

REVIEW

Sjögren's syndrome in present

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Abstract: Sjögren's syndrome is a systemic autoimmune disease characterized by a reduced function of exocrine glands, mainly salivary and lacrimal glands based on chronic plasmocellular infiltration. Syndrome includes affection of glands in gastrointestinal system, respiratory apparatus, skin, and vaginal mucosa. It is described separately as a primary Sjögren's syndrome or together with other inflammatory rheumatic diseases as a secondary Sjögren's syndrome. Advanced diagnostic is based mainly on serologic examinations. Treatment of patients reflects the form of Sjögren's syndrome. Despite recent knowledge the treatment is rather symptomatic than causal (Ref. 12). Full Text in PDF www.elis.sk.

Key words: Sjögren's syndrome, xerostomia, xerophthalmia.

Etiology and pathogenesis

Sjögren's syndrome (sicca syndrome, later only SS) was described by Swedish ophthalmologist Sjögren in the year 1933 for the first time. It is a disease of unclear multifactor etiology, where the association with infection is put in front, and the genetic predisposition is also plumb. The most afflicted group (up to 95 %) is females aged between 20 and 50 (1). Base for the pathogenesis is a disorder of exocrine functions created by development of autoimmune reactions. Antibodies being produced by the organism are either organ-specific – produced against epithelium of salivary ducts and lacrimal glands, or organ-nonspecific – against nucleus and cellular antigens (anti-Ro/SS-A, anti-La/SS-B), rheumatoid factor (RF) and antinuclear antibodies (ANA). Anti-Ro/SS-A and anti-La/SS-B appear in 50 % to 70 % equally. Disorder of T- and B-cellular immunity systems plays an important role. Polyclonal hyperactivity of B-lymphocytes and plasmatic cells is in place with producing of large amount of polyclonal immunoglobulins (majority of IgG), cryoglobulins and other antibodies. Increased occurrence of HLA-Bg and DRw3 was recorded in patients with the primary form of SS, whereas in the secondary form associated with rheumatoid arthritis the occurrence of HLA-DRw4 prevailed. Chronic plasmocellular infiltration of exocrine glands is a fundamental morphologic sign of SS; it may generalize and attack internal organs, muscles, and reticular endothelial system.

In the primary SS, it concerns mainly xerostomia and xerophthalmia without affection of joint tissue. Classical disease manifestation affects mainly salivary and lacrimal glands, less skin,

tracheobronchial, stomach and vaginal glands. This form has an unfavorable prognosis with a progressive exitus from respiratory or kidney failure. In 60 % it relates to interstitial pneumonia and fibrosis, in 15 to 25 % tubular acidosis of kidney is the case. Secondary syndrome always develops together with other inflammatory rheumatic diseases, such as rheumatoid arthritis, systemic lupus erythematosus, progressive systemic scleroderma, dermatomyositis and polymyositis. Course and prognosis of secondary SS depends on the basic disease and includes such features as increased tiredness, subfebrility, arthralgia and myalgia. 70 % of patients have polyarthritis, 40 % Raynaud's syndrome, and 20 % develop lymphadenopathies. Next conditions with mucosa dryness not classified elsewhere belong among so-called sicca-like syndrome.

Diagnostics

The main diagnostic criteria of Sjögren's syndrome is xerophthalmia – burning, pinching, feeling of foreign body in eye connected with dry keratoconjunctivitis, proved by Schirmer test or Bengal pink dye assay. Oral difficulties encounter objective xerostomia and affection of large salivary glands (recurring parotitis), histopathologic examination of small salivary glands (usually of lower lip) is also positive. Presence of autoantibodies is currently considered determining. Glands are usually affected in the course of basic disease, however may preclude development of joint findings. Given disease is a part of stationary (facultative) precancerosis in general sense, by which abnormal is turned to cancer only at certain conditions, not always. Objective xerostomia in sicca syndrome causes an increased vulnerability in oral mucosa as the protective effect of saliva is missing. Therefore, common chronic triggers may rapidly lead to development of cancer. At the same time, it was proven that affection of salivary glands increases the risk of malignant lymphoma and the incidence is 40 to 70 times higher, which represents 5 to 15 % from total number of patients. Moreover, malignant lymphomas associated with Sjögren's syn-

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drome have significantly worse prognosis than those originating from normal glands.

Treatment

Systemic medication is applied both at nonvisceral global expressions like arthralgia, myalgia, arthritis, tiredness, and visceral expressions (lung, cardiac, renal, CNS and peripheral nerves). Nonsteroid antirheumatics, salicylates and low doses of corticosteroids are used. Relatively favorable effect, mainly on nonvisceral global expressions, was recorded after deployment of antimalarials (6). Laboratory parameters being influenced included mainly values of sedimentation, hypergammaglobulinemia, hyperimmunoglobulinemia, reduction of polyclonal IgG. In visceral affection, including vasculitis, skin lesion, pneumonitis, neuropathy and nephritis, corticosteroids are used similarly as in the systemic lupus erythematosus. Drugs like hydroxychloroquine, azathioprine and methotrexate are used to stabilize the status, and to reduce doses of corticoids. It is possible to use cyclosporine A in some patients, but a tendency to interstitial nephritis in a number of patients with Sjögren's syndrome limits its usage. Sometimes it is necessary to order treatment with cyclophosphamide for life threatening conditions. Anyhow, the tendency to develop lymphoma in patients with Sjögren's syndrome leads to caution with its usage. „Pulse“ treatment is recommended rather than daily administration of this drug. You can find literature essays describing treatment with chlorambucil, particularly at neurological indication. D-penicillamine, gold preparations, interferon alpha remains an opened issue and using of intravenous gamma globulins and plasmapheresis are also questionable, mainly in patients with severe extraglandular disease expressions. Deployment of dexametasone in prevention of congenital cardiac arrest in pregnant patient with antiRo and anti-La positivity is a separate issue (3, 11). It needs to be mentioned that disease itself and its treatment leads to further complications like secondary osteoporosis, or renal tubular acidosis, which also need a therapeutic approach. Treatment of secondary Sjögren's syndrome should be handed to specialists, with premium position of rheumatologist.

Xerostomia is a very unpleasant expression of glandular signs of disease, and included a strong feeling of thirst. Saliva has not only the role of lubricant, but helps at uptake and processing of meals, protects mucosa from inflammation. Reduced saliva volume results in increased risk of infection, elevated cariogenicity. Thus it is necessary to increase the hygiene of oral cavity, use various antiseptic mouth rinses, saliva substitutes in various forms, and lubricants as well. Last ones have similar physical properties as tears (pH, osmolarity), but don't have some chemical and biological features of tears. They contain electrolytes, buffers and EDTA. Some contain preservatives, and majority was chosen based on empiric experience. Randomized clinical trials were performed with solutions of 1 % carboxymethylcellulose containing CaCl₂, KCl, NaCl and sodium lactate, solutions containing propylene glycol, dextrane and polycarboxiphilic in NaCl solution with EDTA. The survey exists about topical hyaluronate (1) and topical fibronectin. Most frequently used substitutional lacrimal products

in our conditions for *xerophthalmia* are Lacrisyn gtt oph, Liquifilm gtt oph, Hypromelozol 5% gtt oph, Hypromelozol P gtt oph, Ocutect gtt oph. The preparation Hypotears gel builds viscous solution based on carbomere 980. After application, it spreads above conjunctiva and cornea a protective moistening film with a long contact period with cornea securing stability of lacrimal film for 6 hours (9). Spectacles with UV filter are an approved protective tool, wearing of contact lenses is not recommended, because lack of tears might increase the risk of corneal damage.

Patients with SS should avoid dry, air-conditioned spaces, wind environment, cigarette smoke exposition, and other triggering substances. It is recommended not to speak too much at worsened condition; patients should carry water with them, and keep drinking regimen due to age and global status of body. Local and global fluoridation is recommended in relation to an increased cariogenicity. Repeated studies proved that fluorides, except of increasing resistance of enamel against acid environment, also act remineralizing on enamel lesions (7). Almost all patients use chewing gums with low sugar content to stimulate saliva secretion. Products Biotène or BioXtra including moistening oral gel, tooth paste, mouth rinse without alcohol, and non sticky chewing pastils are available. These preparations contain natural saliva factors (lactoperoxidase, lactoferrin, lysozyme, immunoglobulins, natural peptides), as well as other biologic agents (xylitol, whey, colostrum, Aloe vera, glucose oxidase, essential oils). Preparations containing sorbitol, electrolytes, calcium, and phosphorus are used as saliva substitutes (e.g. Sialin, Glandosane). Clinical trials monitored several agents, which could increase the saliva secretion. It was Bromhexine as a mucolytic agent first of all. Not quite univocal results were obtained with Anethole trithione (Sialor). More controlled clinical trials were performed with pilocarpine (12). Preparation Salagen tablets are available. Studies were performed with cevimeline hydrochloride hydrate – an agonist of muscarine receptors (4, 8). Levamisole and Chinese herbal extracts were used in herpetic ulcerations (10).

In recurrent swelling of salivary glands it is fundamental to differentiate inflammation from lymphoproliferative changes. Antibacterial treatment was proved good in inflammations, for example, antibiotics of penicillin range (Amoksiklav, Augmentin) provided the patient is not allergic to PNC. Repeated rinsing of gland outlets, so-called „lavage“ with physiologic solutions, 1 % mesocaine, or local antibiotics, most frequently with 0.5 % Pamycon were considered efficient. Lipiodol at X-ray examination with contrasting agent (eventually with addition of chlorophyll 1:1) acts anti-inflammatory on gland parenchyma.

Regular usage of various OTC nose aerosols avoids drying of nasal mucosa, increased scab formation, and finally recurring inflammation of upper respiratory tract. A reduced lumen of Eustachian tube may develop otitis (5). In healing season, the quality of air is reduced, which may be eliminated by use of domestic humidifiers. Dry vaginal mucosa may cause an unpleasant feeling at sexual activity, increases risk of infection, therefore usage of lubricants is recommended, and promoted body hygiene, as well. Application of cream and body milk with hydrating component particularly after shower is generally suitable for global dry skin.

Conclusion

Sjögren's syndrome is a disease demanding a lot of effort from both physician and patient. Education of patient based on principles „recommend“, „encourage“, and „advise“ is one of the basic treatment pillars for patients with Sjögren's syndrome. However, major part of the treatment is in hands of the patient alone and lies in correct lifestyle, regular hygiene, and constant treatment of mucosa. It should not be forgotten that we deal with autoimmune disease, which is very effectible by mental burden of the body. Every stress may worsen the course of illness, or be its trigger factor. Not every patient can identify himself with the disease, therefore our role and duty is to help the patient to secure as full life as possible.

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