

## Burning Mouth Syndrome: Hypersensitivity to Sodium Metabisulfite

Sir,

Burning mouth syndrome (BMS) is characterized by the onset of symptoms such as burning sensation and/or pain in the oral mucosa and/or the tongue, where no other disease is present (1, 2). It is usually found in women in the perimenopausal or postmenopausal period. It has been shown that local irritation, systemic diseases (diabetes mellitus, folic acid deficiency), psychological factors and contact allergy (1, 3, 4) could be correlated with the pathogenesis of the disease, which still remains unknown. Furthermore the symptoms often arise after dental intervention, and the majority of the patients wear dental prostheses (5). A mild erythema of the oral mucosa is sometimes observed, but no characteristic histopathological features are present (6, 7). It is sometimes possible to observe episodes of urticaria-angioedema of the face and other regions apparently caused by the absorption of the sensitizing hapten/antigen through the mucosa. The allergic pathogenesis seems to be quite rare in the development of BMS; the reason for this may be that the haptens have an infrequent, brief contact with the oral mucosa (except in patients with dental prostheses), that they are diluted by the saliva, that the mucosa, because of its structure, has few protein carriers available, and that abundant vascularization rapidly carries away most of the haptens and antigens.

We here describe the clinical picture of two women, who came under our observation. In these two cases it seems that sulfites, particularly sodium-metabisulfite, played a fundamental role in causing BMS.

### CASE REPORTS

#### Case 1

A 62-year-old woman, with a positive family history of hay fever and asthma in both parents, who had undergone several dental interventions, after which a dental prostheses was applied, started to complain of local and systemic reactions. The former were essentially characterized by oral burning and pain with ageusia, the latter by angioedema of the face and lips and wide-spread urticaria. The patient reported that the urticaria worsened and was accompanied by an asthmatic attack after an injection of a corticosteroid drug (Bentelan intramuscular ampule). After this episode the patient was hospitalized. After the urticaria-angioedema syndrome had disappeared, the oral symptoms persisted for months and did not disappear even after removal of her denture. The patient was sent to be examined at our Department of Allergy.

#### Case 2

A 51-year-old woman came under our observation because of the presence of typical BMS symptoms localized in the oral cavity. Pertinent family history consisted of hay fever in her mother. The personal history of this patient revealed that she had undergone a dental intervention (extraction of the 2nd molar), which had caused angioedema of the lips and tongue. We also discovered that the patient regularly drank wine.

The following tests were carried out on both patients: a complete blood count, glucose, iron, vitamins B1, B6, B12 and folic acid, *Candida* cultures (oral cavity), bacterial cultures

(oral cavity) and herpes cultures (mucosa of the jaw). No hematologic abnormalities were observed, so no relation between BMS and these parameters could be demonstrated, contrary to what has previously been reported in the literature (8).

We then investigated the kind of local anaesthetic that had been administered during the dental interventions; it was found that in both cases Xylestesin, an anaesthetic containing lidocaine with a combination of epinephrine, had been used. However, the provocation test, which was performed with pure lidocaine without epinephrine (following the protocol suggested by the Italian Society of Allergy and Clinical Immunology (SIAIC)), was negative.

Next, patch-tests were applied to the patients' back using the routine series (GIRDCA series) supplemented with an acrylate series, a dental metal series, and a spices and food additives series.

After 72 h the patch-test showed a marked hypersensitivity to sodium-metabisulfite (at a concentration of 5%).

This is a salt widely used as a preservative and anti-oxidant agent in beverages (such as wine, beer, fruit juice), foods (fruit, vegetables, potatoes), and some drugs (antibiotics, steroids, local anaesthetics) (9, 10).

A double-blind provocation test with sodium-metabisulfite was carried out in both patients. The test, performed with titanium dioxide gelatine capsules, was markedly positive even on the first day, with a dosage of 10 mg in both patients, who complained of burning sensation and pain in the oral mucosa.

### DISCUSSION

The use of bisulfites as food preservatives is known to cause allergic reactions in atopic patients. Symptoms may include anaphylaxis, bronchoconstriction, nausea, vomiting, and diarrhea (8, 11). We have considered it of interest to report the above cases, as we think that contact allergy to sodium-metabisulfite contained in food and drugs (particularly local anaesthetics (12)) should be borne in mind when considering the possible etiologic factors involved in causing BMS.

What we have described suggests that the sodium-metabisulfite contained in the local anaesthetic administered during dental interventions may play a triggering role; in the first case, also, the administration of an injection of Bentelan (Glaxo), a steroid drug containing betamethasone and sodium-metabisulfite as an excipient, worsened the symptomatology. The acquired sensitivity was then automaintained through the ingestion of food and beverages containing sulfites.

As far as the pathogenetic mechanism is concerned a late reaction (type IV according to Gell and Coombs' classification) occurs. In this mechanism not only T helper lymphocytes but also the delayed hypersensitivity T lymphocytes (TDH) and cytotoxic T lymphocytes of the mucosal associated lymphoid tissue (MALT) of the oral cavity are involved. We also hypothesize the coexistence of an IgE-mediated mechanism that probably caused the associated angioedema.

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