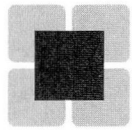

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A 59-year-old man with mouth pain

A 59-YEAR-OLD man seeks medical attention because of a "fire-like" pain in his tongue and hard palate that has lasted 4 months. Initially episodic, the pain is now persistent. He has no other complaints except a change in taste and trouble sleeping at night, not related to the pain. He has a history of hypertension but takes no medications for it. He says he has not experienced any trauma, does not smoke, does not wear dentures, and has no risk factors for human immunodeficiency virus (HIV).

On physical examination, the patient appears uncomfortable. His blood pressure is 146/92 mm Hg. No adenopathy, sinus tenderness, or oral abnormalities are noted, and there is no glossitis or evidence of lichen planus. His lungs are clear, and the heart examination is normal. No organomegaly is noted. His extremities are normal and no neurological deficits are found, including those of taste perception.

1 On the basis of these findings, what is the most likely diagnosis?

- ❑ Gastroesophageal reflux disease
- ❑ Oral candidiasis
- ❑ Giant cell arteritis
- ❑ Xerostomia
- ❑ Burning mouth syndrome

Gastroesophageal reflux is unlikely because this patient has no heartburn, pyrosis, acid regurgitation, or pharyngeal erythema, and the pain is not worse at night. The lack of typical lesions of candidiasis in an immunocompetent patient essentially excludes candidal infection. Patients with giant cell arteritis may have "oral" pain, but this is usually related to ischemia of the muscles of mastication. Hence, in this condition, the pain should worsen with chewing, and other typical signs and symptoms should be noted. Xerostomia, although possible, is unlikely, given that he has no complaints about a dry mouth or dry eyes and his tongue is not bald. Medications, notably antibiotics, diuretics, or psychiatric drugs (especially tricyclic antidepressants), could also cause mouth pain; however, he is not taking any.

The most plausible diagnosis is burning mouth syndrome, an oral pain disorder unaccompanied by clinical signs. The presence of oral mucosal lesions precludes the diagnosis; therefore, a thorough oral examination is necessary. Altered taste and abnormalities of sleep support the diagnosis.

The prevalence of burning mouth syndrome is highest in postmenopausal women: 10% to 40% attending postmenopausal clinics. The greatest frequency occurs from 3 years before menopause to 12 years after, and in women who have more menopausal complaints than do matched controls. Prevalences of 2.5% to 4.5% are noted in general medicine clinics.

Typically, patients experience burning pain that begins spontaneously. More than one site is often affected, most commonly the anterior two thirds of the tongue, anterior hard palate, and mucosal surface of the lower lip. The pain may be continuous, although it frequently begins in the midmorning, is maximal by early evening, and remits at night. The severity of the pain is similar to that of a toothache. Patients often report a dry mouth, a metallic, bitter

taste, and thirst as well. Irritability, depression, decreased desire to socialize, and difficulty sleeping are not uncommon. Patients may also have more health complaints, chronic pain syndromes, or medication use (especially sleeping pills) than matched controls.

Burning mouth syndrome frustrates both patients and clinicians alike. It is known by different terms—glossodynia, oral dysesthesia, and orolingual paraesthesia—displaying the uncertain nature of the problem. Numerous causes have been proposed, including local factors (dentures, *Candida* infection, decreased salivary production), systemic factors (nutritional or estrogen deficiency), psychogenic factors (depression, anxiety disorders, parafunctional habits such as persistent tongue movements), and miscellaneous factors including sensory neuropathies.

2 What is the next step in the care of this patient?

- ❑ Serologic study for HIV
- ❑ *Candida* culture
- ❑ Glucose tolerance test
- ❑ Vitamin B_{12}, red blood cell folate, and ferritin concentrations

Burning mouth syndrome has been linked to a variety of medical conditions, although recent studies have not substantiated the associations. Hence, the laboratory evaluation remains controversial and does not substitute for a thorough general examination.

Many primary care physicians search for treatable causes such as vitamin deficiency, diabetes, and hypothyroidism, even though no cause is identified in most patients. Grushka and Sessle found no significant differences in the prevalence of *Candida* infections, hematologic abnormalities, thyroid abnormalities, or diabetes between patients with burning mouth syndrome and controls.

Preanemic deficiencies of iron, vitamin B_{12}, and folate have been implicated; hence, a measurement of vitamin B_{12} (and perhaps of methylmalonic acid), red blood cell folate, and ferritin concentrations should be considered.

Medications are a common cause of oral symptoms. Clinicians should also consider miscellaneous causes of oral complaints such as giant cell arteritis, lymphoid inflammation, allergies, medications, periodontal disease, candidiasis, oral cancer, myeloblastic syndrome, amyloidosis, sensory neuropathy, and infections (HIV, fusobacteria and spirochetes).

If clinical uncertainty exists regarding oral findings, referral to an oral specialist (dentist, dermatologist, otolaryngologist) should be considered.

3 The appropriate therapy for this patient could include which of the following?

- ❑ Tricyclic antidepressants in low doses
- ❑ Psychotherapy
- ❑ Topical antifungal therapy
- ❑ Multivitamins
- ❑ All of the above

All of the treatment options listed, which address putative causes of burning mouth syndrome, are reasonable. However, none have been proven to be effective.

Mood and personality changes have long been recognized in burning mouth syndrome. Although there is a strong psychological component, no evidence of a causal relationship exists. Psychogenic distress in patients with chronic pain is to be expected and may result from the pain itself.

Reports of relief with low doses of tricyclic antidepressants and psychotherapy support the belief that burning mouth syndrome is a psychobiological disorder. However, there is little reason to assume that the efficacy of tricyclic antidepressants is due to a therapeutic effect on depression, as they are useful in other chronic pain syndromes both with and without depression. Gorsky et al recently reported that the benzodiazepines chlordiazepoxide and diazepam had greater efficacy than did amitriptyline, although this has not been confirmed in controlled, double-blind, crossover studies. As tricyclic antidepressants may cause dry mouth as a side effect, a selective serotonin reuptake inhibitor could also be considered for patients whose pain does not respond or who have intolerable side effects with tricyclic antidepressants.

Adjunctive use of psychotherapy should be considered for patients unresponsive to medications, who have disturbing mood alterations, or who have parafunctional habits such as persistent tongue movements (also known as "restless tongue syndrome").

There have also been anecdotal reports of relief with antifungal therapy despite negative candidal cultures, although no blinded studies substantiate this.

Since one study showed that patients with the syndrome had decreased levels of vitamins B_1, B_2, and B_6 and obtained symptom relief with vitamin therapy, a trial of vitamin therapy could be considered.

Postmenopausal women who have no contraindications to hormone replacement therapy may experience some relief with estrogen replacement.

Five percent to 10% of patients with the syndrome have abnormal glucose tolerance test results, but treatment of the glucose intolerance has little impact on the pain.

Allergies to substances present in dentures (acrylic, cadmium) and mechanical irritation are possible considerations in patients who wear dentures, and denture refitting or change of denture adhesives should be considered.

Once infectious and neoplastic processes have been ruled out, perhaps more important than pharmacological management is patient reassurance. It is useful to warn patients in advance that the likelihood of finding a cause for the condition is slim, and the patient will have to learn to live with it. Very often, patients will be satisfied with this explanation. Some good news is that at least a partial remission does occur in up to two thirds of patients within 6 to 7 years after onset.

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SUGGESTED READING

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