DIAGNOSTIC CHALLENGES OF BURNING MOUTH SYNDROME

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ABSTRACT

This survey presents some modern diagnostic approaches to a painful pathology of oral cavity defined as burning mouth syndrome (BMS). Absence of relevant clinical and laboratory signs hampers the diagnosis and results in delayed proper treatment. Clinicians should distinguish between primary and secondary BMS. Laboratory examinations include haematological screening, salivary analyses, epicutaneous and microbiological tests. Psychological assessments and autonomic nervous system testing play a diagnostic and differential-diagnostic role, too. Application of an interdisciplinary diagnostic approach is justified.

Key words: burning mouth syndrome, diagnosis, haematological screening, visual analogue scale, Candida species, Helicobacter pylori

INTRODUCTION

Primary, essential or idiopathic burning mouth syndrome (BMS) is characterized by a burning sensation in the oral mucosa and perioral areas, typically with bilateral, symmetric distribution and absent relevant clinical and laboratory findings. It is difficult to recognize and considered a diagnosis of exclusion of any detectable organic bases for the complaints (9,13,14). Sensation in secondary BMS is due to clinical abnormalities, systemic or psychological pathology. The diagnosis is delayed, often due to a lack of understanding of the nature of this entity, in addition to the patients taking up many health resources, since they frequently consult various specialists (13). According to a retrospective study, most BMS patients are mid-life white women and report a sudden onset of constant oral burning symptoms of increasing intensity. They share oral symptoms for 41 months (20±73,5 months; range of 2-360 months). Besides 38 of 49 patients receive/trial 71 various interventions (mean of 1,9) prior to receiving a definitive diagnosis for their oral burning symptoms that is considerably delayed (10).

Clinical diagnosis

Dental practitioners should distinguish between primary and secondary BMS. The clinical history is helpful in diagnosing BMS. Most patients report an increased pain intensity from morning to night, a decreased pain with eating, oral dryness that waxes and wanes with the burning, and the frequent presence of taste disturbances. Even when a patient reports typical BMS features, other potential causes should be ruled out. If burning persists after management of systemic or local oral conditions, a diagnosis of BMS can be considered. Referral to

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a subspecialist with expertise in this area may be beneficial in particularly difficult cases.

However, there are no specific diagnostic tests for BMS. It is essential to obtain the medical, dental and psychological history of the patients; to quantify the pain on a visual analogue scale and to note the symptoms, duration, location and chronology and temporal relationship (burning/pain), if accompanied by xerostomia and taste alteration, if alleviated or aggravated by foods, and any precipitating factors. Special attention should be paid to the use of medication that can produce xerostomia, the presence of parafunctional habits, and the clinical history should provide information on prior or current psychological and psychosocial stress factors (13).

An oral and extraoral examination should be made to discard lesions such as erythema, erosions, and depapillated tongue. The oral cavity should not display any anomalies such as inflammation or atrophy of the mucosa at all. Possible dental problems should be ruled out, reviewing any prostheses and their occlusion, any probable oral galvanism and volumetric tests of saliva flow should be made (13). In patients with symptoms of burning in the oral cavity and clinically healthy oral mucosa, clinical examination of the oral cavity, candidal swab, oral galvanism measurement, salivary flow rate and parafunctional habit investigations should be performed. Detailed medical history should reveal any systemic factors which might result in symptoms of burning. If any of these known local and systemic causes could not be confirmed a diagnosis of ‘true’ BMS should be established, unfortunately, still without a proven cause and a limited therapeutic options. There is a significantly higher prevalence of gastritis and by 3,2 times higher incidence of gastrointestinal symptoms among ‘true’ BMS patients (12). Therefore, every patient with burning mouth should be referred to the gastroenterologist (2).

**Laboratory diagnosis**

Hematological screening (with special attention to serum iron, serum ferritin, blood glucose levels and *Helicobacter pylori* antibodies) should be performed to identify possible underlying disturbances. Complimentary examinations include analytical studies, folates, vitamin B12, zinc, serum antibodies in Sjögren’s syndrome and against *Helicobacter pylori* as well as culture for the detection of *Candida* taken from the oral mucosa and palate. Epicutaneous tests are made on patients presenting intermittent symptoms (metals and other allergens used in dental prostheses, foods, additives) (13). Patch testing of 75 BMS patients identified allergic reactions in 28 of them (37,3% of the cases). The most common allergens were nickel sulfate hexahydrate (2,5%), balsam of Peru and gold sodium thiosulfate (0,5% each) (19).

Salivary levels of cortisol, 17β-estradiol, progesterone, dehydroepiandrosterone and a-amylase activity were estimated in unstimulated (UWS) and stimulated (SWS) whole saliva flow samples of 30 female BMS patients and 20 controls. BMS showed significantly higher levels of cortisol in UWS and of 17β-estradiol in SWS compared with controls. Progesterone was significantly lower in UWS of the patients aged over 60 years than in the younger ones (8). Female patients with BMS presented with a lower stimulated salivary flow (p<0,01) (1).

The average serum estradiol levels in women with BMS were low (<13 pg/mL) (15).

Fungiform papillae density was analyzed over a small area of 19 mm² on the anterior tongue tip by means of a digital camera in 20 BMS patients and 20 controls. This density was significantly higher in BMS patients as 65% of them presented with a density of 71-90 papillae, while 10% had even more than 90 papillae within this region (4).

Keratinocyte intercellular adhesion was evaluated by immunofluorescence of the biomarkers desmoglein 1, desmoglein 3 and occluding in tongue mucosa of BMS patients and control subjects. Besides keratin 10 and keratin 14, the markers of epithelial differentiation and keratin 16, the marker for activated keratinocytes after epithelial injury were assessed. Lingual three-dimensional architecture was preserved. Desmoglein 1 and desmoglein 3 epithelial distributions in the desmosomes, keratin 10 immunoreactivity and keratin 14 distribution in the epithelial compartment were similar of both groups. In all BMS patients, keratinocyte cytoplasm
was homogeneously labelled for keratin 16 and more intensively stained than in controls. This staining progressively decreased towards the most superficial epithelial layers. Keratin 16 might be involved in the cell mechanisms underlying BMS occurrence (18).

Oral candidiasis is not an uncommon condition in BMS. This can either be a primary infection or a secondary one to local irritation or systemic predisposition. Although this most often presents with a white, red or mixed red/white lesion, the visible change can be small. A direct smear is the ideal way to make this diagnosis rather than taking samples for microbiological culture as *Candida albicans* is commensal in most mouths. If candidiasis is suspected, a course of antifungal therapy, such as mycostatin, should be tried first (14). In BMS, the most frequent species of the genus *Candida* is *C. albicans* (in nine of 31 patients; 29.03%) followed by *C. parapsilosis* (in two - 6.45%); *C. tropicalis, C. krusei* and *C. kefyr* (in one - 3.22% each) (Cavalcanti). Special emphasis should be addressed at infection with Helicobacter pylori due to very high percentage (79%) of patients whose burning symptoms resolve after eradication therapy (2).

**Functional and psychological tests**

Specific techniques can be used to test for taste disturbance and salivary function. Autonomic nervous system testing, low autonomic disorder questionnaire, heart rate variability (HRV), deep breathing (exhalation/inspiration [E/I] ratio), and sympathetic skin response (SSR) were applied to 33 BMS patients and 30 controls. In BMS, mean HRV values and E/I ratios were significantly lower and SSR latency in the foot was significantly prolonged. The autonomic questionnaire score was significantly higher in BMS. There was a significant impairment of the sympathetic and parasympathetic nervous systems and a preserved sympathetic/parasympathetic balance (11).

The ability to taste bitter, acid and spicy substances and the thyroid function of 50 BMS patients and 50 controls were comparatively analyzed. Thirty BMS patients reported ageusia for bitter and two had ageusia for acid taste. Pepper sauce consumption produced a strong burning to the tongue in 28 BMS patients and in 10 controls only. There was biochemical evidence of hypothyroidism in five BMS patients, raised levels of thyroid auto-antibodies in four ones and echographically proved nodularity in 34 the rest ones (7).

Due to the significant difference in anxiolytics intake between ‘true’ BMS and controls, psychological examination and counselling should be offered to these patients. The mean pain levels of visual analogue scale (VAS) are 7.5 in women and 6.1 in men with BMS. Other diagnostic methods include the number of words chosen and pain rating index sections of the McGill Pain Questionnaire (15).

A thorough examination was performed in 44 patients with primary BMS. It included VAS, salivary flow rate measurements, laboratory tests (complete blood cell counts, blood glucose levels, serum iron and transferrin levels, serum vitamin B₁₂ and folate levels), patch tests for contact allergy to denture materials, and isolation of *Candida* species from oral mucosal scrapes (6).

**Differential diagnosis**

Various mucocutaneous disorders are noteworthy. Here belong lichen planus, lichenoid reactions, benign mucous membrane pemphigoid, pemphigus and migratory glossitis. A visual clinical examination followed by biopsy can confirm or exclude this pathology. Viral diseases such as herpes simplex or herpes zoster can result in symptoms that the patient interprets as a burning sensation. Although these will be clinically apparent when the lesions erupt, there can be a prodromal burning sensation. The pain of post-herpetic neuralgia is much more severe, however, it can present as a burning sensation on the oral mucosa. Nutritional, metabolic or endocrine disorders may result in BMS, too. This includes diabetes mellitus, hypothyroidism, iron or zinc deficiency as well as vitamin B complex deficiency, particularly vitamin B₁₂ (cobalamin), a common cause of macrocytic anemia (pernicious anemia) (13,14). Patients with true xerostomia present with BMS, too. This can be as a component of Sjögren’s syndrome, a result of radiation therapy to the head and neck, a side effect of medication or
just an age-related reduction of salivary production, particularly the serous component (14).

Thus it behooves the clinician to obtain a clear and detailed disease and medical/dental history as well as perform a thorough oral clinical examination including any laboratory studies indicated. A neurological examination is useful, unless there are marked deficiencies, the lack of baseline data can present a problem. If other causes of this symptom are ruled out and/or the patient fails to respond to a normal course of treatment a diagnosis of BMS is reasonable (14). BMS associated to fibromyalgia is diagnosed in one of 41 patients with atypical or symptomatic facial pain (16).

In patients with Sjögren’s syndrome or treated with radiotherapy for oral cancer, there is virtually no salivary secretion. They complain of burning sensation, dysgeusia, difficulty in speech and there may be lobulation and fissuring of the tongue (1,20). The term of ‘scaled mouth syndrome’ was to describe the burning caused by angiotensin-converting enzymes inhibitors (3). Lithium, griseofulvin, antibiotics and metronidazole could cause burning sensation in the oral cavity (17).

In conclusion, modern interdisciplinary approach is needed to solve the diagnostic dilemmas of BMS.

REFERENCES
Diagnostic challenges of burning mouth syndrome


