was able to modify the tremor frequency and consequently the intensity of the externally audible tinnitus. He was even able to interrupt it briefly. This fact supports the hypothesis of a voluntary behavioral origin. However, an isolated voluntary mechanism is unlikely, given the lack of benefit. Moreover, family history is found in case reports in the literature, but not with this patient (Klein et al., 1998). As we have not found reported cases of palatal tremor associated with hearing loss in children, these may be independent conditions despite its synchronous onset in patient No. 2.

Medical history and physical examination, including oropharynx direct exploration and cavum visualization through nasopharyngoscopy, are the cornerstones of diagnostic workup. In cases of pulsatile tinnitus asynchronous with the arterial pulse, palatal tremor should be ruled out, especially if the patient reports involuntary oropharyngeal contractions or self-control over the tinnitus frequency. In case 1, palatal tremor was observable on both direct oropharynx exploration and nasopharyngoscopy, whereas in case 2, it was only visualized by nasopharyngoscopy. Therefore, it is advisable to include nasopharyngoscopy in the workup regardless of direct oropharynx exploration findings.

Brain MRI is mandatory in all cases (Bhattacharjee, 2020). If a secondary origin is suspected, additional lab tests should be performed based on clinical suspicion. This may include celiac disease screening, Lyme disease serology, ACE (angiotensin-converting enzyme), cholestanol, and anti-GAD (anti-glutamate decarboxylase antibodies) or anti-TPO (thyroid peroxidase antibody) test. Cerebrospinal fluid (CSF) analysis may be helpful to rule out lymphoma, multiple sclerosis, neurosarcoidosis or Whipple's disease (Nagappa et al., 2018; Bhattacharjee, 2020). Genetic testing is recommended if spinocerebellar ataxia, hereditary spatic paraparesis, Alexander disease, or mitochondrial disease are suspected (Bhattacharjee, 2020). Finally, electromyography determines the tremor frequency, whereas electroneurography can detect axonal neuropathy. In our cases, patient No. 1 was already diagnosed with palatal tremor when referred to our center. Nonetheless, the diagnosis was confirmed through our physical examination. Brain MRI and lab tests showed no alterations, and CSF analysis and genetic testing were not considered necessary for this patient. Regarding case 2, symptoms were the key to suspect palatal tremor, leading to nasopharyngoscopy, which otherwise would not have been performed. In this case, brain MRI did not show alterations either, and pure tone audiometry confirmed moderate bilateral hearing loss. Currently, the patient is pendant for hearing loss related gene mutation screening and a neurology evaluation to rule out associated neurologic diseases. In our two cases, neither electromyography nor electroneurography was performed since their relevance was considered low.

The first-line treatment for palatal tremor is botulinum toxin infiltration into the TVP and LVP muscles (Bhattacharjee, 2020; Penney et al., 2006; Slengerik-Hansen and Ovesen, 2016). Usual doses range between 5 and 15 U per injection site. A systematic review on this topic shows clinical improvement in 62% of the cases with an average effect duration from 3 to 6 months (Slengerik-Hansen and Ovesen, 2016). In our case, procedure effects were evaluated by subjective patient report and the THI, with an average THI score reduction of 27.2 compared to the initial score. However,

the effect may range from a few days to several years, showing both intra- and inter-individual variability (Slengerik-Hansen and Ovesen, 2016). Since a dose-effect relation is not found in the mentioned study, a low-dose start is recommended. Velopharyngeal incompetence is the main side effect, appearing in up to 41% of the cases. It usually lasts several weeks, being tolerable by the patient in most cases (Slengerik-Hansen and Ovesen, 2016).

As already proposed, we agree that a correct technical execution and selection of appropriate injection location can be directly related to outcomes (Slengerik-Hansen and Ovesen, 2016). The mentioned study shows a trend to better outcomes for electromyography-guided injections, probably due to better localization of the appropriate injection site. However, further studies are warranted in order to clarify this issue. Coinciding with other cases reported, our patient in case 1 showed improvement, not only in terms of palatal tremor, but also in the associated facial tremor (Jamieson et al., 1996; Cho et al., 2001). Nonetheless, the underlying cause of this improvement remains unclear, as it cannot be totally explained by the simple diffusion of botulinum toxin.

As palatal tremor is a chronic condition requiring repeated interventions, we recommend approaching the anatomical alterations that may impede a correct infiltration in the first place, as was done in case 1. Regarding the dose of botulinum toxin, our outcomes do not suggest a dose-effect relation, supporting other reports where no clear difference in outcome related to the botulinum toxin dose has been seen (Slengerik-Hansen and Ovesen, 2016). Therefore, we consider it appropriate to begin with a 5 U dose per injection site and modify the dose based on results of previous procedures. The time interval between infiltrations should depend on the symptoms reported by the patient instead of a fixed time interval.

There are multiple case reports which describe the response to drugs such as carbamazepine, gabapentin, clonazepam or valproic acid. However, none of these drugs has consistently proven to be effective (Bhattacharjee, 2020). Surgery might be a therapeutic option in some SPT cases. In children, like patient No. 2, an expectant approach is recommended since palatal tremor in this age group has a tendency to resolve spontaneously (MacDonald, 2007).

5. Conclusion

Palatal tremor is a rare cause of objective tinnitus. Diagnostic workup is based on medical history and physical examination, including direct oropharynx exploration and cavum visualization through nasopharyngoscopy. SPT is caused by injuries located at the Guillain-Mollaret triangle, so brain MRI is essential in its diagnosis. EPT causes are still unknown, and currently, several hypotheses are proposed. First-line treatment is botulinum toxin infiltration in the LVP and TVP muscles, with velopharyngeal insufficiency being its main adverse effect. Other medications have not been shown to be effective.

Declaration of competing interest

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