



# REVISTA BRASILEIRA DE REUMATOLOGIA

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## Review article

# What rheumatologists should know about orofacial manifestations of autoimmune rheumatic diseases



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## ABSTRACT

Orofacial manifestations occur frequently in rheumatic diseases and usually represent early signs of disease or of its activity that are still neglected in clinical practice. Among the autoimmune rheumatic diseases with potential for oral manifestations, rheumatoid arthritis (RA), inflammatory myopathies (IM), systemic sclerosis (SSc), systemic lupus erythematosus (SLE), relapsing polychondritis (RP) and Sjögren's syndrome (SS) can be cited. Signs and symptoms such as oral hyposalivation, xerostomia, temporomandibular joint disorders, lesions of the oral mucosa, periodontal disease, dysphagia, and dysphonia may be the first expression of these rheumatic diseases. This article reviews the main orofacial manifestations of rheumatic diseases that may be of interest to the rheumatologist for diagnosis and monitoring of autoimmune rheumatic diseases.

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## O que o reumatologista deve saber sobre as manifestações orofaciais das doenças reumáticas autoimunes

### RESUMO

Manifestações orofaciais ocorrem com frequência nas doenças reumáticas e, comumente, representam sinais iniciais ou de atividade da doença que ainda são negligenciados na prática clínica. Entre as doenças reumáticas autoimunes com possíveis manifestações orais, incluem-se a artrite reumatoide (AR), miopatias inflamatórias (MI), esclerose sistêmica (ES), lúpus eritematoso sistêmico (LES), policondrite recidivante (PR) e síndrome de Sjögren (SS). Sinais e sintomas orofaciais como hipossalivação, xerostomia, disfunções

### Palavras-chave:

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temporomandibulares, lesões na mucosa bucal, doença periodontal, disfagia e disfonía podem ser a primeira expressão dessas doenças reumáticas. Esse artigo revisa as principais manifestações orofaciais das doenças reumáticas que podem ser de interesse do reumatologista, para diagnóstico e acompanhamento das doenças reumáticas autoimunes.

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## Introduction

Autoimmune rheumatic diseases constitute a heterogeneous group of conditions characterized by immune tolerance breakdown and production of autoantibodies and of a number of substances responsible for lesions in several body structures. In this category, rheumatoid arthritis (RA), inflammatory myopathies (IM), systemic sclerosis (SSc), systemic lupus erythematosus (SLE) and Sjögren's syndrome (SS) can be included.<sup>1</sup>

Some rheumatic diseases show mucocutaneous manifestations. Generally, the changes are consequences of systemic disorders and manifest themselves insidiously, showing signs and symptoms in the oral cavity (Table 1). However, in the context of autoimmune diseases, the oral approach appears to have not yet aroused scientific interest. In this paper, some dental clinical findings often found in patients treated at the Rheumatology Outpatient Clinic of Brasília, Hospital Universitário de Brasília (HUB)-UNB will be discussed, based on a narrative literature review. For this review, the following terms were entered in PubMed database (Autoimmune Rheumatic Disease [all fields]) AND "dentistry" [all fields], limited to those studies conducted on human subjects. It was found that are only sixty-eight studies were published until June 21, 2015. Some studies point to epidemiological data of medical and dental interest. In this context, clearly one realizes the limited approach to the subject. However, the papers chosen demonstrate that the dentist can and should act in the early diagnosis and management of these disorders, since these patients have specific needs.

Thus, this narrative review aims to address the main orofacial manifestations in autoimmune rheumatic diseases that may be of interest to the rheumatologist for diagnosis and clinical follow-up.

## Literature review

### Rheumatoid arthritis

Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease of unknown etiology.<sup>2</sup> The classic features of this disease are chronic, bilateral and symmetric polyarthritis, joint pain and inflammation that can result in deformity, instability and destruction of synovial joints.<sup>3,4</sup> RA affects more often the synovial membrane of small joints of the extremities, resulting in swelling, edema and pain, and can lead to bone and cartilage destruction, severe disability and untimely mortality.<sup>3</sup>

The most common oral manifestations in patients with RA are:

### Temporomandibular disorder (TMD)

The temporomandibular joint (TMJ) is a synovial joint and can be affected by disorders in non-articular tissues, with manifestations of muscle spasm, fibromyalgia, and myotonic dystrophy, among others. However, TMJ joint tissues may also be affected by mechanical trauma, infection, iatrogenic disorders, and gout, as well as by autoimmune rheumatic diseases such as RA and psoriasis.<sup>5</sup> One can observe the presence of typical inflammatory mediators of osteoarthritis, including tumor necrosis factor (TNF)- $\alpha$ , interleukin (IL)-1 $\beta$ , IL-6 and IL-8. These findings maintain correlation with the extent of the disease, i.e., clinical symptoms, number of joint effusions or morphological changes.<sup>6,7</sup>

TMDs are considered to be the most common conditions causing orofacial pain of non-dental origin, and the dentist is the professional responsible for the clinical examination of TMJ and for requesting imaging exams of this anatomical region. A TMD can manifest symptoms such as ear pain, headache, non-specific nerve pain, and toothache. Its diagnosis requires a medical and dental approach, which makes the evaluation of the prevalence of TMD a complex issue, and its study is often overlooked in the clinical practice of rheumatic autoimmune diseases.<sup>8,9</sup>

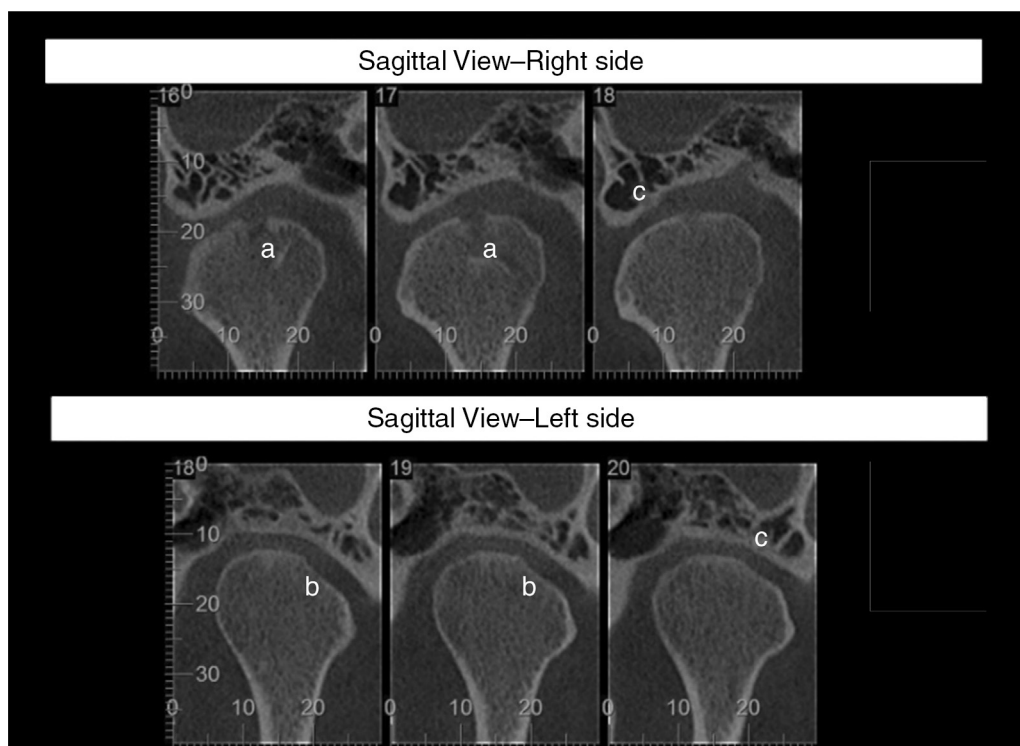
TMD can occur both in adults and – more commonly – in children with RA. A study that evaluated 223 children with juvenile idiopathic arthritis revealed that 38.6% had some TMJ involvement (pain, swelling and/or limitation in range of motion).<sup>10</sup> When TMJ involvement is manifested during a child's development, there may be a mandibular growth restriction, resulting in micrognathia and/or ankylosis.<sup>11</sup>

In adults, studies on the prevalence of TMD in RA patients resulted in extremely varied values (5–86%), depending on the population studied, diagnostic criteria used, and assessment methods.<sup>4,5</sup> TMD is the most common orofacial manifestation in RA patients. The patient may show a bilateral, profound and pervasive acute pain, which is exacerbated during the function. The clinical examination may reveal: malocclusion, sensitivity and inflammation of pre-auricular regions, joint stiffness upon waking, limitation of jaw movement, intracapsular crepitus or clicking and pain in masticatory and/or neck muscles.<sup>4,12</sup> Imaging studies may show bone structure loss at the condylar head (Fig. 1). The occurrence of TMJ ankylosis is quite unusual, becomes evident only at a late stage, and may be bilateral.<sup>4,13</sup>

**Table 1 – Oral manifestations of autoimmune rheumatic diseases and their clinical implications.**

Oral events	Autoimmune rheumatic diseases					Clinical implications	
	RA	IM		SSc	SLE		SS
		PM	DM				
Periodontal disease	X			X	X		<ul style="list-style-type: none"> <li>• Worsening factor for diabetes and rheumatic and heart diseases</li> </ul>
Dental caries				X	X	X	<ul style="list-style-type: none"> <li>• Depending on the extent of the injury, pain, chewing involvement, and foci of infection can occur, likely worsening diabetes and rheumatic and heart diseases</li> </ul>
Candidiasis					X	X	<ul style="list-style-type: none"> <li>• Itching and/or burning in the mucosa</li> <li>• Risk of esophageal infection</li> <li>• Inappetence</li> </ul>
Hyposalivation	X			X	X	X	<ul style="list-style-type: none"> <li>• Dysphonia</li> <li>• Dysphagia</li> <li>• Thrush and ulcers in the oral mucosa</li> <li>• Greater tendency to oral and oropharyngeal infections<sup>30</sup></li> <li>• Recurrent esophagitis</li> <li>• Sleep interrupted for water intake and urination</li> </ul>
Xerostomia	X		X	X	X	X	<ul style="list-style-type: none"> <li>• Decrease in quality of life</li> </ul>
Halitosis						X	<ul style="list-style-type: none"> <li>• Decrease in quality of life</li> </ul>
Mouth burning	X			X	X	X	<ul style="list-style-type: none"> <li>• Dysgeusia</li> <li>• Eating difficulty</li> <li>• Cancer phobia</li> </ul>
Oral ulcers			X		X	X	<ul style="list-style-type: none"> <li>• Pain</li> <li>• Difficulty in feeding and oral hygiene</li> </ul>
TMD	X		X	X	X		<ul style="list-style-type: none"> <li>• Headache</li> <li>• Otagia and/or tinnitus</li> <li>• A feeling of ear tamponade</li> <li>• An irradiating cervical pain</li> <li>• Chronic headache</li> <li>• Limited mouth opening</li> <li>• Difficulty to chew and speak<sup>12</sup></li> </ul>
Microstomia				X			<ul style="list-style-type: none"> <li>• Limited mouth opening</li> <li>• Difficulty in eating and to have a good oral hygiene<sup>46</sup></li> </ul>
Regional resorption of jaw bone/TMJ				X			<ul style="list-style-type: none"> <li>• Limited mouth opening</li> </ul>
Dysphagia		X	X			X	<ul style="list-style-type: none"> <li>• Dehydration</li> <li>• Malnutrition</li> <li>• Aspiration of secretions and/or food to the lung–aspiration pneumonia</li> </ul>
Dysphonia	X	X	X			X	<ul style="list-style-type: none"> <li>• Decrease in quality of life</li> </ul>
Changes in language		X	X			X	<ul style="list-style-type: none"> <li>• Difficulty to perceive food, speech and swallowing.</li> </ul>
Angle cheilitis						X	<ul style="list-style-type: none"> <li>• Pain and limited mouth opening</li> </ul>
Alterations in tooth morphology			X				<ul style="list-style-type: none"> <li>• Facial esthetics and masticatory function changes</li> </ul>
Pathological changes in salivary glands					X	X	<ul style="list-style-type: none"> <li>• Hyposalivation</li> </ul>
Changes in mimic and chewing muscles and in the pharynx			X				<ul style="list-style-type: none"> <li>• Dysphagia</li> <li>• Dysphonia</li> <li>• Difficulty to chew</li> </ul>
Trigeminal neuralgia							<ul style="list-style-type: none"> <li>• Episodes of intense pain in the eyes, lips, nose, scalp, forehead and/or jaw</li> </ul>

DM, dermatomyositis; IM, inflammatory myopathies; PM, polymyositis; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; SSc, systemic sclerosis; SS, Sjögren's syndrome; TMD, temporomandibular dysfunction.



**Fig. 1 – Computed tomography of temporomandibular joint of a patient with rheumatoid arthritis and complaint of clicking while chewing. Presence of subchondral cyst in the upper portion of the right mandibular head (a), erosion of lateral portion of the left mandibular head (b) and flattening of articular eminences (c).**

#### Periodontal disease (PD)

PD is a chronic infectious disease caused by Gram-negative anaerobic bacteria, affecting the tissues of protection and support of the tooth, such as gums, periodontal ligament, cementum and alveolar bone. Under PD designation, both reversible (gingivitis) and irreversible (periodontitis) processes are included. When undiagnosed and untreated, PD can cause progressive destruction of alveolar bone, causing tooth mobility and subsequent dental loss.<sup>14</sup> According to the World Health Organization, periodontal disease affects approximately 10–15% of the world population.<sup>14</sup> Brazilian official data show that 19.4% of adults aged 35–44 years are carriers of this disease.<sup>15</sup>

Some recent studies also suggest a significant association between RA and PD.<sup>13,16–18</sup> The relationship between RA and progression of inflammatory conditions (p.ex., periodontitis) is not clear. The main reason for this scenario is the lack of uniformity in the classification of the various forms of both diseases.<sup>19</sup> It is estimated that the prevalence of PD increases twice in RA patients compared to the general population.<sup>17</sup> Thus, the presence of a moderate-to-severe RA also increases more than twice the risk of developing forms of moderate-to-severe periodontitis compared to individuals without the disease.<sup>17–19</sup>

Furthermore, there is evidence of similarity in the pathogenesis of RA and PD. Microorganisms such as *Porphyromonas gingivalis* may play a role in both conditions,<sup>16</sup> being able to invade isolated human chondrocytes in the knee joint, interfering with cell cycle and inducing these cells' apoptosis.<sup>20</sup>

Another important factor would be that *P. gingivalis* expresses the peptide arginine deiminase (PAD), which converts arginine to citrulline by a citrullination process. This process, which is common to some human proteins, is associated with the pathophysiology of RA. It has a low immune tolerance to citrullinated proteins in synovial fluid, which triggers the development of immunoglobulins against these proteins, present in joints and tendons.<sup>21,22</sup> In addition, studies have demonstrated the presence of antibodies in response to oral anaerobic bacteria in the synovial tissue and serum. Others authors also found the presence of oral bacterial DNA in the synovial fluid of RA patients.<sup>18</sup> In fact, RA and PD have a variety of markedly similar clinical and pathophysiologic features (Table 2).<sup>23,24</sup>

Although periodontal disease has local clinical manifestations, its chronic inflammatory nature can contribute to change – and even worsen – the course of RA and of other rheumatic diseases. A recent systematic review by Kaur et al. (2013) demonstrated a good level of evidence to support an association between RA and PD, taking into account tooth loss, the clinical attachment level, and erythrocyte sedimentation rates. Moderate evidence was noted in C-reactive protein and interleukin-1 values. A positive outcome of periodontal treatment was observed, with respect to the clinical features of RA. However, more studies are needed to fully explore the biochemical processes and the relationship between these chronic inflammatory diseases, despite the similarity in the pathophysiologic characteristics of RA and PD. It is found that six months after the completion of periodontal therapy, the improvement of oral health is strongly associated with an

**Table 2 – Pathophysiological similarities in the characteristics of rheumatoid arthritis and periodontal disease.<sup>23,24</sup>**

Pathophysiological characteristics	RA	PD
Cell infiltrate	Macrophages, T lymphocytes, plasma cells and PMN	Equivalent
Immune phenomenon	Immune complex deposition, complement fixation	Equivalent
Cytokines	IL-1 $\alpha$ , IL-1 $\beta$ , IL-6, IL-8, TNF- $\alpha$ and TGF- $\beta$	Equivalent
Local cells affected	Chondrocytes and synoviocytes	Gingival fibroblast, osteoblast, and keratinocytes
Induction of bone resorption	PGE2, TNF- $\alpha$ , IL-1 $\beta$	LPS, PGE 2, TNF- $\alpha$ , IL-1 $\beta$
Tissue Destruction	Metalloproteinase, phospholipase and elastase	Equivalent
Granulation tissue	Present in cartilage/bone interface	Present in the cement/bone interface

IL-1 $\alpha$ , interleukin-1 alpha; IL-1 $\beta$ , interleukin-1 beta; IL-6, interleukin-6; IL-8, interleukin-8; LPS, lipopolysaccharide; PD, periodontal disease; PGE2, prostaglandin E2; PMN, polymorphonuclear leukocytes; RA, rheumatoid arthritis; TNF- $\alpha$ , tumor necrosis factor alpha; TGF- $\beta$ , growth transforming factor beta.

improvement in endothelial function, with a decrease in local and systemic inflammatory processes.<sup>25</sup>

### Hyposalivation/xerostomia

Among oral changes, it turns out that hyposalivation (low salivary flow) and xerostomia (dry mouth) are common in autoimmune rheumatic diseases, and xerostomia affects 1% of RA patients.<sup>26</sup> About one third of RA patients have secondary SS.<sup>27</sup> A study including 604 RA patients showed a decrease in salivary flow in 43% of subjects.<sup>28</sup> The risk of developing hyposalivation increases with the severity of the disease. It is worth mentioning that another study conducted in 483 hospitalized patients due to complications of arthritis found that only 17.7% of xerostomia-positive patients were treated for xerostomia. In contrast, 84.8% of patients treated for xerophthalmia were treated for this condition. It was also observed that the therapeutic modalities administered for xerostomia were not effective and also were not in accordance with current recommendations found in the medical literature.<sup>29</sup>

Therefore, a timely diagnosis and proper monitoring of SS associated with RA are important steps to promote gains in the quality of life of these patients (as will be discussed in the

SS section), taking into account that saliva performs functions of systemic interest, for instance, the sense of taste, epithelial repair of oropharynx and esophagus, and esophageal acid content buffering, among other functions.<sup>30</sup>

### Inflammatory myopathies

Polymyositis (PM) and dermatomyositis (DM) are autoimmune diseases classified as idiopathic inflammatory myopathies, being characterized by musculoskeletal inflammation.<sup>31</sup>

PM is a systemic connective tissue disease, characterized by bilateral, symmetrical, proximal muscle weakness. It affects muscles of the shoulder and pelvic girdle and progresses toward proximal muscles of the limbs. Its onset is frequently gradual and progressive. PM exhibits a geographically variable incidence, with about one case for every 100,000 inhabitants, predominantly affecting females.<sup>32</sup>

Impairment of skeletal muscles of posterior pharyngeal wall and proximal third of the esophagus can lead to oropharyngeal dysphagia, with aspiration and dysphonia. Consequently, the patient can complain of hypersalivation. This complication, however, will be due to an impaired functional activity of swallowing muscles in association with the salivary reflex caused by reflux. Two thirds of the patients present involvement of the neck flexor muscles, which can cause difficulty in neck support. Constitutional symptoms include fatigue, low-grade fever, weight loss, and arthralgia or arthritis of small and medium joints.<sup>33</sup>

Some rare case reports relate presence of ulcerations on the entire tongue, of a linear aspect and with a white secretion on the edges, and also tongue atrophy, in which one can observe a reddened mucosa.<sup>34</sup>

DM is an autoimmune disease of unknown etiology that is characterized by a systemic small-vessel vasculopathy predominantly involving muscles and skin. Besides the cutaneous involvement, the characterization of DM is based in the pattern of muscle involvement, presence of associated clinical manifestations, and histopathological changes.<sup>35</sup>

The prevalence of oral involvement in DM is unknown. Most of the information available comes from individual case reports or small case series, and some early reports of cases did not clearly separate MS from PM.<sup>36</sup>

An involvement of mimic muscles may occur, which leads to a decrease in facial expression. Similarly, the involvement of the masticatory and pharyngeal muscles may result in dysphagia, dysphonia, and hypersalivation. The involvement of striated muscle of the pharynx or esophagus also contributes to the occurrence of dysphagia. In patients with dysphagia, DM reaches 18–50% of patients and correlates with disease severity.<sup>36,37</sup> In addition, the presence of dysphagia increases the risk of aspiration pneumonia. Mortality rates range from 1 to 5 years, reaching 31% of patients with DM and dysphagia.<sup>37</sup> However, the occurrence of hypersalivation is not always attributable to an excess in saliva production, but may be caused by an inability to retain saliva and swallowing it, due to the weakness of perioral muscle tone, or because of dysphagia. The involvement of tongue muscle results in macroglossia, in addition of hypotonia, which can also make it more difficult chewing, swallowing and speech.<sup>38</sup> Involvement of the mucous membrane is reported in about 10–20% of cases.<sup>39</sup>



Mucosal edema, erythema and telangiectasia are the commonest oral changes.<sup>38</sup>

Although 27.5% of patients with DM also suffer arthritis, TMJ involvement is rare, with only one case reported in the literature. In some reports, the presence of prominent blood vessels throughout the oral mucosa and aphthous stomatitis/ulcer-like lesions were described.<sup>40</sup> About 10–46% of patients develop painful oral and gingival ulcers.<sup>41</sup> The teeth have short and bulging roots, with obliteration of root canals as well as pulp chamber calcification. Xerostomia is also seen as a common complaint.<sup>42</sup>

### Systemic sclerosis

Systemic sclerosis (SSc) is an autoimmune disease characterized by inflammation and hyper-reactivity of micro- and macrovascular circulation associated with excessive collagen deposition in tissues, with subsequent fibrosis of the skin and/or internal organs.<sup>43</sup> SSc has a predilection for females, with an incidence of 2–10/one million inhabitants in the general population.<sup>44</sup> In addition, there is a consensus about an increase in morbidity and mortality, with an estimated 66% survival at 10 years.<sup>45</sup>

The oral manifestations are scarcely studied and often neglected by clinicians, although leading to major functional disability. Microstomia is the most common oral finding and develops due to collagen deposition in perioral tissues, causing limitation of mouth opening, perioral groove wrinkling, and soft palate, larynx and oral mucosa stiffness.<sup>46</sup> Furthermore, hyposalivation and/or dry mouth are secondary manifestations of the disease. TMD can also occur, with varying degrees of subsequent resorption of mandibular branch, coronoid process, menton and condyle.<sup>5</sup> It is believed that these areas are reabsorbed due to the chronic collagen deposition. Tongue cancer has a significantly increased frequency in patients with SSc that present a mouth opening <30 mm.<sup>47</sup>

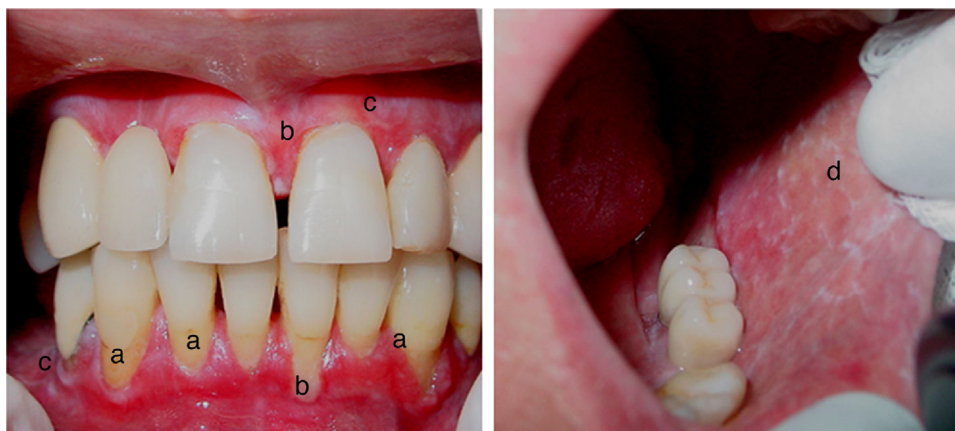
The resorption of some teeth has also been reported with some frequency in these patients. There may be an abnormal increase in the frequency of decayed teeth and of an

atypical tooth eruption. Apparently there is also a predisposition for the occurrence of PD, due to increased plaque buildup. This problem arises from the difficulty of cleaning the mouth (caused by a smaller mouth opening) and in the use of the dental brush. This latter complication is due to sclerotic changes in fingers and hands. Furthermore, the use of systemic corticosteroids for long periods influence in reducing the periodontal inflammatory response, thus making this process a progressive and often insidious one.<sup>48</sup>

### Systemic lupus erythematosus

SLE is an autoimmune disease of unknown etiology, influenced by environmental and genetic factors, and which mainly affects women in the second and third decades of life.<sup>49</sup> The prevalence of oral lesions in patients with SLE varies between 6.5% and 21%. SLE affects primarily tongue, oral mucosa, lips and palate. For this reason, oral ulcers are considered primary events, that are included in the following activity indexes of this disease: BILAG (British Isles Lupus Assessment Group),<sup>50</sup> SLEDAI (Systemic Lupus Erythematosus Disease Activity Index),<sup>51</sup> SELENA-SLEDAI (Safety of Estrogens in Lupus Erythematosus National Assessment), SLAM (Systemic Lupus Activity Measure),<sup>52</sup> and ECLAM (European Consensus Lupus Activity Measurement).<sup>53</sup>

The lesions appear in different ways, such as blemishes and plaques on the mucosa. The lesions may be erythematous, ulcerated, of a recurrent aphthous stomatitis, and lichen planus- or leukoplakia-like lesions (Fig. 2). The size of these lesions is also variable, from a small surface erosion to ulcers covering a wide and extensive area.<sup>54,55</sup> The few studies on oral lesions in patients with SLE show, microscopically, parakeratosis or orthokeratosis, acanthosis, epithelial atrophy, vacuolar degeneration of the basal membrane with necrosis of basal keratinocytes, basement membrane thickening, lichenoid mononuclear infiltrate, and deep connective tissue vasculitis. Injuries in the vermilion border of lips (especially in the lower lip), deserve special attention, as these lesions may be related to lupus cheilitis, with or without epithelial dysplasia.<sup>54,56</sup>



**Fig. 2 – Patient with systemic lupus erythematosus with gingival and tooth sensitivity complaint. Presence of periodontal disease with extensive loss of attached gingiva (a) and regions with a purulent exudate (b). There is a manifestation of lichen planus reticular with gingival (c) and mucosal (d) Wickham striae. The dentist referred this patient to the rheumatologist, suspecting that the lupus was active; this suspicion was subsequently confirmed.**

Other secondary orofacial signs/symptoms include: mouth burning, hyposalivation, xerostomia, salivary gland disease (such as focal necrosis of the parotid gland), TMD, desquamative gingivitis and PD.<sup>54</sup> Hyposalivation can lead to an increased occurrence of dental caries and to a predisposition to candidiasis, especially if immunosuppressive agents such as corticosteroids are being used.<sup>56</sup>

### Sjögren's syndrome (SS)

SS is an inflammatory autoimmune disease presenting a frequent chronic course, in which the lymphocytic infiltration of exocrine glands, particularly lacrimal and salivary glands, impairs its secretory function.<sup>55</sup> Simultaneously, systemic manifestations of cutaneous, respiratory, renal, hepatic, neurologic and vascular nature can occur. SS has two distinct forms: primary SS – not associated with another disorder; and secondary SS – in which the patient expresses this syndrome in association with other autoimmune diseases.<sup>57,58</sup>

It is estimated that SS affects 0.2% of the world population, mainly women, in a ratio of 9:1.<sup>57,58</sup> In Brazil, due to the absence of official estimates or scientifically confirmed data on its incidence, no one knows the exact number of patients with this syndrome. However, it was stated that the majority of diagnosed cases are related to menopausal, or older, women.<sup>59</sup>

SS follows a variable course and exhibits a wide spectrum of clinical manifestations. In addition, many of its symptoms are non-specific, making difficult and delaying the diagnosis. Eighty percent of patients with SS exhibit an insidious onset of symptoms of dryness that develop over a period from several months to years.<sup>58</sup>

The oral manifestations observed in patients with SS are attributed to the involvement of salivary glands, which leads to less salivary secretion. In consequence, the worse lubrication and loss of buffering and antimicrobial action of salivary secretion increase the incidence of oral/dental infections, mucosal friability, and symptoms of irritation and burning mouth (Fig. 3).<sup>57</sup> On the other hand, some patients complain of xerostomia, which may not be accompanied by a decrease in salivary secretion.<sup>30</sup> However, in the initial stage of the disease, when the diagnosis has not yet been well established, patients may complain of xerostomia due to changes in

salivary composition, or to a reduction of salivary secretion from the smaller salivary glands (from lip mucosa and palate). Thus, sialometry may reveal that the patient has a normal salivary flow; however, salivary composition tests will indicate qualitative changes.<sup>60</sup>

Usually, dental caries and fungal infections are observed in mucous membranes (especially candidiasis) that can manifest as pseudomembranous or erythematous lesions. The friability of the mucosa in patients with SS often leads to soft tissue injuries. Such signs include dry and cracked lips, median rhomboid glossitis or a fissured tongue, loss of lingual papillae, stomatitis, angular cheilitis, aphthous injury, lip mucosal ulcers, difficulty in swallowing solids, andodynophagia.<sup>57</sup>

SS patients often display voice disorders and correlated symptoms that are associated with a decrease in their quality of life. It is known that the lubrication of the vocal cords is carried out by saliva.<sup>61</sup> Thus, this biological fluid is important for a proper phonation.

Another relevant point refers to the drop in the quality of life of patients with SS, because of their changing eating habits, caused by dry mouth.<sup>62</sup> There is a Strong correlation among oral dryness and fatigue, pain, psychological distress, and a worse quality of sleep; and that it is considered as a cardiovascular risk factor.<sup>63</sup> In this study, the authors concluded that a multidisciplinary therapeutic approach may be the best way to minimize dry mouth and its consequences in patients with primary SS.<sup>63</sup>

Finally, another common oral manifestation is an asymptomatic and self-limiting increases of parotid glands or other major salivary glands,<sup>55</sup> which may be pointing to the early stage of SS.

Therefore, the establishment of an early diagnosis of SS is essential for the choice of the correct treatment, which consists in relieving the signs and symptoms in order to minimize or avoid sequels that can impact on the health and quality of life of patients.<sup>64</sup>

Gustatory, mechanical and chemical sialogogues have been used to stimulate saliva production. However, the effectiveness of these resources is low, because they provide only temporary relief, requiring frequent applications.<sup>65</sup> Many topical treatments such as sprays, lozenges, mouthwashes, gels, oils or toothpastes have been evaluated, but there is no strong



**Fig. 3 – Loss of papillae of the tongue(a) and candidiasis (b) in a patient with Sjögren's syndrome who presented with complaints of a burning mouth, feeling of “something stuck in the throat” and reduced sense of taste. Examinations of salivary patterns showed severe hyposalivation (unstimulated salivary flow rate: 0 ml/min; flow with stimulus: 0.1 ml/min) and an acidic pH (6.3). Loss of mineral structure with clefts formation in teeth (c) and resin porosity (d), conditions that promote great discomfort to the patient, because of the greater attrition with the dried up mucosa.**

evidence that any of these topical treatments is effective to alleviate the patient with dry mouth.<sup>66</sup> Oxygenated tri-ester glycerol-based lubricants are more effective than water-based electrolyte sprays. Chewing gum increases saliva production, but there is no evidence that these products are better or worse than saliva substitutes. However, acidic secretagogues and those containing sugar should be avoided,<sup>66</sup> because these products lower oral pH, promote greater tooth demineralization and irritate a mucous already very sensitive. One should opt for the use of sugar-free chewing gum, but containing fluoride and bicarbonate in its composition. These components increase salivary pH and assist in preventing tooth decay.<sup>67,68</sup>

Chemical sialagogues, such as pilocarpine and cevimeline, are effective in relieving hyposalivation, but may cause adverse effects.<sup>65</sup> Electrical stimulation applied to the afferent pathways (through the oral mucosa or skin) in areas of salivary glands, showed increased saliva production and relief of dry mouth in patients with SS<sup>65</sup> and in patients undergoing cervical-brain radiotherapy.<sup>69</sup>

A systematic review of randomized controlled trials was conducted to gather evidence on drug therapy in primary SS. The authors suggested that saliva substitutes and sugar-free chewing gums may be effective in cases of mild-to-moderate dry mouth. Consumption of alcohol and smoking should be avoided, and it is a critical factor the establishment of a thorough oral hygiene. The treatment of choice for patients with residual function of salivary glands is cevimeline and oral pilocarpine. However, no study was published comparing the efficacy of these two drugs. The doses which have shown better effects in terms of efficacy and safety were: pilocarpine 5 mg every 6 h; and cevimeline 30 mg every 8 h. N-acetylcysteine could be an alternative in patients with contraindications or intolerance to muscarinic agonists.<sup>70</sup>

## Conclusion

Orofacial manifestations in patients with autoimmune rheumatic diseases are common problems, but still sparsely addressed by rheumatologists in their everyday clinical practice. This article produced a summary of the main manifestations observed, in order to familiarize these professionals with their diagnoses, underlying the possible need for an early referral to the dentist.

## Conflicts of interest

The authors declare no conflicts of interest.

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