Glossitis with linear lesions: An early sign of vitamin B_{12} deficiency

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The classic oral manifestations of vitamin B_{12} deficiency are considered nonspecific. We describe 4 patients with oral linear lesions associated with vitamin B_{12} deficiency. Patients were free of neurologic symptoms and anemia at diagnosis. We believe that glossitis with linear lesions is an early clinical sign of vitamin B_{12} deficiency. We recommend the determination of vitamin B_{12} in such patients, even in the absence of anemia. (J Am Acad Dermatol 2009;60:498-500.)

INTRODUCTION

The classic triad of vitamin B_{12} deficiency consists of the presence of megaloblastic anemia, gastrointestinal symptoms or glossitis, and neuropsychiatric symptoms.[1] Early diagnosis is important because neurologic signs could be irreversible.

Vitamin B_{12} deficiency can present with several oral manifestations, which are considered nonspecific. Hunter's glossitis (or Moeller-Hunter) is the most classic form. Hunter's glossitis, which presents in up to 25% of cases,[2] is characterized by diffuse erythema and lingual atrophy. There are other oral manifestations of vitamin B_{12} deficiency: glossodynia, recurrent ulcers, lingual paresthesia, burning, pruritus, dysgeusia, intolerance to dental prosthesis, intermittent xerostomia, stomatitis, and cheilitis.[3-10] All manifestations are considered clinically nonspecific. The majority of published cases are in the odontologic literature.

We describe 4 patients with oral linear lesions associated with vitamin B_{12} deficiency. We suggest that this presentation is evocative of the deficit and precedes the onset of macrocytic anemia.

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CASES

The major clinical and laboratory findings are summarized in Table I.

Patient 1 was referred in May 2003 because of stomatitis and glossitis of 1 year's duration. She had been treated for malignant melanoma in the gluteal region in 1988, without further problems. In 1995 a hysterectomy with removal of the ovaries and Fallopian tubes was performed because of squamous cell carcinoma of the cervix; as sequelae of the procedure, a ureterorectal fistula and bowel subocclusive episodes resulted. On physical examination, depapillated erythematous linear lesions affecting the tongue and hard palate were seen (Fig 1). She was initially treated with oral fluconazole, with no response. A 4-mm punch biopsy performed on the tongue, at the margin of the erythematous area, disclosed epithelial hyperplasia, parakeratosis, and capillary ectasia; periodic acid—Schiff (PAS) stain was negative. Blood analysis was performed (see Table I).

Patient 2 presented in November 2004 for migratory glossitis of 1 year's duration which had not responded to topical nystatin. On physical examination, glossitis with atrophic linear lesions was observed (Fig 2). Vitamin B_{12} deficiency was suspected. Blood analysis was carried out (see Table I) and a therapeutic regimen of daily oral vitamin B_{12}, 2 μg, was started. On December 2004, after 1 month of treatment, the patient returned for blood analysis results, and his glossitis had resolved.

Patient 3, a 33-year-old woman with Hashimoto's thyroiditis, was referred to the Department of Dermatology in February 2006 for evaluation of acute glossitis in the context of antibiotic treatment for eradication of *Helicobacter pylori* infection. On physical examination, erythematous areas on the tongue were observed, some of them with a linear pattern (Fig 3). She was treated with oral fluconazole

Table I. Main clinical and laboratory findings in patients with glossitis with linear lesions*

Patient No.	Age (y)	Sex	Duration of symptoms (mo)	Hb (g/L)	Hct (%)	MCV (fL)	Vitamin B_{12} (pmol/L)	Folate (nmol/L)	Ferritin (μg/L)	Etiology
1	54	F	12	135	39.9	93	<44	59	51	Bacterial overgrowth
2	36	M	12	151	44.7	106	<44	34	21	Gastric atrophy
3	33	F	1	128	37.8	94	<44	6	2.7	Gastric atrophy
4	68	F	72	120	37.8	116	25	24	ND	Gastric atrophy

F, Female; *Hb*, hemoglobin; *Hct*, hematocrit; *M*, male; *MCV*, mean corpuscular volume; *mo*, months; *ND*, not determined.
*Reference values: Hb, 110-180 g/L; Hct, 32%-55%; MCV, 82-92 fL; vitamin B_{12}, 132-857 pmol/L; folate, 6-77 nmol/L; ferritin, 30-300 μg/L.

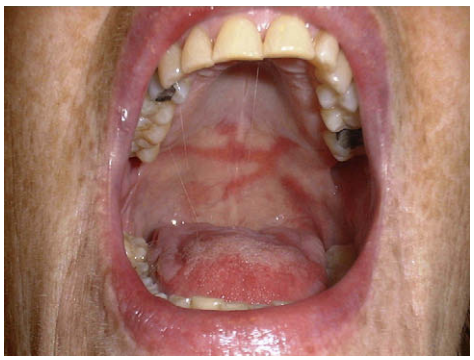

Fig 1. Linear lesions on hard palate and dorsum of the tongue.

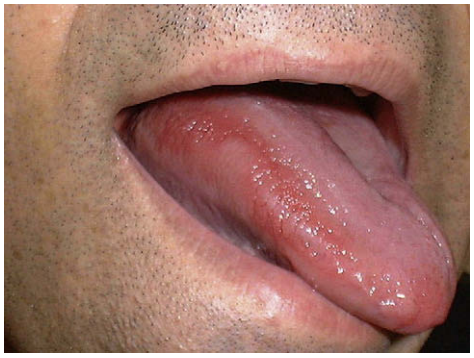

Fig 2. Linear glossitis on lateral aspect of the tongue.

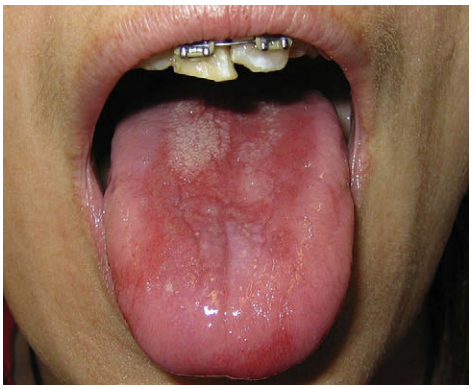

Fig 3. Glossitis with linear and band-like lesions.

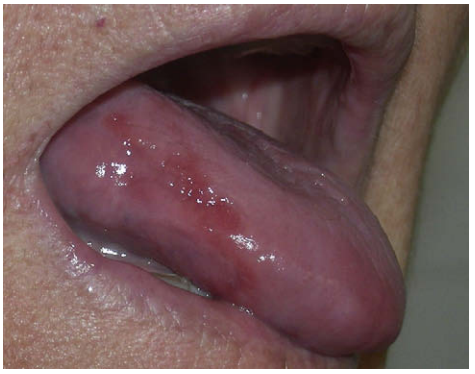

Fig 4. Lateral erosive linear glossitis of 6 years' duration.

without improvement. Blood analysis was then performed (see Table I).

Patient 4 was referred in May 2007 complaining of glossitis of 6 years' duration. She did not improve with topical antiseptics or antifungal therapy. The patient had arterial hypertension treated with hydrochlorothiazide, amlodipine, and valsartan, and she had been treated with acenocumarol for previous deep venous thrombosis. On examination, an erosive glossitis with linear localized lesions was observed (Fig 4). A lingual biopsy was performed, disclosing a hyperplastic epithelium with exocytosis of polynuclear neutrophils, fibrosis, and vascular ectasia; PAS stain was negative. A blood sample was obtained (see Table I).

None of the patients reported neurologic symptoms, although examination by a neurologist was not performed. Continuous vitamin B_{12} treatment was prescribed. Oral lesions cleared in the first 4 weeks of treatment in all cases. At follow-up, no lesions had recurred; patient 1 reported taking oral B_{12} vitamin sporadically.

DISCUSSION

Glossitis in vitamin B_{12} deficiency is present in up to 25% of cases[2]; it is traditionally described as a diffuse and clinically nonspecific atrophy of lingual papillae affecting more than half of the tongue, and it

is classically known as Hunter's glossitis or glossitis of Moeller-Hunter.

The glossitis found in our patients does not correspond to the classic description. All of our cases presented with linear lesions. We think that our patients, if not diagnosed, would have developed the diffuse presentation classically described.

The lack of response to antifungal therapy, the absence of mycotic structures in the two cases that had undergone biopsy, and the early resolution with substitutive treatment all support the diagnosis of glossitis due to deficit of vitamin B_{12}. Although the role of low ferritin levels in two of the patients remains to be determined, lesions resolved with vitamin B_{12} treatment only.

Classic Hunter's glossitis has two stages: inflammatory in the beginning, with bright red plaques, and atrophic later, characterized by papillae atrophy affecting more than 50% of the tongue.[3,4] Our patients could be included in a clinically characteristic variant of the inflammatory stage.

We have only found one published case in which oral linear lesions in association of vitamin B_{12} deficiency are described; however, authors concluded that the clinical picture was nonspecific.[5] A reference textbook of dermatology[11] mentions the occasional presence of lingual linear lesions in vitamin B_{12} deficiency; however, this finding is not described as clinically characteristic and, when examining the original articles referenced in the textbook, patients did not present with linear lesions, which were considered to be nonspecific by the authors.[2,8]

In none of our cases was anemia present at diagnosis; all 4 patients had elevated mean corpuscular volume, although in two this elevation was mild. For this reason, we consider that the glossitis with linear lesions could be a sign potentially very useful for early detection of the disease.

The most frequent cause of vitamin B_{12} deficiency in developed countries is gastric atrophy of autoimmune origin. Other causes are gastrectomy, bowel bacterial overgrowth, and ileal anomalies.[1] Treatment of the deficit is substitutive and usually for life. Intramuscular administration has been used for years. However, the efficacy of oral daily megadoses of vitamin B_{12} (1000-2000 μg) has been demonstrated; the absorption is mediated by simple diffusion, independently of the presence of intrinsic factors.[12,13]

In conclusion, the finding of glossitis with linear lesions is characteristic of vitamin B_{12} deficiency in its early phases. It is advisable to determine vitamin B_{12} levels in these patients independently of the presence of macrocytic anemia, as anemia is usually still not present.

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