CLINICO-HISTOPATHOLOGICAL FEATURES AND INVESTIGATIONS OF ORAL APHTHOUS STOMATITIS INCLUDING BEHCET'S DISEASE

Siar C.H. Clinico-histopathological features and investigations of oral aphthous stomatitis including Behcet's disease, Annal Dent Univ Malaya 1999; 6: 38 - 39.

Siar Chong Huat
Department of Oral Pathology, Oral Medicine & Periodontology, Faculty of Dentistry,
University of Malaya,
50603 Kuala Lumpur, Malaysia

ABSTRACT

The three clinical subtypes of oral recurrent aphthous stomatitis (RAS) i.e. minor, major and herpetiform share certain common features - namely the patients affected are otherwise well, their ulcers have a tendency to recur, are generally associated with varyng degrees of pain and preferentially occur in nonkeratinized mucosa. These subsets of RAS differ from one another by the size and number of ulcers at each bout and whether or not permanent scarring occurs upon healing. Histopathologically RAS presents as a nonspecific ulcer characterized by a fibrinopurulent membrane covering an area of epithelial loss and deep to it granulation tissue showing a chronic inflammatory response and attempts at organization. Immunofluorescence of lesional tissue is rarely of diagnostic benefit. Haematological investigation may reveal an underlying haematinic deficiency.

In Behcet's disease, RAS-like ulceration is seen in patients with multisystem disease involving other mucocutaneous surfaces, eyes (uveitis), musculoskeletal, neurological, haematological and gastrointestinal systems. Thorough systemic work-up is necessary for these patients.

CLINICAL FEATURES OF ORAL RECURRENT APHTHOUS STOMATITIS

On clinical grounds, three subtypes of recurrent aphthous stomatitis (RAS) are recognised: minor aphthae, major aphthae and herpetiform aphthae. Their common features are recurrent bouts of painful ulcers at intervals of a few months to a few days. The patients are clinically well.

Minor aphthae

Minor aphthae accounts for about 80% of all cases of RAS. Onset is usually during childhood. Clinically they present as ovoid or circular areas of shallow ulceration of about 2-4 mm in diameter. They are covered with a greyish-yellow slough and surrounded by an erythematous halo. These ulcers tend to occur on the nonkeratinised mucosa in the anterior part of the oral cavity notably the buccal mucosa, labial mucosa, floor of mouth or ventral surface of the tongue but are uncommon on the gingiva, palate or dorsum of tongue. Pain is a feature. Patients with minor aphthae typically have one to five ulcers at any one time and they healed in about 2 weeks without leaving a scar.

Major aphthae

As its name implies, these are large painful ulcers of 1 cm or more in diameter. Some ulcers may reach up to a size of 3 cm. Major RAS usually has its onset at puberty and is chronic, persisting for up to 20 years or more. They account for about 10% of all RAS and tend to affect the posterior part of the oral cavity, in particular the soft palate and fauces. Healing of major aphthae may take several weeks or months, and with scarring. In recent years major aphthae have been added to the list of oral changes which may indicate the presence of HIV infection.

Herpetiform aphthae

Herpetiform aphthae represents the least common form of RAS. It accounts for the remaining 10% or less of RAS encountered. They have a late onset and are seen more frequently in females. Clinically these lesions present as tiny pin-point painful ulcers in crops of 100 or more (Hence the name herpetiform). They rapidly coalesc to form larger areas of ulceration. The healing time for herpetiform aphthae is similar to that of minor aphthae. No scarring occurs.

Recurrent aphthous stomatitis as an oral manifestation of Behcet's disease

RAS may represent an oral feature of a variety of systemic disorders, one notable example is Behcet's disease. This is an immunologically mediated disease characterized by multisystem/organ involvement as summarized Table 1.

The RAS that occur in Behcet's disease may be of the minor or major type or both. Patients with Behcet's disease may experience one to 3 bouts of RAS per year.

INVESTIGATION AND DIAGNOSIS OF RAS CLINICAL DIAGNOSIS

In most instances oral RAS is diagnosed on clinical grounds alone. It is therefore important to recognise the distinguishing features of the three subsets of RAS because there is no reliable method of laboratory diagnosis.

Laboratory investigations

Haematological assessment

As RAS is often associated with an underlying haematinic deficiency state, haematological investigation for haemoglobin level, serum ferritin (or iron/total iron binding capacity), vitamin B12 and corrected whole blood folate should be routine.

Table 1:
Systems involvement and clinical features of Behcet's Disease

No.	Systems of involvement	Clinical features
1.	Oral mucous membrane	Recurrent aphthous ulcers
2.	Ocular	Uveitis
		Retinal vasculitis
		Optic atrophy
		Blindness
3.	Genitalia	Recurrent aphthous ulcers
4.	Neurological	Pseudobulbar palsy
		Multiple sclerosis
		General paresis
5.	Skin	Pustule
		Erythema nodusum
6.	Psychiatric	Depression
7.	Joints	Arthralgia
8.	Vascular	Aneurysm
		Thromboses
		Subcutaneous thrombophlebitis
9.	Renal	Proteinuria
		Haematuria
10.	Gastrointestinal	Diarrhoea
		Abdominal distension
		Loss of appetite

Patch-testing

If allergy is suspected then patch-testing to detect potential allergens is said to be useful. When these tests are not available, abstinence from these allergens especially those related to the diet, may indirectly help identify the underlying causative allergen(s).

Serology/Immunological investigations

In oral RAS presenting as a localised disease in normocompetent patients, the serum immunoglobulins are generally normal but IgA, IgG, IgD and IgE may sometimes be elevated or reduced. Findings generally not contributory to diagnosis.

In HIV cases presenting with RAS, investigations may reveal an altered or inverse CD4/CD8 ratio.

In Behcet's disease, the serum IgA is increased along with an elevated ESR, serum C9 but evaluation for circulating autoantibodies e.g. antinuclear, anti-DNA etc. are usually negative.

Biopsy for histopathology

It is unnecessary to biopsy minor aphthae to confirm their clinical diagnosis. Major aphthae, because of their alarming clinical form that often may mimic a malignant ulcer or an infective lesion e.g. TB, a biopsy is performed more to rule out these diagnoses.

Histologically, a minor aphthous ulcer show essentially nonspecific features namely loss of epithelium at the ulcer site with granulation tissue formation and a mixed inflammatory cell infiltration. The major aphthae also show similar changes except there is involvement of the oral mucosa to a greater depth and with some attempts at organisation e.g. fibrosis.

CONCLUDING REMARKS

RAS remains a common disorder of the oral mucous membrane and recognition of the distinct subsets is important as their diagnosis is based largely on clinical findings alone.

ACKNOWLEDGEMENTS

I like to thank Dr. Ng Kok Han from the Department of Cinical Pathology, Institute for Medical Research, Kuala Lumpur for his critical review of this paper.

FURTHER READING

1. Schneider LC, et al. Diagnosis of oral ulcers. Mt Sinai J Med. 1998 Oct-Nov;65(5-6):383-7.
2. Lichon JF. Treatment of recurrent oral aphthous and herpetic ulcerations. Dent Today. 1994 Oct;13(10):88-9.
3. Rogers RS 3rd. Recurrent aphthous stomatitis in the diagnosis of Behcet's disease. Yonsei Med J. 1997 Dec;38(6):370-9.
4. MacPhail LA, et al. Oral ulceration in HIV infection: investigation and pathogenesis. Oral Dis. 1997 May;3 Suppl 1:S190-3.
5. Rogers RS 3rd. Recurrent aphthous stomatitis: clinical characteristics and associated systemic disorders. Semin Cutan Med Surg. 1997 Dec;16(4):278-83.
6. Esin S, et al. Peripheral blood T cell expansions in patients with Behcet's disease. Clin Exp Immunol. 1997 Mar;107(3):520-7.
7. Ceballos-Salobrena A, et al. Oral manifestations associated with human immunodeficiency virus infection in a Spanish population. J Oral Pathol Med. 1996 Nov;25(10):523-6.
8. Woo SB, et al. Recurrent aphthous ulcers: a review of diagnosis and treatment. J Am Dent Assoc. 1996 Aug;127(8):1202-13.
9. Eversole LR. Immunopathology of oral mucosal ulcerative, desquamative, and bullous diseases. Selective review of the literature. Oral Surg Oral Med Oral Pathol. 1994 Jun;77(6):555-71.
10. Greer RO Jr, et al.. A double-blind study of topically applied 5% amlexanox in the treatment of aphthous ulcers. J Oral Maxillofac Surg. 1993 Mar;51(3):243-8; discussion 248-9.
11. Ledford DK. Immunologic aspects of cardiovascular disease. JAMA. 1992 Nov 25;268(20):2923-9.
12. Lihara K, et al. Neuronal hyaline inclusions observed in an autopsy case of Behcet's disease. Acta Pathol Jpn. 1992 Jun;42(6):432-8.
13. Svirsky JA. Recurrent aphthous ulcerations. Va Dent J. 1992 Jan-Mar;69(1):8-11.
14. Silverman S Jr, et al. Prednisone management of HIV-associated recurrent oral aphthous ulcerations. J Acquir Immune Defic Syndr. 1992;5(9):952-3.
15. Meiller TF, et al. Effect of an antimicrobial mouthrinse on recurrent aphthous ulcerations. Oral Surg Oral Med Oral Pathol. 1991 Oct;72(4):425-9.