

## Burning Mouth Syndrome: The Role of Contact Hypersensitivity

A. VIRGILI<sup>1</sup>, M. CORAZZA<sup>1</sup>, L. TROMBELLI<sup>2</sup> and A. ARCIDIACONO<sup>2</sup>

Departments of <sup>1</sup>Dermatology and <sup>2</sup>Dental Medicine, University of Ferrara, Ferrara, Italy

The burning mouth syndrome is characterized by an unpleasant sensation of burning in the oral cavity, without clinical signs. Causal factors may be psychogenic, systemic or local. The aim of the study was to determine the significance of contact allergy in the pathogenesis of burning mouth syndrome.

Fifteen patients with burning mouth syndrome were studied through anamnesis and laboratory analysis. Epicutaneous patch tests were performed with the Italian standard series (GIRDCA – Gruppo Italiano di Ricerca Dermatiti da Contatto ed Ambientali), preservative and dental series. The same tests were carried out in 12 healthy age- and sex-matched subjects.

The number of patients affected by burning mouth syndrome with a positive reaction to patchtesting was 6 out of 15, while the number of allergic patients in the control group was 3 out of 12. No association could be found between positive reaction at patchtesting and exposure to allergens.

Contact allergy in burning mouth syndrome seems not to play a primary role; nevertheless, it is advisable to perform patch tests in selected patients to identify a possible aetiological agent. **Key words:** allergic contact stomatitis; dental allergens; prosthesis.

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A. Virgili, Clinica Dermatologica, Università degli Studi di Ferrara, Via Savonarola n. 9, I-44100 Ferrara, Italy.

Burning mouth syndrome (BMS) is a disorder which is defined by Grushka as: "an intraoral pain disorder that is unaccompanied by clinical signs" (1).

The frequency of this syndrome is about 5% and the sex ratio is 1 male: 3–9 females. The affected age span is reported between 40–80 years (1, 2).

The most characteristic symptom is burning, sometimes accompanied by subjective xerostomia, altered taste perception and thirst sensation.

Even if every site of the oral cavity may be affected, the tongue is the most affected area. Lamey & Lewis (3) identified 3 BMS categories. In the first type of BMS, patients have no symptoms on waking but a burning sensation appears and increases in severity as the day goes on. In the second type of BMS, burning is present on waking and persists throughout the day, while in type 3 patients complain of intermittent symptoms at unusual sites such as the throat or the floor of the mouth.

Local, systemic and psychological factors are considered in the aetiology of BMS (3, 4). Psychic factors such as anxiety and depression are thought to be very important (5, 6). Haematologic disorders (3, 7), diabetes (3, 8), hormonal abnormalities (2, 9–11) and vitamin B complex deficiencies are also considered (4, 12).

Among local causes, *Candida* infection (3, 7), badly fitting prostheses (2, 3, 13) and deficit or qualitative abnormalities of salivary flow must be evaluated (1, 7, 13).

The possibility of an allergy to methyl-methacrylate monomer, constituent of the prostheses (3, 14, 15), metals of prostheses (especially nickel and palladium) (14, 16) or amalgam of fillings (17) has been recently underlined. The aim of this study was to investigate the role of contact hypersensitivity in the etiopathogenesis of BMS.

### MATERIALS AND METHODS

Fifteen patients (2 males aged 67 and 68; 13 women, mean age 65, 7, range 54–75) were consecutively examined for BMS in a period of 8 months. For each patient recent and past anamnesis, complete description of symptoms (type, sites and temporal distribution during the day) were collected. The patients were asked to report on the severity of symptoms through a visual analogue score.

When the patient was wearing prosthesis, an objective and subjective evaluation of aesthetics and functionality of the prosthesis was made. Parafunctional habits such as clenching and tongue thrusting were detected.

Psychical alterations related to anxiety and depression were investigated through the Hospital Anxiety and Depression scale (HAD). Seven questions for each parameter were answered and a score between 0–3 was attributed (21 maximum value for each subscale). Scores over 10 revealed anxiety and depression, under 7 were not significant while between 8–10 were considered borderline.

A swab from the back of the tongue was taken to detect possible candidal infection.

Haematological investigations including seric iron, seric ferritin, transferrin and blood concentration of vitamin B 12, zinc and folic acid were performed. Autoantibodies were researched when connective tissue disorders were clinically suspected.

Patch tests were performed with the GIRDCA standard series, Preservative series and a selection of allergens related to denture materials (benzoyl peroxide 1%, tetracaine hydrochloride 1%, copper sulfate 1%, potassium dicyanourate 0,002% aq., methyl methacrylate 2%, hydroquinone 1%, bisphenol A 1%, N,N-dimethyl-p-toluidine 2%, eugenol 1%, ethylene glycol dimethacrylate (EGDMA) 2%, triethylene glycol dimethacrylate (TEGDMA) 2%, bisphenol A dimethacrylate 2%, dibutyl phthalate 5%, diethanolamine 1%, sodium thiosulphatoaurate 0,25%). Patch tests, according to the methods recommended by the International Contact Dermatitis Research Group, were applied to the back and readings were performed after 48 and 72 h. The final result was rated on a scale 1+ to 3+.

Twelve healthy subjects, matched with the BMS patients as regards sex, age and frequency of wearing dentures, were selected among the healthy subjects waiting for a new prosthesis at the odontoiatric department and were submitted only to patch tests.

### RESULTS

Five patients had had one or more diseases such as diabetes, cardiovascular and hepatic disturbances.

All female patients had already been menopausal for more than 10 years.

One third of patients smoked but only 2 patients smoked more than 10 cigarettes a day. Burning was the prevalent symptom in the majority of the cases, followed by dryness or pain; symptoms were more frequently located on the tongue and on the lips.

Seven out of 15 patients were wearing partial or total prostheses; only 1 prosthesis was found to be badly fitted.

Clinical examination revealed 2 cases of morsicatio buccarum and another one with angular cheilitis related to a denture with reduced occlusal vertical dimension; parafunctional habits were found in 2 patients.

Anxiety and depression were found in 6 and 7 patients, respectively, following the score, while 3 and 4 patients achieved a borderline score (between 8 and 10).

Only one patient out of 13 presented a low level of transferrin and another one a low level of folic acid. These data were, however, isolated in a normal haematological situation. Nobody presented low seric levels of vit B12. Seric zinc was evaluated in 10 patients out of 15; one patient had a lower level than normal while another one had a higher level.

When autoantibodies were researched (4 cases) they were always negative.

Cultural examination of the tongue was positive for *Candida* sp. in 7 out of 15 without clinical objectivity.

Five patients were found positive to allergens of the GIRDCA series (p-phenylenediamine, benzocaine, colophony, balsam of Perù, fragrance mix, nickel sulfate). No positivities were found testing allergens of the Preservative series.

While only benzoyl peroxide of the dental series induced a positive response in 2 patients, nobody presented allergy to methacrylates or metals used in odontoiatrics (copper sulfate, potassium dicyanoaurate, tetrachloroplatinum).

Of the 6 allergic patients 4 were hypersensitive to only one allergen, one had a cross reaction to allergens of the par-group (paraphenylenediamine, benzocaine, diaminodiphenylmethane) and the last patient showed polysensitization to allergens of the balsam and the perfume group (colophony, balsam of Perù, fragrance mix) and to benzoyl peroxide.

Three out of the 12 healthy control subjects showed a positive result to balsam of Perù and thimerosal, cobalt chloride and nickel sulfate, and nickel sulfate, respectively.

## DISCUSSION

The BMS patients showed symptoms and sites of burning sensation similar to those described in the literature (1, 3, 4). Neither the type nor the course of symptoms during the day supported the hypothesis of contact urticaria or irritant stomatitis.

We could not observe the high percentage of poor-fitting dentures which was noticed by other authors (3, 13, 18); lower data than those reported by Lamey & Lewis (20%) were achieved with regard to parafunctional habits (3).

The aetiological hypotheses relating to deficiencies of vit. B12, folic acid, iron and zinc were not confirmed in this study.

*Candida albicans* is a saprophyte of the oral cavity with a prevalence rate of 40–60% (19). The anti-*Candida* treatment performed in 5 out of 7 patients failed to improve symptoms. These data do not allow the conclusion of a significant relation between BMS and *Candida* infection.

Some authors considered contact hypersensitivity to prostheses as an important aetiological factor (4, 18). It must be considered that some of these studies, contravening the criteria with which to define BMS patients ("no clinical signs") (1), were performed in series of patients with lesions in the oral cavity.

Lamey & Lamb (20) researched allergy carrying out patch

tests in 14 BMS patients out of 150. Allergy to acrylic materials and allergens of diet (sorbic acid and propyleneglycol, benzoic acid, cinnamon) was detected in 2 and 3 subjects of this series, respectively. The percentage of positive results to patch tests was considered high but in a very restricted group of patients. Avoidance of balsam of Perù in our 3 patients allergic to this allergen failed to improve symptoms.

Helton & Storrs (15) performed patch tests in 8 patients affected by BMS, matched with 7 healthy controls, and denied the role of hypersensitivity in BMS. They could exclude the presence of contact dermatitis, contact urticaria and pressure urticaria in the tested patients. Our study agrees with the results of Helton & Storrs, even if it was performed in a group with a higher prevalence of prosthesis wearers and with a wider battery of allergens.

Skoglund & Egelrud (16) found 21% (5 out of 24) of BMS patients allergic to nickel sulfate; only one of our patients was allergic to this allergen.

Dimethyl-p-toluidine was negative in all our patients, even if it was found as a significant allergen in contact stomatitis in other studies (21, 22).

Acrylates were positive in the study by Ali et al. (18) in 5 cases out of 23 and in 14 out of 53 in the study by Kaaber et al. (22). As in our experience, Motolese et al. (23) noticed a negative result to acrylates.

In our study only 2 patients were found positive to the dental series. They unexpectedly did not wear dental prostheses; it is therefore hard to link hypersensitivity with symptoms. Our research never showed a relation between positivity to the allergen and contact with the same allergen.

The result in healthy controls revealed a number of positivities to patch tests lower than that of the affected patients (3:12 and 6:15, respectively). Even if this may suggest that contact allergy plays a role in the pathogenesis of BMS, it is difficult to consider the positivities found in BMS patients as relevant. However, it is also possible that other substances of importance may not have been included in the patch test.

Patch tests are not advisable as a screening examination in BMS patients but may be indicated in all cases in which previous examination did not show pathological condition. They are indicated, at the end of a diagnostic path (screening laboratory tests, *Candida* cultures, prosthesis and dental fillings examination), in patients in which a strict co-relation does exist between time of onset symptoms and exposure to known sensitizers (acrylates of prostheses, amalgam of fillings, allergens of the diet).

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