CASE REPORT

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Ramipril Related Burning Mouth Syndrome: A Case Report

Ramipril İlişkili Yanan Ağız Sendromu: Vaka Sunumu

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ABSTRACT

Burning mouth syndrome (BMS), or glossodynia, is a disease characterized by oral burning or similar pain without clinically evident causative lesions or any other possible causes. Many factors are accepted as possible causes for this disease, including some drugs. The present case of burning mouth syndrome, which started after the use of angiotensin-converting enzyme (ACE) inhibitor ramipril and whose symptoms disappeared after discontinuation of the drug may be insightful when it comes to determining the best treatment.

ÖZET

Yanan ağız sendromu (YAS) veya glossodini, klinik olarak belirli bir lezyon veya başka bir neden olmaksızın ağızda yanma veya benzeri ağrı ile karakterize olan bir hastalıktır. Birçok faktör bu hastalığın olası nedenleri olarak kabul edilmektedir. Bazı ilaçların da bu sendroma neden olduğu bildirilmiştir. Anjiyotensin dönüştürücü enzim (ACE) inhibitörü ramipril kullanımından sonra başlayan ve ilacın kesilmesiyle semptomları kaybolan mevcut ağız yanması sendromu olgusu, ideal tedavinin belirlenmesi konusunda aydınlatıcı olabilir.

Keywords:
Angiotensin-converting enzyme inhibitor
Burning mouth syndrome
Ramipril

Anahtar Kelimeler:
Anjiyotensin dönüştürücü enzim inhibitörü
Yanan ağız sendromu
Ramipril

INTRODUCTION

Burning mouth syndrome (BMS), also known as glossodynia, is disease characterized by oral burning or similar pain without clinically evident causative lesions or any other possible causes (1). It has been found that this situation is more common among middle-aged and older women (2).

Although many factors are accepted as possible causes for this disease, the field of oral diseases has not seen much research done on the topic. Most notably, medications such as H-2 receptor antagonists, proton pump inhibitors, clonazepam, lisinopril, sertraline, venlafaxine and fluoxetine seem to be connected to the development of BMS (3).

In this article, we present a case of burning mouth syndrome, which started after the use of angiotensin-converting enzyme inhibitor (ACEI) ramipril and whose symptoms disappeared after discontinuation of the drug.

CASE

A 63-year-old female patient was admitted to the family medicine outpatient clinic with complaints of her tongue burning as if she had been drinking hot coffee. The patient stated that the burning sensation was constant throughout the day and localized in the anterior two-thirds of the tongue and the lower lip.

She explained that her complaint started one month prior to being admitted and added that she had never had such an issue before. In the vital findings of the patient, whose general condition was good, oriented, and cooperative, she had a fever of 36.5° C, arterial blood pressure of 120/70 mmHg, pulse of 90 beats/min, respiratory rate of 18/min and oxygen saturation of 99% in the room air.

There were no significant features in her family history. However, her medical history revealed that ramipril 5 mg tablet had been issued for hypertension approximately one month prior to her admission to the clinic. She did not smoke or consume alcohol. In the oral examination, it was determined that there were no mucosal or dental lesions, and that patient had normal and healthy oral mucosa. There was also no sign of aphthous or tumoral lesion on the tongue. Other physical examination findings were normal. The patient's mood was also normal; she had no history of mood disorders. There was no correlation to any gastrointestinal or other systemic disease. The laboratory results of the patient are presented in Table 1. A real-time reverse-transcription polymerase chain reaction (RT-PCR) test for COVID-19 came back negative.

After excluding all possible causes of burning mouth syndrome, we stopped ramipril, suspecting that the present symptoms might be a side effect of the ACEI, and changed the drug to a beta-blocker. After three weeks, her symptoms improved, taste perception returned to normal, and the burning sensation ceased. As of her latest follow-up, the patient's oral mucosa and tongue appeared normal and she was not experiencing any oral symptoms. No evidence of an underlying medical disorder was detected.

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Table 1: Patient's Laboratory Examination Results

White Blood Cell (WBC)	6.7 (4.60-10.20) K/uL
Hemoglobin	13.8 (12.20-18.10) g/dl
Mean Corpuscular Volume (MCV)	92.4 (80- 100) Fl
Lymphocyte (LYM)	3.01 (0.60-3.40) K/uL
Eosinophil (EOS)	0.4 (0.0-0.7) K/uL
Platelet (PLT)	285000 (100000-450000) K/uL
Glucose	87 (74-118) mg/dL
Sodium (Na)	141 (136-146) mmol/L
Potassium (K)	4.2 (3.5-5.1) mmol/L
Calcium (Ca)	9.4 (8 .8-10.6) mg/dL
Urea	26 (17-43) mg/dL
Creatinine	0.7 (0.67-1.17) mg/dL
D-dimer	50 (0-500)) µg FEU/L
C-reactive protein (CRP)	3.6 (0-5) mg/dL
Iron (Fe)	107 (37-158) µg/dL
Ferritin	78 (4.63-204)) ug/L
Thyroid Stimulating Hormone (TSH)	2.18 (0.35-4.94) uIU/mL
Free T4	1.03 (0.7-1.48) ng/dL
Vitamin B12	480 (187-883) pg/mL
25-Hydroxy vitamin D	40.2 ng/mL
Magnesium	2.2 (1.9-2.5) mg/dL
HgA1c	4.7 (4-6) % NGSP
Folate	5.9 (3.1-20.5) ng/mL

According to the Adverse Drug Reaction Probability Scale (Naranjo Algorithm), her score was 6 and classified as probable (4).

DISCUSSION

BMS has been defined as a chronic neuropathic intraoral pain condition. A number of etiologies have been reported to elucidate the clinical situation of burning mouth syndrome. These reported etiologies include personality and mood changes (anxiety and depression), concurrent health conditions and chronic pain conditions, headaches and pain in other locations, nutritional deficiencies, hormonal changes, and medications (5). While all these factors can be counted as causes, BMS is a diagnosis of exclusion. If the patient is experiencing these symptoms due to a medication, the best way to treat it is to change the medication for hypertension and follow-up (6).

Studies have shown that various neuropathic mechanisms act at different neuraxial levels and contribute to the pathophysiology of BMS. In tongue biopsy studies, it has been shown that BMS is caused by trigeminal small fiber sensory neuropathy (7). Presynaptic nigrostriatal dopaminergic pathway dysfunction has been reported to contribute to chronic pain in BMS. In immunohistochemical studies of biopsy samples taken from the tongues of BMS patients, a significant correlation was found between the pain score and heat and capsaicin receptor, transient receptor potential vanilloid 1 (TRPV1), as well as regulatory nerve growth factor (8). On the other hand, ACEI block hydrolysis of bradykinin by inhibiting desensitization of the receptor and potentiate the action of bradykinin (9). Katanosaka et al. reported that TRPV1 is a possible target ion channel activated indirectly by bradykinin. This study also showed that TRPV1 plays a role in bradykinin-evoked nociception (10). These prominent nociceptive complaints in the current case may have occurred as a result of the increased bradykinin level and TRPV1 effect after ACEI use.

Obara et al. reported that a 53-year-old female patient complained of burning mouth syndrome after using the ACE inhibitor captopril for the treatment of hypertension (6). Castells et al. stated in their study that the medication which causes burning symptoms and dysgeusia is an angiotensin receptor antagonist eprosartan (11). Boras et al. alluded to the connection between burning mouth symptoms and antihypertensives (ACE inhibitors and rarely angiotensin II receptor antagonists) in their report, describing how a 74-year-old female patient started to have complaints of a burning tongue one year after first using ramipril. These complaints disappeared when the medication was changed (12). Similar to the current case, the symptoms of all these patients regressed after the change of medication.

CONCLUSION

The clinical status of patients presented with symptoms of burning mouth syndrome and the medication they use should be reviewed. These complaints should inform clinicians when they prescribe treatments for patients with hypertension that involve ACEI. Physiological and histological studies are needed to elucidate the pathogenesis of BMS.

Conflict of interest: Authors declare no conflict of interest.
Ethic: Informed consent was obtained from the patient.
Approval of final manuscript: All authors

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