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ORIGINAL ARTICLE

# Laryngeal manifestations in atypical recurrent aphthous stomatitis

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## Summary

Recurrent aphthoid stomatitis is characteristically observed in children and adolescents in the form of painful relapsing ulcers in the oral mucosa unaccompanied by evidences of systemic disease. The ulcers appear every one or two weeks for at least one entire year. Some patients suspected for recurrent aphthoid stomatitis develop lesions in atypical sites - mainly in the larynx - concurrently to the ones found in the oral mucosa. **Aim:** this study aims to describe a series of recurrent aphthoid stomatitis patients with atypical laryngeal injuries. Study design: this is a case series study. **Materials and method:** patients diagnosed with recurrent aphthoid stomatitis with oral mucosa ulcers and laryngeal symptoms without altered lab test results and no evidence of systemic disease underwent fibroscopic examination, oral and laryngeal biopsies, followed by specimen evaluation by direct immunofluorescence. **Results:** all six patients in this series had acute and chronic inflammatory processes according to pathology studies and negative direct immunofluorescence test results. **Conclusion:** laryngeal involvement in recurrent aphthoid stomatitis is rare. Therefore, during diagnostic examination thorough clinical history and meticulous physical examination accompanied by fibroscopic examination are necessary. When atypical lesions are found, biopsies for histological evaluation and direct immunofluorescence tests are required.

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## INTRODUCTION

Recurrent aphthous stomatitis (RAS) is characteristically observed in children and adolescents in the form of painful relapsing ulcers in the oral mucosa unaccompanied by evidences of systemic disease. The ulcers appear every one or two weeks for at least one entire year[1]. Aphthous injuries apparently disconnected from underlying diseases or syndromes are somewhat frequently seen in our daily practice.

Oral injuries may mimic other conditions or be part of the clinical manifestations seen in various diseases, as is the case of autoimmune vesicular-bullous diseases. Fully evolved sores may look like pemphigus vulgaris (PV) or benign mucous membrane pemphigoid (BMMP), two conditions that frequently involve the laryngeal mucosa[2,3].

Cases suggestive of RAS with concurrent non-specific laryngeal lesions ask not only for careful analysis of clinical history, physical examination, and lab workup, but may also require biopsy followed by pathology tests and immunofluorescence labeling so a proper diagnosis is established.

Direct immunofluorescence (DIF) on RAS, as described by Ship[4], is utterly important in the establishment of a differential diagnosis from the atypical forms of RAS (in which test results are negative) and vesicular-bullous diseases (in which fluorescence is positive for oral and/or laryngeal epithelium)[4].

## OBJECTIVE

This study aims to describe a series of six patients with oral ulcers and clinical history compatible with RAS, added by atypical laryngeal signs not compatible with any previously described manifestation of recurrent aphthous stomatitis.

## MATERIALS AND METHOD

This is a retrospective study featuring six consecutive patients seen from 2002 to 2004 by the stomatology group of a university hospital's ENT Clinic; all patients had aphthous injuries that appeared and evolved atypically.

Enrolled patients signed a free informed consent term. This study was approved by our institution's ethics committee under permit 876/04, as part of a Project investigating the clinical, pathological and genetic characteristics of RAS patients.

All enrolled patients were submitted to a protocol that consisted of general and clinical interviews, physical examination - mainly of the oral cavity, nasal fibroscopic examination using a flexible Olympus 3.4mm ENF Type P4 scope and a rigid 70-degree Storz (Hopkins) laryngeal scope connected to a 250-Watt halogen light source.

Lab workup included the following: complete blood count, coagulation profile, serum ferritin, G6PD dosage (glucose-6-phosphate dehydrogenase), antinuclear factor (ANF), rheumatoid factor (RF), serology for lues (RSS and FTA-ABS), anti-HIV 1 and 2, serum immunoglobulin (Ig) A, G and M, C-reactive protein.

Oral and laryngeal biopsies were performed to rule out other diseases affecting the oral cavity and to produce a differential diagnosis for RAS (Behçet disease, pemphigus, pemphigoid, erythema multiforme and others).

Oral biopsy procedure: patients were administered an injection of 2% xylocaine without vasoconstrictor; oral biopsy was performed using a 4-mm punch; specimens were obtained from the mucosa adjacent to the sore for direct immunofluorescence and from the transition zone between the injured and healthy portions of the mucosa for pathology workup.

Laryngeal mucosa biopsy was performed under general anesthesia. Patients underwent laryngeal micro surgery and had two specimens removed for pathology workup and DIF.

**Enrollment criteria:**

- clinical history compatible with RAS, i.e., episodes of aphthous sores in the oral cavity occurring in monthly or shorter intervals for at least one year;
- presence of aphthous injury in the oral mucosa;
- absence of altered results in the tests order as part of the protocol;
- absence of clinical signs and/or test results compatible with systemic disease characterized by oral lesions.
- no use of topical corticosteroids on the sores at least two weeks prior to biopsy.

**Exclusion criteria:**

- clinical history not compatible with RAS;
- presence of altered results in the tests order as part of the protocol;
- presence of clinical signs and/or test results compatible with systemic disease characterized by oral lesions.
- use of topical corticosteroids on the sores within two weeks prior to biopsy.

## RESULTS

All patients enrolled in our study had 'atypical aphthous injuries.' Three were males and three were females, with ages ranging between 22 and 64 years - mean age of 38.8 years (Table 1).

Lab workup indicated the presence of oral and laryngeal mucosa ulcers and acute/chronic submucosal inflammation in all patients. Stains for fungi/granulomatosis were negative, as well as DIF (Fig. 1).

Physical examination revealed four patients had oral lesions (Fig. 2), some active and some healing. Nasal fibroscopy showed additionally that all six patients had