

Case Report

Atrophic Glossitis From Vitamin B₁₂ Deficiency: A Case Misdiagnosed as Burning Mouth Disorder

Julia S. Lehman,* Alison J. Bruce,[†] and Roy S. Rogers III[†]

Background: Glossodynia, or painful sensation of the tongue, can have a spectrum of etiologies, such as local infection, trauma, nerve damage, glossitis, or the enigmatic neuropathic pain syndrome, burning mouth disorder (BMD; also known as burning mouth syndrome). Careful history-taking, physical examination, and appropriate laboratory screening can differentiate these causes of glossodynia and direct further therapy.

Methods: A 73-year-old woman presented with several months of glossodynia having previously been diagnosed by her primary care physician with primary BMD. Subsequently, she consulted an otolaryngologist, who pursued further diagnostic evaluation.

Results: Examination revealed the presence of a beefy, red, smooth tongue, and further laboratory evaluation yielded a low serum vitamin B₁₂ level and macrocytosis. Three months of oral vitamin B₁₂ supplementation led to partial restoration of serum vitamin B₁₂ levels and a modest improvement in symptoms. Her final diagnoses were atrophic glossitis and glossodynia secondary to vitamin B₁₂ deficiency, most likely due to pernicious anemia.

Conclusions: The results of this case have important clinical implications for the diagnostic evaluation and management of patients with glossodynia and apparent BMD. Pathogenic mechanisms of nutrient deficiency in atrophic glossitis are discussed. *J Periodontol* 2006;77:2090-2092.

KEY WORDS

Anemia, pernicious; burning mouth syndrome; glossalgia; glossitis; vitamin B₁₂ deficiency.

Glossodynia, or tongue pain, can have a spectrum of etiologies,¹ such as local infection, trauma, nerve damage, vitamin deficiencies, glossitis, or the complex pain syndrome burning mouth disorder (BMD; also known as burning mouth syndrome). Primary BMD is a specific condition characterized by unremitting oral mucosal pain and the absence of oral lesions or changes of the oral mucosa.²⁻⁴ Thought to be caused by a combination of local, systemic, and psychological factors, BMD confers a diminished quality of life and is often associated with a poor prognosis.²⁻⁶

We present a patient with several months of glossodynia who initially was diagnosed with primary BMD before undergoing a complete laboratory workup. Revision of her diagnosis based on laboratory test results led to appropriate therapy and the partial reversal of her symptoms. This case highlights the importance of recognizing sometimes subtle tongue abnormalities on physical examination and the necessity of screening for reversible conditions in patients with glossodynia. The patient provided informed consent to be profiled.

CASE REPORT

In August 2005, a 73-year-old previously healthy woman presented to the Mayo Clinic with an 18-month history of a sore, burning tongue and increased tongue sensitivity. Six months prior, she had been given empiric treatment for presumed candidiasis by her primary care physician because of her complaints of glossodynia; this failed to improve her symptoms. An esophagogastroduodenoscopy demonstrated no evidence of reflux esophagitis. After this initial workup, she was diagnosed with primary BMD based on her symptoms. It is unknown whether the patient had clinical changes in the appearance of her tongue at that time. However, three months later, she was seen by an otolaryngologist, who noted physical findings of atrophic glossitis on examination. Screening laboratory tests demonstrated macrocytosis (mean corpuscular volume: 99.6 fl; range: 81.6 to 98.3 fl) but no

* University of Wisconsin Medical School, Madison, WI.

[†] Mayo Clinic, Rochester, MN.

evidence of anemia (hemoglobin: 13.7 g/dl; range: 12.0 to 15.5 g/dl). Her serum vitamin B₁₂ level was low (144 ng/l; range: 200 to 650 ng/l), whereas her serum folate, calcium, magnesium, zinc, thyroid stimulating hormone, and fasting blood glucose levels were all within normal limits.

The patient began oral vitamin B₁₂ replacement (super B-complex vitamin containing 100 mcg vitamin B₁₂ daily and a multivitamin containing 400 mcg vitamin B₁₂ daily) and followed up with dermatology at our institution 3 months later.

At that time, she reported partial improvement in her symptoms. Examination revealed a smooth, shiny tongue with some central fissuring (Fig. 1). Her oral and conjunctival mucosa were otherwise normal. Laboratory studies demonstrated a slightly improved but still suboptimal serum vitamin B₁₂ level (148 ng/l). The incomplete restoration of serum vitamin B₁₂ levels with a diet containing meat and several months of oral vitamin B₁₂ supplementation was suggestive of malabsorption, most likely due to a lack of intrinsic factor (pernicious anemia). She was advised to follow a soft, bland diet until resolution of her glossodynia and to follow up with her internist for continued management of her vitamin B₁₂ deficiency. We anticipate that her symptoms will continue to improve with prolonged supplementation with high doses of vitamin B₁₂. Her final diagnoses were atrophic glossitis and glossodynia from vitamin B₁₂ deficiency, likely secondary to pernicious anemia.

DISCUSSION

This case emphasizes the importance of testing for reversible etiologies in patients presenting with complaints of a painful or burning tongue. Initially, the patient had been diagnosed with BMD, a complex neuropathic pain syndrome that is not well under-



Figure 1.

Smooth, shiny tongue, demonstrating loss of filiform papillae and central fissuring. These findings fit the classic description of atrophic glossitis and can be seen with vitamin B₁₂ deficiency.

stood and that generally confers a poor prognosis.⁴ It is important to recognize that this is a diagnosis of exclusion and should only be made in the presence of an entirely normal physical examination and after elimination of potential causative factors. This case highlights the need for clinicians to perform a meticulous oral examination and to be familiar with the normal architecture of the tongue, so as to be able to detect subtle changes in appearance that may provide clues to a correct diagnosis. Because this patient had the physical findings of atrophic glossitis, further diagnostic evaluation was indicated.

Atrophic glossitis, characterized by a smooth, shiny appearance of the tongue secondary to the loss of filiform papillae, can be associated with a burning sensation of the tongue.¹ Tongue atrophy has been documented in oral candidiasis, general malnutrition, and several other systemic conditions such as Sjögren's syndrome, syphilis infection, amyloidosis, and Riley-Day syndrome.^{1,7-9} However, more commonly, atrophic glossitis is associated with deficiencies of specific nutrients, such as B-complex vitamins, vitamin E, folate, and iron.^{1,7,10-14} Although such nutritional deficiencies usually are detected by an associated anemia, they only rarely present initially with symptoms of atrophic glossitis or glossodynia.^{10,15}

Several hypotheses regarding the pathogenic role of nutrient deficiencies in atrophic glossitis have been proposed. Because cells of the tongue papillae have a high rate of turnover, deficiencies in micronutrients needed for cell proliferation or cell membrane stabilization may lead to depapillation.¹¹ Nutrient deficiencies may also contribute to oral pathology by altering the pattern of microbial flora.¹⁶ Interestingly, the dysgeusia and glossodynia associated with atrophic glossitis may lead to anorexia and, therefore, may exacerbate some nutrient deficiencies.

With regards to therapy, supplementation with deficient nutrients in patients with both atrophic glossitis and documented vitamin or mineral deficiencies has been shown to improve symptoms.¹⁵ To ameliorate the burning sensation of the tongue associated with atrophic glossitis, consumption of a soft, bland diet has been suggested previously^{6,7} until normal nutritional status and concurrent tongue anatomy are restored. This was recommended to the patient.

Deficiency of vitamin B₁₂ in particular has been reviewed elsewhere.^{17,18} Briefly, vitamin B₁₂ deficiency can result from dietary deficiency (e.g., in strict vegetarians, older or malnourished people, or alcoholics) or malabsorption (e.g., as a consequence of bacterial overgrowth in the gut, use of gastric acid-lowering agents, or autoimmune destruction of intrinsic factor [pernicious anemia]).^{17,18} This condition may be asymptomatic or may present with hematologic, neuropsychiatric, or gastrointestinal disturbances.^{17,18}

Initial presentation of vitamin B₁₂ deficiency as atrophic glossitis, stomatitis, and mucosal ulceration has been described previously.^{14,15,19} Regardless of the etiology of vitamin B₁₂ deficiency, high-dose oral supplementation (1,000 to 2,000 mcg daily for 2 weeks, followed by 1,000 mcg daily for maintenance) is currently recommended.¹⁸ Historically, pernicious anemia was treated with intramuscular vitamin B₁₂ supplementation. However, several studies^{20,21} have demonstrated that high doses of oral vitamin B₁₂ are just as effective as, and are better tolerated than, intramuscular vitamin B₁₂ in patients with vitamin B₁₂ malabsorption. It is now thought that high doses of ingested vitamin B₁₂ activate an alternate mechanism of absorption in the ileum that involves passive diffusion without the need for an intrinsic factor.²⁰

The case presented in this article demonstrates that it is appropriate and necessary to screen for correctable causes in patients with burning mouth pain. Obtaining a meticulous history and physical examination in conjunction with ordering relevant laboratory tests, including serum levels of vitamin B₁₂, other B-complex vitamins, zinc, iron, and folate, a complete blood count, and red blood cell indices, may reveal an occult nutrient deficiency. Hastily diagnosing primary BMD, a probable neuropathic pain syndrome, could hinder investigation into and reversal of other potentially treatable conditions. Early detection and correction of nutrient deficiencies can prevent future medical complications^{10,15} and improve patient prognosis considerably, underscoring the importance of accurate diagnosis and prompt management of such disorders.

REFERENCES

1. Byrd JA, Bruce AJ, Rogers RS 3rd. Glossitis and other tongue disorders. *Dermatol Clin* 2003;21:123-134.
2. Drage LA, Rogers RS 3rd. Burning mouth syndrome. *Dermatol Clin* 2003;21:135-145.
3. Drage LA, Rogers RS 3rd. Clinical assessment and outcome in 70 patients with complaints of burning or sore mouth symptoms. *Mayo Clin Proc* 1999;74:223-228.
4. Scala A, Checchi L, Montevecchi M, Marini I. Update on burning mouth syndrome: Overview and patient management. *Crit Rev Oral Biol Med* 2003;14:275-291.
5. Drage LA, Bruce AJ, Rogers RS III. Burning mouth syndrome. In: Lebowitz M, Heymann WR, Smith-Jones J, Coulson I, eds. *Treatment of Skin Disease*, 2nd ed. Philadelphia: Elsevier; 2005:241-243.
6. Soares MS, Chimenos-Kustner E, Subira-Pifarre C, Rodriguez de Rivera-Campillo ME, Lopez-Lopez J. Association of burning mouth syndrome with xerostomia and medicines. *Med Oral Patol Oral Cir Bucal* 2005;10:301-308.
7. Rogers RS 3rd, Bruce AJ. The tongue in clinical diagnosis. *J Eur Acad Dermatol Venereol* 2004;18:254-259.
8. Bohmer T, Mowe M. The association between atrophic glossitis and protein-calorie malnutrition in old age. *Age Ageing* 2000;29:47-50.
9. Terai H, Shimahara M. Atrophic tongue associated with Candida. *J Oral Pathol Med* 2005;34:397-400.
10. Schmitt RJ, Sheridan PJ, Rogers RS 3rd. Pernicious anemia with associated glossodynia. *J Am Dent Assoc* 1988;117:838-840.
11. Drinka PJ, Langer E, Scott L, Morrow F. Laboratory measurements of nutritional status as correlates of atrophic glossitis. *J Gen Intern Med* 1991;6:137-140.
12. Drinka PJ, Langer EH, Voeks SK, Scott L, Morrow FD. Nutritional correlates of atrophic glossitis: Possible role of vitamin E in papillary atrophy. *J Am Coll Nutr* 1993;12:14-20.
13. Enwald CV, Drinka PJ, Swartz C, Langer EH, Voeks SK. Iron status in atrophic glossitis: A pilot study. *Wis Med J* 1993;92:570-573.
14. Lu SY, Wu HC. Initial diagnosis of anemia from sore mouth and improved classifications of anemias by MCV and RDW in 30 patients. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2004;98:679-685.
15. Petavy-Catala C, Fontes V, Gironet N, Huttenberger B, Lorette G, Vaillant L. Clinical manifestations of the mouth revealing vitamin B₁₂ deficiency before the onset of anemia (in French). *Ann Dermatol Venereol* 2003;130:191-194.
16. Sweeney MP, Bagg J, Fell GS, Yip B. The relationship between micronutrient depletion and oral health in geriatrics. *J Oral Pathol Med* 1994;23:168-171.
17. Dharmarajan TS, Adiga GU, Norkus ER. Vitamin B₁₂ deficiency: Recognizing subtle symptoms in older adults. *Geriatrics* 2003;58:30-38.
18. Oh RC, Brown DL. Vitamin B₁₂ deficiency. *Am Fam Physician* 2003;67:979-986, 993-994.
19. Field EA, Speechley JA, Rugman FR, Varga E, Tyldesly WR. Oral signs and symptoms in patients with undiagnosed vitamin B₁₂ deficiency. *J Oral Pathol Med* 1995;24:468-470.
20. Kripke C. Is oral vitamin B₁₂ as effective as intramuscular injection? *Am Fam Physician* 2006;73:65.
21. Vidal-Alaball J, Butler CC, Cannings-John R, et al. Oral vitamin B₁₂ versus intramuscular vitamin B₁₂ for vitamin B₁₂ deficiency. *Cochrane Database Syst Rev* 2005;(3):CD004655.

Correspondence: Dr. Alison J. Bruce, Mayo Clinic E-5, 200 First St. S.W., Rochester, MN 55905. Fax: 507/284-2072.

Accepted for publication July 12, 2006.