Treatment of glossodynia with olanzapine

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A 73-year-old white male with a 6-month history of glossodynia, unresponsive to clotrimazole troches, cevimeline, triamcinolone dental paste, paroxetine, and lorazepam presented to the dermatology clinic for consultation. Work-up revealed no oral abnormalities and no underlying systemic disorder. He denied symptoms consistent with a psychiatric disorder. A detailed free amnestic assessment by a board certified Geriatric Psychiatrist (John S. Kennedy, MD) found that the patient was oppressed by the pain. He did not meet the criteria for major depression nor did he have any anxiety disorder or delusions. Because of the presence of dysphoria and anticipatory anxiety secondary to glossodynia, the patient was started on olanzapine. Improvement of pain symptoms were noted within 3 days with full resolution of symptoms at 1- and 3-month follow-ups. Dysphoria and anticipatory anxiety remitted fully upon pain relief. (J Am Acad Dermatol 2004;51:463-5.)

CASE REPORT

A 73-year-old white male presented with a 6-month history of “painful burning tongue and bitter taste” following acute trauma from eating hot soup. The patient also complained of thick saliva, cotton mouth, and a red tender tongue with eating. The tenderness and taste perversion resulted in a 20-pound weight loss. The patient denied cancer phobia. Past medical history was significant for non-Hodgkin’s lymphoma treated with chemotherapy 5 years previously and no evidence of recurrence. He noted that during chemotherapy he had experienced similar tongue symptoms for a brief period, but they had remitted following completion of treatment. He reported no personal or family history of psychiatric disorder. His only medication prior to symptom onset was terazosin, which he had taken for 5 years. He was unresponsive to clotrimazole troches, cevimeline, triamcinolone dental paste, paroxetine, and lorazepam. He denied tobacco, alcohol, or other drug use.

On physical examination, the patient appeared physically well. Oral mucosa and conjunctiva were pink and moist. The tongue appeared normal both before and after eating. The mandible was edentulous with a lower complete denture and the maxilla was partially edentulous without a partial denture. There was no angular cheilitis or lymphadenopathy. He was dysphoric and had anticipatory anxiety just prior to eating each morning. He did not report symptoms consistent with a depression syndrome. He expressed a wish not to continue living in his current state, but denied any active plans of suicide. A detailed free amnestic assessment by a board certified Geriatric Psychiatrist (J. S. K.) found that the patient was oppressed by the pain. The patient did not meet the criteria for major depression. He did not have any anxiety disorder and he had no delusions.

A review of the patient’s prior laboratory evaluation revealed normal blood counts, serum chemistry profile, and erythrocyte sedimentation rate. Vitamin B12 and folate levels were normal. Oral culture was obtained and was negative for fungus.

A diagnosis of idiopathic glossodynia was rendered. The patient was started on olanzapine (Zyprexa, Eli Lilly and Company, Indianapolis, Ind) 5 mg once daily. He noted improvement of symptoms within 3 days. His taste perception normalized, burning sensation was eliminated, and appetite improved. His mood was euthymic without evidence of anxiety. He remained free of symptoms at 1- and 3-month follow-ups.
DISCUSSION

Glossodynia (burning mouth syndrome, glosсалgia, stomatodynia, glossopyrosis, glossitis) is defined as a spontaneous syndrome of burning sensation, discomfort, pain, irritation, or rawness of the tongue, lips, or oral cavity often without organic cause.1,2,3 In a cohort of 70 patients with glossodynia, 80% were female with a mean age of 59 years.4 The reported prevalence of glossodynia is between 0.7% and 1.5% of the population.5 There are no diagnostic criteria for glossodynia. Patients often complain of pain, tenderness, or burning with symptoms often worsening throughout the day. Patients may also complain of dysgeusia (altered taste) or xerostomia (dry mouth). In a prospective study of 96 patients, dysgeusia was detected in 44.8% of patients with glossodynia, approximately half of which did not present with a complaint of dysgeusia.6 Xerostomia has been reported in more than 20% of patients with glossodynia.4,7 On examination, the tongue appears normal, with erythema, edema, or atrophy present in rare cases.

The work-up for glossodynia should be guided by clinical suspicion and may include: detailed patient history, complete blood count, serum iron, serum B12 and folate levels, mucosal culture, serum tests for Sjögren’s syndrome antibodies (SS-A, SS-B), glycosylated hemoglobin, patch testing, and biopsy (if exam is abnormal).8,9 Further consultation may be helpful. In the case presented above, no underlying systemic conditions, nutritional deficiencies, adverse drug reactions, or oral disorders were detected to explain the etiology of the patient’s continued discomfort (Table I). Comorbid psychiatric disorders, particularly those with depressive or anxiety symptoms, have been reported in 30%-72% of patients with glossodynia.3,10 However, in the case of our patient, symptoms of dysphoria and anxiety were felt to be secondary to oppression associated with pain since these symptoms developed after the onset of glossodynia and remitted fully upon pain relief.

Treatment of secondary glossodynia is aimed at correcting the underlying condition. Reassuring that the pain is not related to neoplasia is appropriate in patients with cancerophobia. Topical antifungals are controversial treatments in cases of normal exams and cultures. Topical steroids and viscous lidocaine have been cited as therapy for glossodynia, but often provide patients with only temporary relief.9

The mainstay of treatment for primary glossodynia has been benzodiazepines and tricyclic antidepressants. Low-dose clonazepam was successful in reducing symptoms of burning mouth syndrome in 67% of 30 patients.11 Chlordiazepoxide is another long-acting benzodiazepine that has been successful in the treatment of glossodynia.7 Low-dose tricyclic antidepressants such as amitriptyline and doxepin have been effective in treating glossodynia, neuropathy, fibromyalgia, and other chronic pain conditions.12,13

This case is noteworthy because the patient was refractory to benzodiazepine and antidepressant therapy. The patient responded to a medication currently indicated only for psychosis in schizophrenia and acute mania in bipolar disorder. This is the first reported case in the literature of olanzapine successfully relieving the symptoms of glossodynia. Recent case reports demonstrate the potential success of olanzapine in treating patients with other pain disorders: fibromyalgia14 and cancer pain.15

The mechanism responsible for this effect of olanzapine is unknown. Olanzapine is a potent antagonist at a number of neuronal receptors including dopamine and serotonin receptors and produces antipsychotic effects with reduced risk of extrapyramidal symptoms.16,17,18 We hypothesize that the efficacy of olanzapine in treating glossodynia is due, in part, to its blockade of a subset of these serotonin receptors. Olanzapine may exhibit anxiolytic, antipsychotic, and gastrointestinal anti-motility properties secondary to other serotonin receptor antagonism.16-18 Peripheral serotonin blockade or involvement of alpha2-adrenoreceptors19 by olanzapine may be partially responsible for the pain relief observed in our patient. Possible side-effects of olanzapine include weight gain, which may be substantial in a small subset of patients. Minimal anticholinergic side effects may be observed in geriatric patients.20,21 Olanzapine, a newer antipsychotic and dopamine modifier, may induce or uncover extrapyramidal syndromes such as parkinsonism, akathisia, tardive dyskinesia, and neuroleptic malignant syndrome. The risk of the atypical antipsychotics for these adverse effects and

### Table I. Primary and secondary types of glossodynia and their associated etiologies

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<thead>
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<th>Primary</th>
<th>Secondary</th>
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<tbody>
<tr>
<td>Idiopathic</td>
<td>Disorders of the oral cavity</td>
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<td>Infection</td>
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cardiotoxicity is much lower than has been reported for the older typical medications including pimozide.

Glossodynia is a challenge for many health care providers. Etiology often cannot be identified and success of treatment is currently patient-specific and unpredictable. When the side effect profile or safety concerns of benzodiazepines and tricyclic antidepressants outweigh the benefits of their use, or the patient is refractory to such medications, olanzapine may prove to be the next successful alternative in providing relief to the patient with glossodynia. Therefore, further experience with olanzapine in glossodynia, confirming the effect observed in such patients as this, is warranted by the result reported here.

REFERENCES