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Pathological lesions in the oral cavity in the course of connective tissue diseases

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ABSTRACT

Dentistry, is one of the intensively and rapidly growing branches of medicine. This prompts dentists to take an interdisciplinary approach to their patients. Thus, the dentist, being a general practitioner, can make significant contributions to the early diagnosis of systemic disease and the faster implementation of appropriate treatment. In view of the aforementioned, we undertook research on the relationship of pathological changes observed in the oral cavity with diseases of the connective tissue system. Collagenosis is a chronic autoimmune disease initiated by many factors, among which the genetic factor and viral infections are mentioned. The changes observed in the oral cavity may be a picture of the disease, a complication of the disease or a side effect of the treatment. The aim of the study is, thus, too present the pathological changes in the oral cavity which often accompany collagenosis, and to discuss the risk factors of connective tissue system diseases and methods of dental treatment.

INTRODUCTION

The results of recent studies point to the relation between pathological symptoms observed in the oral cavity and chronic systemic diseases. These diseases include collagenoses such as rheumatoid arthritis, systemic lupus erythematosus, systemic scleroderma, inflammation polymyositis, dermatomyositis, necrotising vasculitis and other vasculopathies (polyarteritis nodosa, hypersensitivity vasculitis, giant cell arteritis, Kawasaki disease, Behçet's disease), Sjögren syndrome and overlap syndromes [1].

AIM OF THE STUDY

The aim of the study is to draw dentists' attention to the symptoms of connective tissue diseases observed in the oral cavity. The study presents diseases categorised as collagenoses and their characteristic pathological lesions in the oral cavity. It also discusses the risk factors which negatively influence the development of symptoms and the procedures the dentist should apply if a connective tissue disease is diagnosed.

MATERIALS AND METHODS

PubMed/Medline database was searched from 1995 till present, using keywords. Moreover, other sources were taken from the references of the selected papers and hand search was also done on the scientific journals.

RESULTS AND DISCUSSION

The term collagenosis appeared as early as the 1940s, but the precise aetiology of connective tissue diseases remains unknown. These are autoimmune diseases which are initiated by a genetic factor and they might be stimulated by viral infections [2]. The host's immune system attacks their own cells and tissues, thus causing their inflammation and damage. Apart from this, chronic odontogenic inflammatory foci may cause secondary lesions in other organs and result in the development of rheumatic diseases by activation of the immune system. Lesions observed in the oral cavity may reflect the disease itself, they may be complications of the disease or they may result from the side effect of a treatment [1,3,4]. Therefore, regular, periodical dental check-ups with a special focus on the state of the mucosa may be significant both for the patient and general practitioner. General symptoms combined with the symptoms observed in the oral cavity will facilitate diagnosis and implementation of an adequate therapy. In 1983, the American Rheumatism Association (ARA) introduced criteria for the classification of systemic diseases of the connective tissue.

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Rheumatoid arthritis is the most common collagenosis as it is diagnosed in about 1% of the population [5]. Oral cavity symptoms are not pathognomonic – spontaneously bleeding gums, petechiae and bleeding to the mucous membrane may be caused by concomitant diseases, e.g. usually normochromic and normocytic anaemia. The therapy should be oriented at causative treatment, which improves the state of the oral cavity. Among other rheumatoid arthritis complications, the incidence of amyloidosis amounts to as much as 5-20% [2]. Patients with the disease have considerably enlarged tongues and suffer from resulting ailments. Chronic steroid therapy applied to patients with rheumatoid arthritis may weaken their immunity and disorder the microflora balance. In consequence, the patients are likely to develop bacterial, viral and fungal infections more often.

According to epidemiological research, lupus erythematosus is diagnosed in about 0.12% of the population [6]. There is a correlation between the patient's sex and the incidence of the disease. Indeed, it occurs nine times more frequently in women. Patients aged 20-40 years are at the highest risk of the disease [6,7]. The American Rheumatism Association introduced 11 diagnostic criteria of the disease. Lupus erythematosus can be correctly diagnosed if at least four of these appear [2]. The disease symptoms include skin lesions, which usually occur in the form of malar rash on the patient's face, and erosion in the oral mucosa [2]. According to available publications, painful lesions of the mucosa occur in 15-80% of cases of lupus erythematosus [8]. Skin eruptions are usually located on the lower lip as a result of exposure to solar radiation. They can also be found on the buccal and palatal mucosa [9]. The lesions have the form of diffuse erythematous scales, erosions, ulcers or white lesions, which must be differentiated from lichen planus by means of immunopathological examination [10]. Rheumatologists stress that it is very important for patients to avoid exposure to high and low temperatures and to eliminate spicy dishes from their diet as they exacerbate the disease [4]. Therapy with steroid preparations and other immunosuppressive drugs reduces patients' immunity. In consequence, there are frequent secondary infections of oral lesions with fungi of the *Candida* genus. General treatment does not always improve the state of the oral cavity, so it is necessary to apply additional local therapy with corticosteroid preparations. Oral supplementation with vitamins is also important [10].

Systemic and limited scleroderma is another clinical unit among the connective tissue diseases. Herein, progressive collagen accumulation leads to skin and muscle fibrosis, and, in consequence, to microstomia and limited mouth opening [11,12]. Patients with scleroderma are often characterised by a smooth tongue with shortened lingual frenulum, disappearance of labial red and higher tension of the mucosa [13]. Disordered function of the oral cavity is brought about by impairment of the autonomic nervous system and it is manifested by salivation problems [12]. Moreover, xerostomia favours intensive development of dental caries, which causes the loss of teeth in a short time. Researchers indicate the characteristic radiological image of the maxilla and mandible. It is manifested by diffuse widening of the periodontal fissure, which can be observed in a few dental

quadrants. Another symptom is resorption of the posterior mandibular margin and the condyloid and coronoid processes. Resorption of the condyloid process is manifested by clinical symptoms of open occlusion [14]. Due to such numerous and serious lesions in the oral cavity, patients require special dental care. Doctors recommend frequent check-ups, oral cavity hygiene, pilocarpine supplementation, alcohol abstinence, chewing gum and regular exercises of facial muscles [15,16]. According to Poole *et al.*, the limitations caused by pathological lesions in hand joints have negative influence on oral cavity hygiene and the course of treatment. Therefore, patients should receive multidisciplinary dental care [17].

Dermatomyositis is an autoimmune disease. It is most frequently diagnosed in children aged 5-14 years and adults aged about 40 years [18]. The literature does not provide characteristic symptoms observed in the oral cavity. However, there have been reports on frequent erythematous lesions and facial swelling, heliotropic blepharitis, as well as weakening of the velar and posterior pharyngeal wall muscles, causing dysphonia and dysphagia [19]. Adult patients should undergo an oncological examination, because neoplastic diseases are diagnosed in about 25% of all patients [18].

About 80% of all cases of Kawasaki disease are diagnosed in boys under the age of 5. This pathology can be diagnosed by observing lesions in the oral cavity, as well as dry and chapped lips, which often bleed and result in scabs. The oral mucosa is strongly red, but there are no characteristic ulcers or pseudomembranous lesions. The tongue has a typical raspberry colour with severely swollen lingual papillae. 50-70% of all patients also suffer from acute enlargement of cervical lymph nodes [20].

According to the literature, Behçet's disease is a multi-system syndrome which is most often diagnosed in young men aged 25-30 years who live in the Mediterranean region, Middle East and East Asia [21]. According to epidemiological research, mouth ulcers are the significantly characteristic symptom of the disease, as they are observed in as much as 97-99% of all cases. Other symptoms include genital ulcers (85%), skin lesions (85%) and eye lesions (50%) [22]. Painful lesions in the oral cavity are usually located in the velar region and in the oral part of the pharynx. Usually these are small red-edged lesions occurring in foci of six or more. Ulcers have recurrent nature. There are periods of disease exacerbation and remission. Exanthema in the oral cavity are often accompanied by high body temperature and malaise. Patients with limited mucosal lesions usually receive local symptomatic treatment with steroids [21].

Sjögren syndrome is another disease categorised as a collagenosis [1]. Symptoms observed in the oral cavity are the consequence of impaired and disordered salivary glands, which have inflammatory infiltrations with the majority of CD4+ T lymphocytes, B lymphocytes and plasma cells [22-25]. In consequence, the gland parenchyma becomes impaired or it atrophies at the final stage of the disease. Patients complaining about swelling of the parotid gland region, dryness and burning sensation in the oral cavity require further diagnosis for primary or secondary Sjögren syndrome. These diseases accompany other systemic

diseases, such as rheumatoid arthritis or systemic lupus erythematosus [26-28]. The surface of the tongue and mucous membranes is viscous and dry. There are fissure-like cracks in the corners of the mouth. According to the literature, patients with Sjögren syndrome are more likely to develop dental caries, periodontal diseases and lymphoma. Patients using removable dentures complain about difficulties in their use as well as speaking and swallowing problems [29,30]. The disease is diagnosed by conducting a characteristic subjective anamnesis and an objective clinical test. In order to assess the salivary gland function, additional tests are conducted. These include sialometry, sialography, scintigraphy, histopathological examination of the salivary glands and blood serum tests for the presence of typical anti-Ro/SS-A and anti-La/SS-B antibodies or rheumatoid factor, as well as ANA > 1: 320 [24,31,32]. Scientist also observed considerably increased concentrations of IL-2 and IL-6 in the saliva of patients with Sjögren syndrome. Measurement of the inflammatory cytokine concentration has not only a diagnostic value, but it is also useful for monitoring the course of the disease [33-37]. Apart from this, the analysis of the composition of patients' saliva shows higher levels of sodium, chlorides, IgA, IgG, lactoferrin, albumin and lower levels of phosphates. In recent years, non-invasive methods have also been used to diagnose Sjögren syndrome, e.g. computed tomography, magnetic resonance, magnetic resonance sialography and ultrasonography [24,38].

CONCLUSIONS

To sum up, we can say that it is very important for the benefit of their patients that dentists should cooperate closely with rheumatologists throughout the diagnostic process, treatment planning and prevention of numerous complications of systemic diseases of the connective tissue. The dentist's knowledge of the symptoms of the systemic diseases observed in the oral cavity may affect early diagnosis and implementation of an adequate therapy. Moreover, the prevention and adequate treatment of the dental symptoms of systemic diseases of the connective tissue provides contemporary dentistry with a broad area for clinical action and scientific exploration.

REFERENCES

- Mackiewicz S, Zimmermann-Górska I. *Reumatologia*. Warszawa: PZWL;1995:87-180.
- Świerkot J, Kukiz-Świerkot G. Zmiany obserwowane na śluzówkach jamy ustnej w przebiegu układowych chorób tkanki łącznej. *Przew Lek*. 2000;7:73-7.
- McCarty. Arthritis and allied conditions. Philadelphia: Lea & Febiger;1993:1149-356.
- Klippel JH, Dieppe AD. *Rheumatology*. London: Mosby-Year Book Europe;1994:10-59.
- Jura-Półtorak A, Olczyk K. Diagnostyka i ocena aktywności reumatoidalnego zapalenia stawów. *Diagn Lab*. 2011;47:431-8.
- Ian R Mackay. Tolerance and autoimmunity. *BMJ*. 2000;321:93-6.
- Patavino T. Natural medicine and nutritional therapy as an alternative treatment in systemic lupus erythematosus. *Altern Med Rev*. 2001;6:460-71.
- Prokop J. Objawy skórne i narządowe w różnych postaciach toczenia rumieniowatego. *Post Dermatol*. 1995;12:19-29.
- Szumska-Tyrzyk B, Sadlak-Nowicka J, Antkiewicz H, Tyrzyk S. Stan kliniczny błony śluzowej jamy ustnej u pacjentów chorych na toczenia rumieniowatego układowego (SLE). *Dent Med Probl*. 2002;39:79-83.
- Peterson-Jęckowska R, Wójcicka A, Kurnatowska A. Zmiany w jamie ustnej w przebiegu toczenia rumieniowatego układowego – opis przypadku. *Dent Med Probl*. 2004;41:125-9.
- Meiri SD. *Manifestations stomatologiques de la sclerodermie: description et prise en charge*. These No Med. 616 Geneve, 2002.
- Vincent C, Agard C, Barbator S, N'Guyen JM, Planchon B, Durant C, et al. Orofacial manifestations of systemic sclerosis: A study of 30 consecutive patients. *Rev Med Interne*. 2009;30:5-11.
- Thum-Tyzo K, Balawejder A, Tyzo B, Petkowicz B, Krasowska D, Wysokińska-Miszczuk J. Występowanie zmian w jamie ustnej w przebiegu twardziny układowej. *Dent Med Probl*. 2010;47:53-60.
- Cankaya H, Kabasakal Y. Mandibular resorption due to progressive systemic sclerosis: a case report. *J Oral Maxillofac Surg*. 2001;59:565-7.
- Tolle SL. Scleroderma considerations for dental hygienists. *Int J Dent Hyg*. 2008;6:77-83.
- Nauert P. Scleroderma and dental health. *Scleroderma Foundation Newslines*. 1999;2:14-5.
- Poole JL, Brewer C, Rossie K, Good CC, Conte C, Steen V. Factors related to oral hygiene in person with scleroderma. *Int J Dent Hyg*. 2005;3:13-7.
- Ryniewicz B. Immunologiczne i zapalne uwarunkowania chorób nerwowo-mięśniowych. *Pol Przegl Neurol*. 2009;5:177-83.
- Kukiz-Świerkot G, Świerkot J. Zmiany obserwowane na śluzówkach jamy ustnej w przebiegu układowych chorób tkanki łącznej. *Przew Lek*. 2000;7:73-7.
- Jasiński M, Gołębiowska-Gągała B, Wieleba M. Objawy ze strony ośrodkowego układu nerwowego u dziecka z chorobą Kawasaki – opis przypadku. *Neurol dziec*. 2007;16:31.
- Turowska-Heydel D, Żuber Z, Sobczyk M, Pilch B. Trudności diagnostyczne i terapeutyczne w młodzieńczej chorobie Behceta - opis dwóch przypadków. *Reumatol*. 2010;48:276-81.
- Criteria for diagnosis of Behcet's disease. International Study Group for Behcet's Disease. *Lancet*. 1990;335:1078-80.
- Klippel JH, Dieppe PA, Ferri FF. *Reumatologia*. Lublin: Czelej; 2000:233-6.
- Włodkowska-Korytkowska M, Maślińska M, Saied F, Kwiatkowska B, Prochorec-Sobieszek M, Sudoł-Szopińska I. Przegląd metod diagnostycznych Zespołu Sjögrena. *Reumatol*. 2013;51:363-9.
- Smoleńska Ż, Pawłowska J, Zdrojewski Z. Rola limfocytów T w patomechanizmie pierwotnego zespołu Sjögrena. *Reumatol*. 2012;50:45-51.
- Morawska J, Sierakowski S, Gińdzieńska-Sieśkiewicz E, Sierakowska M. Współwystępowanie zespołu Sjögrena i twardziny układowej. *Reumatol*. 2010;48:446-8.
- Zimmermann-Górska I. Zespół Sjögrena - przykład integracji nauk medycznych. *Pol Arch Med Wewn*. 2001;105:47-51.
- Fuglewicz A, Pękala Ł. Wtórny zespół Sjögrena u chorych z układowymi chorobami tkanki łącznej. *Adv Clin Exp Med*. 2003;12:329-39.
- Napenas JJ, Rouleau TS. Oral complications of Sjögren's syndrome. *Oral Maxillofac Surg Clin North Am*. 2014; 26:55-62.
- Cartee DL, Maker S, Dalonges D, Manski MC. Sjögren's Syndrome: Oral Manifestations and Treatment, a Dental Perspective. *J Dent Hyg*. 2015;89:365-71.
- Zimmermann-Górska I. *Reumatologia*. Wyd 2. Warszawa: PZWL; 1995:35-36,103-4.

32. Cackowska-Lass A, Kochańska B, Kręglewska B, Witek E. Ocena szybkości wydzielania śliny spoczynkowej i stymulowanej u chorych z zespołem Sjögrena. *Dent Med Probl.* 2004; 41:469-75.
33. Szydłarska D, Grzesiuk W, Kupstas A, Bar-Andziak E. Ślina jako materiał diagnostyczny. *Forum Med Rodz.* 2008;6:454-64.
34. Klichowska-Palonka M, Bachanek T. Możliwości wykorzystania śliny w diagnostyce i leczeniu wybranych stanów patologicznych – przegląd piśmiennictwa. *Przegl Lek.* 2011; 68:114-7.
35. Qin R, Steel A, Fazel N. Oral mucosa biology and salivary biomarkers. *Clin Dermatol.* 2017;35:477-83.
36. de Goés Soares L, Rocha RL, Bagordakis E, Galvão EL, Douglas-de-Oliveira DW, Falci SG. Relationship between Sjögren syndrome and periodontal status: A systematic review. *Oral Surg Oral Med Oral Pathol Oral Radiol.* 2018;125:223-31.
37. Phung L, Lollett IV, Goldhardt R, Davis JL, Young L, Ascherman D, et al. Parallel ocular and serologic course in a patient with early Sjogren's syndrome markers. *Am J Ophthalmol Case Rep.* 2017;8:48-52.
38. Saied F, Włodkowska-Korytkowska M, Maślińska M, Kwiatkowska B, Kunisz W, Smorawińska P, et al. Przydatność ultrasonografii w diagnostyce zespołu Sjögrena. *J Ultrason.* 2013;13:55.