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The Sjögren's syndrome – an interdisciplinary problem viewed by a dentist

Zespół Sjögrena – problem interdyscyplinarny widziany okiem lekarza stomatologa

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Słowa kluczowe: terapia, zespół Sjögrena, kserostomia.

Summary

Sjögren's syndrome is common and chronic disease. So far there is no effective therapy. In 90% of cases, it affects women, usually in the peri-menopausal period. Many systems and organs may be involved in the course of the disease, thus it is interesting for many medical specialists. There are primary and secondary Sjögren's syndromes, both characterized mainly by xerostomia and keratoconjunctivitis. The paper reviews basic symptoms in the oral cavity involving the oral mucosa, lips, tongue, gingiva, teeth and periodontium. Treatment and prevention in a dental clinic are also described. Lifestyle and pharmacotherapy to avoid symptom aggravation are additionally considered.

Streszczenie

Zespół Sjögrena jest powszechnie znaną jednostką chorobową o przewlekłym przebiegu, dla której nie opracowano jeszcze skutecznej terapii. W 90% przypadków chorobę tę rozpoznaje się u kobiet, zwykle w okresie okołomenopauzalnym. Dotyczy ona wielu układów i narządów i dlatego stanowi przedmiot zainteresowania lekarzy wielu specjalności. Wyróżnia się pierwotny i wtórny zespół Sjögrena, w których dominującymi objawami są suchość jamy ustnej oraz suchość spojówki i rogówki. W artykule omówiono objawy zespołu Sjögrena ze strony jamy ustnej – dotyczące błony śluzowej jamy ustnej, warg, języka, dziąseł, zębów i przyzębia. Scharakteryzowano leczenie i postępowanie profilaktyczne stosowane w gabinecie stomatologicznym u pacjentów z zespołem Sjögrena. Uwzględniono elementy stylu życia mające wpływ na przebieg choroby oraz zalecenia dotyczące farmakoterapii, których celem jest uniknięcie nasilenia objawów.

Introduction

Sjögren's syndrome, historically called Mikulicz-Radecki's disease, is a disease well known not only by rheumatologists and other specialists but also, and especially, by ophthalmologists and dentists specializing in oral mucosa diseases. The syndrome was first described by the Swedish ophthalmologist Sjögren, in 1933, although the functional disorder of the lacrimal and salivary glands had already been mentioned by the Polish surgeon Mikulicz-Radecki in 1892 [1].

It is estimated that 1 to 2 million people in the US suffer from Sjögren's syndrome; it is the third most common rheumatic autoimmune disorder in that country, behind systemic lupus erythematosus and rheumatoid arthritis [2]. The disease affects 9 times more women than men, its onset is usually in the 4th or 5th decade of life, and it is progressive [3, 4].

Sjögren's syndrome may take a primary or secondary form. The primary form occurs by itself in previously healthy persons; it happens in about 40% cases. The secondary form occurs in the course of other chronic systemic diseases of the connective tissue such as rheumatoid arthritis, systemic lupus erythematosus, systemic scleroderma, and polymyositis, and it may also accompany Hashimoto's thyroiditis [4–6]. It should be noted that more than half of patients diagnosed with systemic scleroderma report dryness symptoms, although all cri-

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teria of Sjögren's syndrome are fulfilled only by a few percent of those patients [6].

Outline of pathogenesis

As is the case with most autoimmune diseases, the cause of Sjögren's syndrome is not known yet. It has been established that the nature of the disease is an autoimmune response to exocrine glands. It may be caused by a prior infection with sialotropic viruses and/or retroviruses HTLV-1 and HIV. Hepatitis C virus is increasingly believed to be engaged in the disease etiopathogenesis since the retrovirus is not only hepatotropic and neurotropic but sialotropic as well. Obviously, genetic predisposition plays an important role, manifested by presence of histocompatibility antigens: HLA-DR2, HLA-DR3, HLA-Dw3, HLA-Dw52, HLA-B8, HLA-DQ1, HLA-DQ2, and, in secondary Sjögren's syndrome, also HLA-DR4. Clinical symptoms of the disease include mainly xerostomia resulting from inflammatory infiltrations with CD4(+) T cells, and, to a lesser extent, CD8(+) T cells and B lymphocytes within salivary glands, which cause apoptosis, fibrosis and resultant atrophy of the glands, as well as keratoconjunctivitis sicca, also caused by inflammatory infiltrations within lacrimal glands [4, 5, 7–10].

Less common symptoms of Sjögren's syndrome include recurrent bronchitis leading sometimes to bronchiectasis; nose dryness resulting in dysosmia and hearing disorders; vaginal dryness; purpura and ulcerations of the skin; atrophic gastritis; dysphagia; acute and/or chronic pancreatitis; hepatitis and cholangitis; primary biliary cirrhosis; nephritis; inflammation of muscles, joints and serous membranes; Raynaud's phenomenon; and signs of nervous system involvement. The disease-related nervous system symptoms include anxiety disorders, depression, and peripheral neuropathy. It should be noted that lesions in the peripheral nervous system developing in the course of primary Sjögren's syndrome are quite common because they may occur even in 10% to 60% of patients, and they often precede diagnosis of the disease. The lesions have a demyelinating or axonal-demyelinating character. They are caused by lymphocytic or necrotic inflammation of vessels supplying blood to nerves. The inflammatory process leading to destruction of endothelium and resultant vascular occlusion results in ischemia of peripheral nerves [11]. In primary Sjögren's syndrome, involvement of the peripheral nervous system usually takes the form of distal sensory polyneuropathy (up to 60%), sensory neuropathy of small nerve fibers as well as distal sensory-motor polyneuropathy and sensory ataxia. Involvement of the peripheral nervous system in Sjögren's syndrome may also manifest as multifocal mononeuropathy, polyradiculopathy, cranial neuropathy and autonomous neuropathy [12–15]. In most cases, cranial neuropathy in the course of primary Sjögren's syndrome affects the trigeminal nerve, unilaterally, and involves mostly the lower part of the nerve. Neuropathy involving the facial nerve or oculomotor nerve [14].

Systemic symptoms occurring in Sjögren's syndrome can include fever and increased fatigue. They are an effect of proinflammatory cytokines. Oncological vigilance is recommended in patients with systemic symptoms because such patients have a 40 times higher risk of developing lymphoma [4].

This paper discusses oral symptoms of Sjögren's syndrome, their diagnostics and treatment.

Dental symptoms

Symptoms of Sjögren's syndrome occurring within the oral cavity are connected with reduced saliva secretion which results in dryness of oral mucosa (xerostomia) and burning tongue (glossodynia). In xerostomia patients, higher rates of dental caries and predisposition to musocal infections are observed [16]. Microbiological cultures reveal increased populations of caries-causing microbes – *Lactobacillus* spp. and *Streptococcus mutans* – in the supragingival plaque [17]. In the bacterial flora of the oral cavity, higher counts of the saprophytic saccharomycetes species – *Candida albicans* can be also observed, together with related lesions on the mucosa such as erythematous lesions, plicated tongue, or – in patients wearing removable dentures – mucositis developing under the denture baseplate.

Reduced saliva secretion reported in Sjögren's syndrome results from atrophy of small salivary glands due to ongoing inflammatory processes. Inflammation is also observed in large salivary glands, with periodical edemas, and lymphocytic infiltrations revealed by histopathological examinations during remission of the disease. The result of the described mechanisms is a reduced amount and changed composition of saliva, which contributes to lower pH and worse buffering properties of saliva [17, 18]. Patients complain of difficulty in chewing, particularly dry foods, distortion of the sense of tase (dysgeusia), abdominal pain (connected with gastroesophageal reflux), changed speech (slurping speech), hoarseness, dry, chapped lips, discomfort when using movable dentures, and dry, strongly plicated tongue (*lingua plicata*) [17, 18]. Studies conducted in Taiwan indicate that patients with Sjögren's syndrome visit dentists twice as often, due to dental caries as well as inflammatory conditions of the gingiva, periodontium, dental pulp and whole oral cavity [19].

Treatment

Treatment of Sjögren's syndrome initiated by a dentist is symptomatic only; it is however extremely diffi-

cult to eliminate xerostomia and its effects. Patients are instructed to use saliva substitute formulations, and saliva stimulating agents such as pilocarpine tablets or fluorine-containing mouthwashes. Patients are recommended to drink large quantities of water, use xylitol-containing chewing gums, or chew tough foods such as apples or bread crust [16, 18, 20]. It is also important to eliminate caffeine from the diet, and to avoid drinking alcohol or using alcohol-containing mouthwashes. It is recommended to give up smoking and avoid passive smoking. Some authors recommend avoiding clearly acidic drinks e.g. apple, citrus, grapefruit or tomato juices [20]. The patient should be instructed about the significance of prophylaxis and dental hygiene.

When taking the history from the patient, the dentist should also ask about medicines taken by the patients. Anticholinergic drugs, histamine antagonists, antiarrhythmic agents, antidepressants, antihypertensives including diuretics, as well as neuroleptics and certain benzodiazepines, can increase dryness of the mouth (Table I). The dentist's role is to suggest that attending physicians of their patients should replace those drugs with milder-acting ones, or taper down the present doses [21]. Following doctor's instructions will alleviate the symptoms, provide relief, and improve life quality of xerostomia patients. It should be noted however that the disease cannot be cured so discontinuation of treatment will lead to exacerbation of symptoms.

Table I. The most common groups of medicaments which can increase the symptoms of dry mouth

Major groups of drugs which usually increase the dry mouth symptoms				
1. Anticholinergic drugs				
Atropine	Ipratropium bromide	Pridinol hydrochloride	Biperiden	
2. Histamine antagonists				
1st generation: Clemastine Promethazine Ketotifen Cyproheptadine Hydroxyzine	**2nd generation:** Cetirizine Loratadine Mizolastine	**3rd generation:** Fexofenadine Desloratadine Levocetirizine Bilastine		
3. Neuroleptics				
Phenothiazines: Chlorpromazine	**Butyrophenones:** Haloperidol	**Benzioxazoles:** Risperidone		
4. Antidepressants				
Tricyclic antidepressants: Amitriptyline Imipramine	**Tetracyclic antidepressants:** Mianserin Mirtazapine	**MAO inhibitors:** Moclobemide	**Selective serotonin reuptake inhibitors (SSRI):** Fluoxetine Sertraline	**Drugs with other activity mechanisms (SSRE):** Tianeptine
5. Antihypertensives				
Non-selective β-blockers: Propranolol	**Calcium channel blockers:** Amlodipine	**Angiotensin-converting enzyme inhibitors:** Ramipril Perindopril	**Selective α_1-adrenolytics:** Doxazosin	**Sympatholytics:** Clonidine Methyldopa
6. Diuretics				
Osmotic diuretics: Mannitol, urea, sorbitol			**Loop diuretics:** Torasemide	
7. Antiarrhythmic agents				
Class Ic: Propafenone	**Class II:** Propranolol	**Class III:** Sotalol	**Class IV:** Diltiazem	
8. Benzodiazepines				
Lorazepam			Alprazolam	

Conclusions

The generalized character of symptoms in Sjögren's syndrome requires an interdisciplinary approach, and care of several specialists. An important role in that care is played by the dentist, and the dentist's co-operation with the patient's attending doctor. Relieving symptoms caused by mouth dryness will significantly affect the life quality in patients with Sjögren's syndrome, and will considerably reduce the disease-related discomfort. Addditionally, we should remember that not only initiation of therapy is important to the patient but we should also understand his/her problems, and dissipate concerns about the diagnosed disease which is little known to the patient.

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