

OPEN

# Change of Cerebral Blood Flow After a Successful Pharmacological Treatment of Phantom Bite Syndrome: A Case Report

Yojiro Umezaki, DDS, PhD,\*† Trang T. H. Tu, DDS,† Akira Toriihara, MD, PhD,‡  
Yusuke Sato, DDS, PhD,§ Toru Naito, DDS, PhD,\* and Akira Toyofuku, DDS, PhD†

**Background:** “Phantom bite syndrome,” a persistent complaint of an uncomfortable bite sensation with no obvious occlusal abnormal finding, recently was suggested to be related with central nervous system dysfunction. Here, we report a case of phantom bite syndrome in which the occlusal discomfort was improved with mirtazapine and aripiprazole combination parallel with regional cerebral blood flow change.

**Case report:** A 60-year-old-female patient came to our clinic with the chief complaint of a “loosely bite” after dental treatment and various uncomfortable sensations of body sites. One year after the medication therapy, the prosthodontic retreatment was carried out successfully, and a good outcome was obtained for over 24 months so far. In addition, a subsequent change of regional cerebral blood flow was observed in single-photon emission computed tomography: the right and left asymmetry of cerebral blood flow in the frontal lobe has disappeared along with the improvement to the symptoms improvement.

**Conclusions:** This case suggests that some central nervous system dysfunction involving dopaminergic system might be related to the pathophysiology of phantom bite syndrome.

**Key Words:** aripiprazole, mirtazapine, occlusal dysesthesia, phantom bite syndrome, single-photon emission computed tomography (SPECT)

(*Clin Neuropharm* 2019;42: 49–51)

“Phantom bite syndrome” (PBS), which was first described by Marbach<sup>1–3</sup> in the year 1976, is a persistent complaint of uncomfortable bite sensation with no obvious occlusal abnormal findings. Conventional dental treatments were repeated again and again to adjust patients' occlusion, but only worsened the symptoms.

Previous studies suggested that PBS was mostly developed after dental treatment (eg, prosthodontic, restoration, orthodontic, etc). While most patients could adapt quickly to the restored occlusion, some of them were hardly and slowly to adapt and keep

complaining of their discomfort.<sup>4</sup> Although PBS has been considered to be associated with paranoia, personality problems, or some other mental diseases,<sup>1</sup> not all the cases of PBS have psychiatric symptoms. Several researches have suggested a relationship between PBS and some dysfunction in the central nervous system.<sup>5,6</sup> In particular, a decreased blood flow of the dorsolateral prefrontal and frontopolar cortex was reported with reproduced occlusal discomfort in healthy participants using near-infrared spectroscopy.<sup>7</sup> Supporting the hypothesis about a relationship between PBS and central nervous system, antidepressants and antipsychotics were used for PBS management.<sup>8</sup> However, there is no investigation involving patients with PBS focusing on the change of cerebral blood flow before and after treatment has been reported.

## CASE REPORT

A 60-year-old housewife complaining about her occlusal discomfort visited our clinic. She felt a pressure sensation on the maxillary anterior fixed prosthetic and numbness of her right face. She had no remarkable incidents in medical/psychiatric history and was living with her husband in a good relationship.

Fifteen months before the initial visit to our clinic, after placing a porcelain fused zirconia crown on the maxillary left incisor, the patient started to feel an occlusal discomfort, which she described as “bite is loose,” “heavy” sensation in her back, “twisting” sensation in her waist, and general lethargy. Even though the crown was immediately replaced by a temporary one and adjusted many times, her symptoms did not improve. Then, the dentist suggested a consult with a psychiatrist, but she refused that proposal. She believed strongly that what she needed was “correcting bite,” not mental health care.

At the first visit to our clinic, she brought along her own illustration to demonstrate the occlusal abnormality and blamed her “lousy bite” to the prior dentist. There she was in a presentable appearance, and a polite attitude was kept through our interview. No overreaction, manic episodes, hallucination, or any sight of delusional complaints were seen.

Extraoral examination found symmetrical face and pleasant countenance. Hypertonia or tenderness of masticatory muscle, clicking, crepitus, and trismus were not observed. However, the patient kept complaining about being unable to find the “correct bite” and unstable “tapping point.” No abnormalities in intraoral examination as well as in the radiographs were found. In accordance with the criteria suggested by Melis and Zawawi,<sup>9</sup> we diagnosed the patient as having PBS. Then a head magnetic resonance imaging and <sup>99m</sup>Tc ethyl cysteinate dimer single-photon emission computed tomography (SPECT) were performed. The head magnetic resonance imaging showed no obvious organic change (eg, bleeding of the brain parenchyma, infarction, expansion of cerebral ventricles, etc). On the other hand, the SPECT imaging showed the asymmetrical cerebral blood flow patterns between the right and left with right-sided dominance in the frontal lobe

\*Section of Geriatric Dentistry, Department of General Dentistry, Fukuoka Dental College, Fukuoka; and †Department of Psychosomatic Dentistry and ‡Diagnostic Radiology and Nuclear Medicine, Graduate School of Medical and Dental Sciences, and §Department of Gerodontology, Graduate School of Tokyo Medical and Dental University, Tokyo Medical and Dental University, Tokyo, Japan.

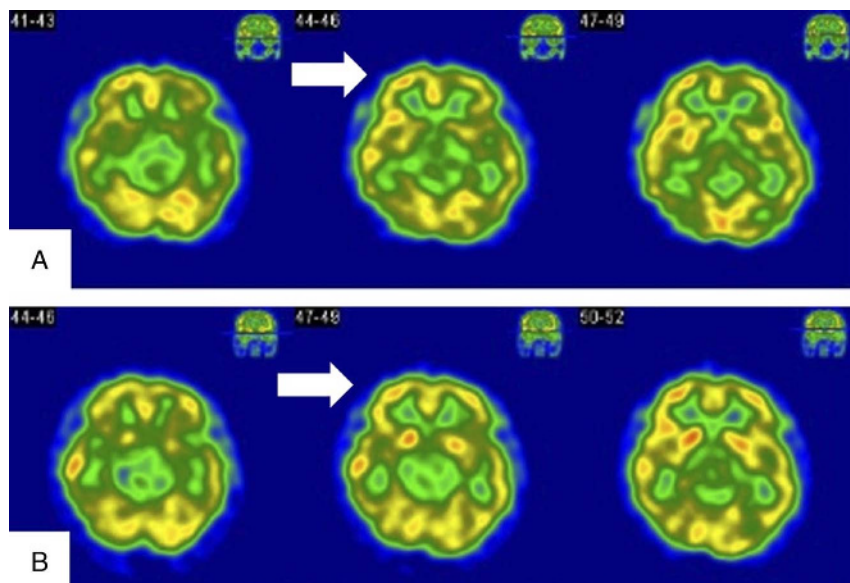
Address correspondence and reprint requests to Yojiro Umezaki, DDS, PhD, Section of Geriatric Dentistry, Department of General Dentistry, Fukuoka Dental College, 2-15-1, Tamura, Sawara-ku, Fukuoka-shi, Fukuoka, Japan; E-mail: yume.ompm@tmd.ac.jp

Conflicts of Interest and Source of Funding: The authors have no conflicts of interest to declare.

This work was supported by the Japan Society for the Promotion of Science KAKENHI (Grant-in-Aid for Scientific Research) grant JP18K17306.

Copyright © 2019 The Author(s). Published by Wolters Kluwer Health, Inc. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

DOI: 10.1097/WNF.0000000000000328



**FIGURE 1.** A, The SPECT images showed the rCBF was asymmetrical between the right and left with right-sided dominance in the frontal lobe (white arrow). B, After the treatment, the asymmetrical rCBF pattern disappeared.

(Fig. 1A). The assessment was carried out by a physician specialized in the field of nuclear medicine.

After explaining that the symptoms might come from the central nervous system, so that any conventional dental treatment could not be mitigated, we obtained her consent for medication therapy. The patient was initially prescribed amitriptyline 10 mg/d, but she complained about many adverse effects such as “stagger,” “strong nausea,” or “cannot do anything.” On day 7, she was switched to mirtazapine 15 mg/d. After 1 week, her appetite returned, and she felt slightly better. The staggering remained so she refused to increase the dosage of the mirtazapine. Instead, aripiprazole 1 mg/d was added on. One month after initiation of medications, the patient was aware of the improvement of “twisted body” feeling. Three months later, the occlusal discomfort improved but remained slightly. The same prescription was continued, and the symptoms stabilized until the prosthodontic retreatment was carried out one year after the initial visit. During the dental treatment, her oral complaints such as “bite was loose” and “the crown did not fit me” recurred; however, it calmed down quickly a week later with the same prescription. The crown was successfully delivered. After the symptom relief, we checked the SPECT image again and observed the previous asymmetrical regional cerebral blood flow (rCBF) pattern disappeared (Fig. 1B). At 41 months' follow-up visits, the patient remained in stable condition with the same prescription. No sight of recurrence has been observed.

## DISCUSSION

The persistence of occlusal discomfort even after many repeated dental treatment is diagnosed as PBS<sup>1-3</sup> or occlusal dysesthesia.<sup>9,10</sup> A study revealed more than 30% of the temporomandibular disorders patients suffer from bite discomfort.<sup>9</sup> In our opinion, PBS might be included in such patients, although the precise prevalence is still unclear. In another study, 70% of PBS patients developed their symptoms after conventional dental treatment.<sup>8</sup> The exact pathophysiological mechanism of PBS remained unknown, but previous research suggested the hypothesis of biochemical abnormalities related to neurotransmitter in

the brain and higher brain dysfunction correlated with the cognitive processes.<sup>11</sup> In this report, in order to clarify those hypotheses, the treatment course and the change in rCBF were assessed.

Before the treatment, SPECT image showed the asymmetrical rCBF pattern between the right and left frontal lobe with dominance in the right side. After prescribed mirtazapine and aripiprazole combination, the cerebral blood flow pattern has been changed. From the view of drugs reaction: mirtazapine is classified as a noradrenergic and specific serotonergic antidepressant and acts like an antagonist of presynaptic  $\alpha_2$ -adrenergic autoreceptors while enhancing serotonin neurotransmission at the 5-HT<sub>1</sub> receptor.<sup>12</sup> On the other hand, aripiprazole is a partial agonist on dopamine D<sub>2</sub>, D<sub>3</sub>, and serotonin 1A and antagonist on serotonin A<sub>2</sub>.<sup>13</sup> In this case, the monotherapy of mirtazapine did not show sufficient effects, but adding on aripiprazole resulted in a good course. This suggests the occlusal discomfort might relate to dysfunction of complex neurotransmissions involving the dopaminergic system.

A remarkable phenomenon in this case is the recurrence of occlusal discomfort after restarting the prosthodontic treatment. Although the sensation existed in only a very short time, then obtained improvement without additional prescription, the prosthodontic treatment likely provoked PBS symptoms. A possible explanation here would be the alteration of sensorimotor functions following modifying dental occlusion. That study also reported that the ability to adapt new altered occlusal in rats related to asymmetrical neuroplasticity between the right and left side of the primary motor cortex of the face in the frontal lobe.<sup>4</sup> Therefore, the spontaneous recovery of adaptation capacity after retreatment and the asymmetrical rCBF change in the frontal lobe in this case might reflect the alternation of this condition.

## CONCLUSIONS

We reported a case of PBS in which the occlusal discomfort was improved by mirtazapine and aripiprazole combination therapy. In the <sup>99m</sup>Tc ethyl cysteinate dimer SPECT images taken after treatment, the right and left asymmetry of the cerebral blood flow in the frontal lobe has disappeared along with the improvement of

the symptoms. It was inferred that the neurotransmitter dysfunction involving dopamine system might have contributed to PBS.

### REFERENCES

1. Marbach JJ. Phantom bite. *Am J Orthod* 1976;70:190–199.
2. Marbach JJ, Varoscak JR, Blank RT, et al. “Phantom bite”: classification and treatment. *J Prosthet Dent* 1983;49:556–559.
3. Marbach JJ. Phantom bite syndrome. *Am J Psychiatry* 1978;135:476–479.
4. Avivi-Arber L, Lee J-C, Sessle BJ. Dental occlusal changes induce motor cortex neuroplasticity. *J Dent Res* 2015;94:1757–1764.
5. Leon-Salazar V, Morrow L, Schiffman EL. Pain and persistent occlusal awareness: what should dentists do? *J Am Dent Assoc* 2012;143:989–991.
6. IL A. Idiopathic orofacial pain: a review. *Internet J Pain* 2009;2:1–8.
7. Ono Y, Kobayashi G, Hayama R, et al. Prefrontal hemodynamic changes associated with subjective sense of occlusal discomfort. *Biomed Res Int* 2015;2015:395705.
8. Watanabe M, Umezaki Y, Suzuki S, et al. Psychiatric comorbidities and psychopharmacological outcomes of phantom bite syndrome. *J Psychosom Res* 2015;78:255–259.
9. Melis M, Zawawi KH. Occlusal dysesthesia: a topical narrative review. *J Oral Rehabil* 2015;42:779–785.
10. Hara ES, Matsuka Y, Minakuchi H, et al. Occlusal dysesthesia: a qualitative systematic review of the epidemiology, aetiology and management. *J Oral Rehabil* 2012;39:630–638.
11. Toyofuku A. A clinical study on psychosomatic approaches in the treatment of serious oral psychosomatic disorders during hospitalization—evaluation of “behavior restriction therapy” for oral psychosomatic disorders and consideration of its pathophysiology [in Japanese]. *J Psychosom Dent* 2000;15:41–71.
12. Stimmel GL, Dopheide JA, Stahl SM. Mirtazapine: an antidepressant with noradrenergic and specific serotonergic effects. *Pharmacotherapy* 1997;17:10–21.
13. Mamo D, Graff A, Mizrahi R, et al. Differential effects of aripiprazole on D(2), 5-HT(2), and 5-HT(1A) receptor occupancy in patients with schizophrenia: a triple tracer PET study. *Am J Psychiatry* 2007;164:1411–1417.