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A Case Report of Pernicious Anemia and Recurrent Aphthous Stomatitis

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Abstract

Aim: The aim of this report is to present the management of a patient with pernicious anemia afflicted with recurrent aphthous stomatitis (RAS).

Background: RAS is one of the most common lesions of the oral mucosa. Although the exact etiology of RAS is still unknown different hematinic deficiencies have been proposed.

Case Report: Painful recurrent ulcers covered with a grayish pseudomembrane surrounded by an erythematous margin were identified on the tongue and in the buccal mucosa of a 71-year-old woman. The patient also presented with depapilation of the tongue. The clinical diagnosis was RAS. Laboratory tests including a hemogram were ordered to determine existing levels of folic acid, iron, ferritin, and vitamins B2, B6, and B12. Levels of serum vitamin B12 and serum hemoglobin were low. The laboratory investigation also showed a medium corpuscular volume of 104.1 fl. A gastroduodenoscopy revealed no macroscopic abnormality. A gastric biopsy showed mucosal atrophy in the gastric corpus with evidence of intestinal metaplasia. Antibodies against an intrinsic factor were negative. The diagnosis pernicious anemia was made, with RAS caused by vitamin B12 malabsorption. Treatment consisted of the administration of 1.0 ml of hydroxocolabamin intramuscularly twice weekly over four weeks followed by 1.0 ml once weekly for four weeks. Clinical resolution was observed after two months.

Summary: The association of RAS with vitamin B12 malabsorption is a rare event. However, along with conventional RAS clinical management, iron, folic acid, vitamin B deficiencies, and nutritional intolerance must be considered. Evaluation of the predisposing factors is imperative in treating patients with RAS including vitamin B12 malabsorption.

Clinical Significance: Determination of the levels of vitamin B12 should be the basis for replacement therapy. Such therapy can be considered a benefit to the patients with RAS as its etiology remains unclear. Clinicians must be alert to the possibility this lesion could be a signal of systemic disease.

Keywords: Chronic gastritis, malabsorption, pernicious anemia, recurrent aphthous stomatitis, RAS, vitamin B12

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Introduction

Recurrent aphthous stomatitis (RAS) is an inflammatory ulcerative condition of the oral mucosa characterized by painful and recurrent ulcers. It is one of the most common oral diseases worldwide and has been the subject of many studies. RAS affects up to 25% of the general population and three-month recurrence rates are as high as 50%.[1]

RAS is classified according to clinical features as minor, major, and herpetiform. The most common presentation is minor RAS with round, clearly defined, small, painful ulcers that heal in 10 to 14 days without scarring. In major RAS (Sutton's disease) the lesions are larger (>1.0 cm), can last for six weeks, and frequently scar. The third variety of RAS is the herpetiform, which presents as multiple clusters of pinpoint lesions that coalesce to form large irregular ulcers and last seven to ten days.[2]

While the exact pathophisiology of RAS remains unclear, factors contributing to this clinical entity include the following:[3,4]

- Local trauma
- Smoking
- Stress
- Hormonal status
- Genetics
- Hematinic deficiencies (iron, folic acid, vitamins B2, B3, B6, B12, and C)
- Immunological factors
- Microorganisms
- Systemic diseases

Broides et al.[5] reported patients with Imerslun-Grabeck syndrome had a vitamin B12 deficiency associated with a neutrophil chemotactic defect that may cause RAS.

Chronic gastritis is an inflammation of the lining of the stomach occurring gradually and persisting for a prolonged time.[6] Pernicious anemia is the result of vitamin B12 malabsorption induced by chronic gastritis. The relation between deficiency of vitamin B12 and RAS have been rarely reported in the literature.[4] Wray et al.[7] demonstrated RAS can be caused by a deficiency of vitamin B12 although only 3.8% of the patients presented this condition. Piskin et al.[8] observed 35 patients with RAS and concluded serum vitamin B12 levels were low in eight patients (22.8%). In other studies Koybasi et al.[9] and Burgan et al.[10] observed 35.2% and 26.6% of the patients, respectively, had RAS and a vitamin B12 deficiency. In the current report the clinical features and management of a case of RAS related to vitamin B12 malabsorption are described.

Case Report

Diagnosis

A 71-year-old-woman was referred to the Oral Medicine Clinic of the School of Dentistry at the Universidade Federal de Minas Gerais in Belo Horizonte, Brazil for evaluation and treatment in April 2006. She complained of painful recurrent oral ulcers evolving over the past three years. Multiple ulcers covered with a grayish pseudomenbrane surrounded by an erythematous margin located

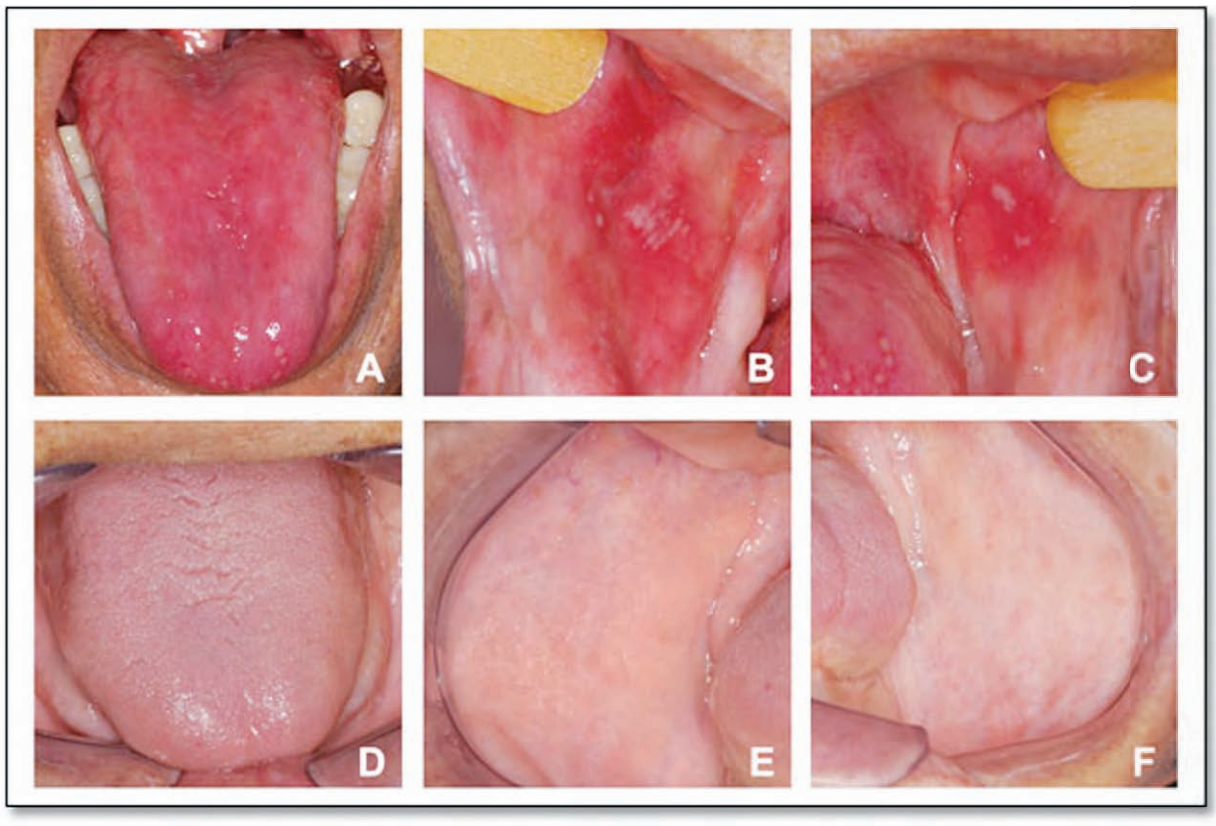

Figure 1. A. Depapilation of the tongue and multiples ulcers covered with a grayish pseudomenbrane located in the apex of the tongue. **B** and **C**. Ulcers covered with a grayish pseudomenbrane located in the right and left erythematous buccal mucosa. **D, E** and **F.** Clinical resolution of the ulcers and improvement of the tongue's depapilation.

in the tongue and in the buccal mucosa were identified during the oral examination. Depapilation of the tongue and erythemathous buccal mucosa was also noted (Figures 1A, 1B, and 1C).

Laboratory tests including a hemogram were ordered to determine folic acid, iron, ferritin, vitamins B2, B6, and B12 levels, serum hemoglobin, and medium corpuscular volume (MCV). A low serum vitamin B12 (133 pg/ml) and a low serum hemoglobin (3,670,000/mm^3) along with a MCV of 104.1 fl were identified.

A gastroduodenoscopy revealed no macroscopic abnormality. A gastric biopsy revealed mucosal atrophy in the gastric corpus with evidence of intestinal metaplasia. Antibodies against an intrinsic factor and *Helicobacter pylori* detection were negative. The diagnosis of pernicious anemia was made along with RAS caused by malabsorption of vitamin B12.

Treatment

Treatment consisted of the administration of 1.0 ml of hydroxocolabamin intramuscularly twice weekly over four weeks followed by 1.0 ml once weekly for four weeks. Clinical resolution of the RAS and improvement of the tongue depapilation and buccal mucosa (Figures 1D, 1E, and 1F) was apparent after two months.

At 12 months the patient was free of the RAS with normal levels of hemoglobin, MCV, and vitamin B12, but continued with intramuscular administration of vitamin B12 and 2 ml of hydroxocolabamin for 60 more days.

Discussion

A great deal of progress has been made during the last three decades regarding the epidemiology, description, causes, and treatment of RAS. Systemic conditions, genetic, immunologic, microbial factors, and hematinic deficiencies have been found to be related to the pathogenesis

of RAS. However, no principal cause has been discovered to date.[2,3] The clinical features along with the patient response to the management of the case reported here supported a diagnosis of RAS related to vitamin B12 malabsorption.

Chronic gastritis can induce malabsorption of vitamin B12. In the present case the gastritis was an auto-immune phenomenon. The deficiency of vitamin B12 is frequently associated with glossitis but not generally thought to induce RAS.[7,8,11,12] While the precise role of vitamin B12 deficiency in the pathogenesis of RAS is unclear, the suppression of cell-mediated immunity and changes in the cells of the tongue and oral mucosa have been described.[13-15] Studies from the United Kingdom, United States, and Spain have demonstrated hematinic deficiency is twice as common in RAS patients than in controls.[7] In the present case the disease started when the patient was 71 years old, which is not common. The patient also presented with erythemathous mucosa and depapilation of the tongue which are characteristic symptoms of other problems.

Differentiation between RAS and other forms of oral ulcers seldom pose a major clinical or diagnostic problem,[4] although similar-appearing lesions may arise in systemic disorders. Rarely, drugs such as non-steroidal anti-inflammatory drugs (NSAIDS) or nicorandil can give rise to oral ulcers, similar to RAS.[15]

Patients with RAS generally do not require treatment. On the other hand, some RAS lesions can be painful in a recurrent or constant pattern. As a result, it is important to determine possible hematinic deficiencies or allergies in order to provide appropriate therapies.[15] Like the case reported by Weusten and Van de Wiel[4] the patient in the present case responded to treatment with parenteral vitamin B12 after which the RAS did not recur and serum vitamin B12, hemoglobin, and MCV levels returned to normal levels.

Summary

The association of RAS with vitamin B12 malabsorption is a rare event. However, along with conventional RAS clinical management, iron, folic acid, vitamin B deficiencies, and nutritional intolerance must be considered. Evaluation of the predisposing factors is imperative in treating patients with RAS including vitamin B12 malabsorption.

Clinical Significance

Determination of the levels of vitamin B12 should be the basis for replacement therapy. Such therapy can be considered a benefit to the patients with RAS as its etiology remains unclear. Clinicians must alert to the possibility this lesion could be a signal of systemic disease.

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