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Case Report

Rapidly progressive dementia and severe awake bruxism resistance to treatment: An unresolved challenge to treatment

Running Title: Progressive dementia and bruxism

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Abstract

Background: Bruxism is a chief complaint in some patients with dementia, but there is no clear guideline for its management.Here, we presented a case with awake bruxism.

Case presentation: This case report study described an 88-year-old woman with severe rapidly progressive dementia (RPD) and awake bruxism, which was improved with discontinuation of sertraline, quetiapine, gabapentin, and resumption of trazodone.

Conclusion: In this case study, despite taking drugs from different classifications for bruxism treatment, no improvement was seen. Bruxism is an important and challenging condition for physicians and caregivers in dementia patients. Although bruxism needs serious treatment, there is no suitable and well-defined treatment for this disorder. Further studies are needed to suggest an efficient drug for the management of bruxism.

Keywords: Bruxism; Dementia; Resistance to treatment

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Introduction

Bruxism is a movement disorder in the mouth and teeth region, such as squeezing, grinding, or restraining teeth that can occur during sleep or wakefulness. The incidence of bruxism is 8 to 31% in the adult population (1, 2). Awake bruxism (AB), that is more common in women, is defined as masticatory muscle activity during wakefulness and is determined by repetitive or sustained tooth contact that may be associated with bracing or thrusting of the mandible (3, 4).

Bruxism etiology is multifactorial, including peripheral (tooth interference in dental occlusion, smoking, medication), psychosocial (stress or anxiety), and pathophysiological factors. The imbalance between both the direct and indirect pathways of the basal ganglion causes movement disorder such as bruxism. Perturbation in the dopamine-mediated transmission of action potential leads to this imbalance, too. In addition, chronic long-term use of levodopa, serotonin reuptake inhibitors (SSRIs), amphetamine, and nicotine may lead to bruxism (4- 7). Typical antipsychotics increase the risk of bruxism, but the effect of atypical antipsychotics on AB is not fully understood yet (8, 9).

Some central nervous system disorders lead to AB, including dystonia, Parkinson's, stroke, and dementia (Alzheimer's disease). AB damages teeth and causes temporomandibular disorders, headaches, and depression. The remission rate of AB is poor (7, 10, 11). Some medicaments potentially attenuate bruxism, including amitriptyline, botulinum toxin A, buspirone, clonazepam, clonidine, clozapine, gabapentin, hydroxyzine, levodopa or dopamine agonists, propranolol, quetiapine, and trazodone (8). Despite many studies on the treatment of bruxism, there are contarasting results in this regard. In this srtudym, a resistant AB case was reported who was treated with trazodone.

Case presentation

The patient in this case study was an 88-year-old divorced Iranian woman with severe rapidly progressive dementia (RPD). She was a hairdresser, but she was unemployed for the last few years. The onset of AB had been about two months ago. Her curator reported hearing loud tooth-grinding sounds during the day. She had difficulty in active mouth opening and had jaw locking. The patient had traumatized cheeks related to her AB.

Her Bruxism was not s and sometimes stopped, but it worsened during stressful, anxiety, and agitation periods. In addition, the patient's symthomes were more severewhen she was conscious and less severe when she was drowsy. The patient had fluent aphasia indicated with headaches in the frontal region. In the appearance, she was an apathetic, mutism, apraxia woman with a past medical history of diabetes mellitus, dementia, ischemia, and pulmonary emboli but no nicotine or substance consumption. According to the patient's signs, clinical oral examination, and diagnostic criteria proposed by the American Academy of Sleep Medicine (AASM) the patient

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was diagnosed with AB. Despite using trazodone months, the severity of her bruxism did not changed. Taking Trazodone was discontinued due for sleep problems overe previous three to financial problems. **Table 1** indicates the medications used by the patient before the study.

Table.1 Patient's medications before the study

Medication list	Order (mg/day)	**Medical indication**
Quetiapine	100	Anxiety and Insomnia
Sertraline	50	Anxiety
Buspirone	15	Anxiety and Agitation
Memantine	10	Dementia
Donepezil	5	Dementia
Lorazepam	1.5	Anxiety and Insomnia
Rivaroxaban	15	Pulmonary embolism and stroke
Melatonin	10	Quality of sleep
Metformin	500	Diabetes mellitus

Quetiapine and sertraline were tapered, and finally discontinued to treat the bruxism. Quetiapine was replaced with gabapentin, which seemed to improve anxiety and insomnia along with bruxism. Unfortunately, gabapentin could not improve the bruxism, and finally it was discontinued by gastroenterologist because of causing stomachache and diarrhea. While quetiapine and sertraline were tapered, trazodone was started for the patient (50 mg daily). The curator of the patient reported a decrease in her bruxism symptoms 1 day after trazodone initiation. The patient's tooth-grinding sounds and temporal headaches improved during wakefulness,. The intensity and frequency of bruxism decreased, but after a few days, the patient was diagnosed with dysphagia. After a few months, the patient was presented with complications of lethargy, fever, and pain. Her bruxism got worse when she had a fever. The patient had shortness of breath without cough. Oral antibiotics, vitamin C, and B-complex were prescribed for her.

The results of patient's blood test showed low serum level of vitamin B12 and high serum level of AST (50 U/L) and TSH (5.52 uIU/mL). In the microscopic patient's urine test, WBC 10-12, RBC 1-2, 2 to 4 epithelial cells, a moderate amount of bacteria, and few mucus were observed.

A brain magnetic resonance imaging (MRI) examination showed generalized brain atrophy in all cortical regions. In addition, dilation of brain and nuclear height of hippocampal neurons were decreased significantly. Her medial temporal lobe atrophy (MTA) score was 4 showing end stage of dementia and Alzheimer's disease. There was a

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symptom similar to "loss of insular ribbon" sign suggesting Creutzfeldt-Jakob disease (CJD). The patient recently got coronavirus disease 2019 (COVID-19).

Discussion

In the present case report, an 88-year-old woman with severe AB was presented. After being treated with trazodone, her conditions were clinically improved. The patient had jaw clenching and loudly grinding of the teeth in awfulness leading to traumatized mouth, which was resistant to treatment. The patient had several risk factors for her AB, including being female, having stress, anxiety, and dementia, having history of stroke, and using medications such as sertraline (4-8, 10, 11). The patient was not addicted to nicotine or any other drugs, so the cause of her bruxism was not related to this risk factor. As bruxism could be a symptom of orofacial tardive dyskinesia, but it was ruled out because the patient had no history of the neuroleptic syndrome (12, 13).

Previous studies showed that the link between dopaminergic agents and bruxism was unclear and dopaminergic agents night induce or suppress bruxism given that many neuronal circuits are associated with dopamine. Dopamine antagonists are divided into two categories, namely typical and atypical drugs. The typical type, by blocking D2 receptor, and the atypical type, by blocking D2, 25-HT2A, and 5-HT1A receptors, may induce or suppress bruxism as a side effect, respectively. Atypical drugs, by blocking both dopamine agonist (DA) and 5-HT receptors, may lead to a reduction in extra-pyramidal side effects and a lower tendency for DA receptors, might treating bruxism more successfully (14).

In a case series, it was reported that a low dose of quetiapine improved bruxism and mandibular dystonia, as side effects of SSRIs (15). In contrast, in our study, the discontinuation of quetiapine (an atypical antipsychotic) improved the patient's symptoms, but the cause of which was unknown. Brain atrophy causes a decrease in capacity and blood supply of the brain and finally leads to sensitivity to drug's side effects.

Antidepressant-associated bruxism is a well-described phenomenon and SSRIs are one the most important agent of that. Bruxism may be treated with prescription of buspirone, gabapentin, benzodiazepine, or dose modification and medication discontinuation (8, 16, 17). Buspirone is a 5-HT_1A receptor agonist that increases the synaptic secretion of dopamine in the frontal cortex and also improves drug-induced bruxism by improving extrapyramidal effects, such as dyskinesia (18).

Some related studies showed the efficacy of gabapentin in bruxism-induced antidepressant. In contrast, in our patient, taking gabapentin could not relief the bruxism. This may be attributed to the fact that the mechanism of gabapentin in decreasing stage III to IV (deep) sleep is seen in nocturnal bruxism (NB) and gabapentin increases these stages, which may be due to the mechanism by which gabapentin reduces NB, not AB (19-21).

The patient suffered from bruxism when she had a fever. In a study performed by Drumond et al., in 2017, the association between respiratory disorders and sleep bruxism was evaluated. It was found that infectious respiratory disorders led to

episodes of intermittent edema of the mucosa of the eustachian tubes (22). In addition, some studies reported patients with CJD who suffered from bruxism, too (23, 24).

The pathophysiology of bruxism is unknown, but one of the causes can be the dysfunction of the cholinergic and dopaminergic pathways (7, 11). Our patient only suffered from bruxism during the day, which was attributed to pathological reason. Our patient developed bruxism a few months after being diagnosed with RPD, but other studies showed that this disorder could occur even in the early stages of RPD (11, 25).

Trazodone is one of the SARI (Serotonin Antagonists and Reuptake Inhibitors) group. There is several pharmacologic mechanisms for it, including antagonist of 5-HT_2A and 5-HT_2C serotoninergic receptors, alpha1 and alpha2 adrenergic receptors as well as H_1 histaminergic receptors. In higher doses, it blocks the SERT serotonin transporter. (26). In our patient, the administration of trazodone could relief the AB, significantly. It could be due to the wide pharmacodynamics profile, resulting in wide

therapeutic spectrum range of treatment was reported. This beneficial effect may be related to an antagonistic effect at the 5-HT_2A receptor, similar to the ant akathisia effect of trazodone in patients treated with antipsychotic (27). The findings on the anti-bruxism effects of H1 antagonists are contradictory. Hydroxyzine can improve the bruxism, but ketotifen can induce bruxism (8).

In patients with RPD, low tolerance to oral protection and injection of botulinum toxin into the masticatory muscles, drug therapy plays an important role. Appropriate and timely treatment of disorders, such as bruxism, can help increase quality of life in RPD patients (11).

Conclusion

In this case study, despite taking drugs from different classification used for bruxism treatment, no improvement was seen in the patient. Bruxism is an important and challenging condition for physician and caregivers in dementia patients. It needs serious treatment, but there is no suitable and well-defined treatment for this disorder. Further studies are needed to suggest an efficient drug for the management of bruxism.

Conflict of interests: The authors have no conflicts of interest to declare.

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References

1. Hathaway KM. Bruxism: definition, measurement, and treatment. Advance in pain research and therapy. 1995;21:375-86.
2. Manfredini D, Winocur E, Guarda-Nardini L, Paesani D, Lobbezoo F. Epidemiology of bruxism in adults: a systematic review of the literature. Journal of Orofacial Pain. 2013;27(2):99-110.
3. Chisini LA, San Martin AS, Cademartori MG, Boscato N, Correa MB, Goettems ML. Interventions to reduce bruxism in children and adolescents: a systematic scoping review and critical reflection. European journal of pediatrics. 2020;179(2):177-89.

 DOI: https://doi.org/10.18502/aptj.v1i2.8669

4. Shetty S, Pitti V, Babu CS, Kumar GS, Deepthi B. Bruxism: a literature review. The Journal of Indian Prosthodontic Society. 2010;10(3):141-8.
5. Ella B, Ghorayeb I, Burbaud P, Guehl D. Bruxism in movement disorders: a comprehensive review. Journal of Prosthodontics. 2017;26(7):599-605.
6. Ghobadi N, Karami S. A review of temporomandibular disorders, diagnostic and therapeutic strategies. Clinical Excellence. 2020;10(2):53-63.
7. Kwak YT, Han IW, Lee PH, Yoon JK, Suk SH. Associated conditions and clinical significance of awake bruxism. Geriatrics & gerontology international. 2009;9(4):382-90.
8. de Baat C, Verhoeff M, Ahlberg J, Manfredini D, Winocur E, Zweers P, et al. Medications and addictive substances potentially inducing or attenuating sleep bruxism and/or awake bruxism. Journal of Oral Rehabilitation. 2021;48(3):343-54.
9. Falisi G, Rastelli C, Panti F, Maglione H, Quezada Arcega R. Psychotropic drugs and bruxism. Expert opinion on drug safety. 2014;13(10):1319-26.
10. Watts MW, Tan E-K, Jankovic J. Bruxism and cranial-cervical dystonia: is there a relationship? CRANIO®. 1999;17(3):196-201.
11. Lai M. Awake bruxism in a patient with Alzheimer's dementia. Geriatr Gerontol Int. 2013;13(4):1076-7.
12. Milanlıoglu A. Paroxetine-induced severe sleep bruxism successfully treated with buspirone. Clinics. 2012;67(2):191-2.
13. Winocur E, Gavish A, Voikovitch M, Emodi-Perlman A, Eli I. Drugs and bruxism: a critical review. Journal of orofacial pain. 2003;17(2.(
14. Mathew T, Venkatesh S, Srinivas M. The approach and management of bruxism in Alzheimer's disease: An under-recognized habit that concerns caregivers (innovative practice). Dementia. 2020;19(2):461-3.
15. Zandifar A, Mohammadi MR, Badrfam R. Low-dose quetiapine in the treatment of SSRI-induced bruxism and mandibular dystonia: case series. Iranian journal of psychiatry. 2018;13(3):227.
16. Garrett AR, Hawley JS. SSRI-associated bruxism: A systematic review of published case reports. Neurology: Clinical Practice. 2018;8(2):135-41.
17. Singh H, Kaur S, Shah A. Antidepressant induced bruxism: a literature review. Journal of Psychiatric Intensive Care. 2019;15(1):37-44.
18. Shakibaei F, Gholamrezaei A, Heydari S. Effect of trazodone on sleep bruxism in children and adolescents 6-18 years of age, a pilot study. Journal of research in medical sciences (JRMS). 2008;13(1):29-33.
19. Brown ES, Hong SC. Antidepressant-induced bruxism successfully treated with gabapentin. The Journal of the American Dental Association. 1999;130(10):1467-9.
20. Sadat Madani A, Abdollahian E, Azangoo Khiavi H, Radvar M, Foroughipour M, Asadpour H, et al. The efficacy of gabapentin versus stabilization splint in management of sleep bruxism. Journal of Prosthodontics: Implant, Esthetic and Reconstructive Dentistry. 2013;22(2):126-31.
21. Soyata AZ, Oflaz S. Gabapentin treatment in bruxism associated with fluoxetine. Journal of clinical psychopharmacology. 2015;35(4):481-3.
22. Drumond CL, Souza DS, Serra-Negra JM, Marques LS, Ramos-Jorge ML, Ramos-Jorge J. Respiratory disorders and the prevalence of sleep bruxism among schoolchildren aged 8 to 11 years. Sleep and Breathing. 2017;21(1):203-8.
23. D'Arcy CE, Bitnun A, Coulthart MB, D'Amour R, Friedman J, Knox JD, et al. Sporadic Creutzfeldt-Jakob disease in a young girl with unusually long survival. Journal of Neuropathology & Experimental Neurology. 2019;78(4):373-8.
24. Monreal J, Collins GH, Masters CL, Fisher CM, Kim RC, Gibbs Jr CJ, et al. Creutzfeldt-Jakob disease in an adolescent. Journal of the neurological sciences. 1981;52(2-3):341-50.
25. Guaita M, Högl B. Current treatments of bruxism. Current treatment options in neurology. 2016;18(2):10.
26. Jarema M, Dudek D, Landowski J, Heitzman J, Rabe-Jabłońska J, Rybakowski J. Trazodon--the antidepressant: mechanism of action and its position in the treatment of depression. Psychiatria polska. 2011;45(4):611-25.
27. Grinshpoon A, Weizman A, Amrami-Weizman A. The beneficial effect of trazodone treatment on escitalopram-associated nocturnal bruxism. Journal of clinical psychopharmacology. 2014;34(5):662.