

Family cases of primary Sjogren's syndrome in monozygous twins*

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Primary Sjogren's disease is a systemic disorder of unknown origin with chronic autoimmune inflammation of the exocrine glands and the obligatory involvement of the salivary and lacrimal glands. We present the cases of primary Sjogren's disease in monozygous twins. These concordant cases suggest the genetic determination of the disease. Early diagnosis of the disease and initiation of immunosuppressive therapy in patient A. prevented the serious complications. The effect of treatment was clearly visible with patient's cancellation of the basic therapy for almost 6 years, after which the general condition worsened, and a joint pain developed. Long-term therapy with small doses of alkylating cytostatics and glucocorticosteroids positively affects systemic manifestations of the disease, and significantly improves the survival of patients. The presence of complications caused by glucocorticosteroid therapy should be taken into account.

Keywords: Sjogren's syndrome, Sicca syndrome, twins, concordance, xerostoma, xerophthalmia.

The Sjogren's syndrome is one of the most common autoimmune disorders of connective tissue, which occurs in 0.59–0.77% of the world's population, including 2.7% of people over 50 [1; 2]. Primary Sjogren's disease is a systemic disorder of unknown origin with chronic autoimmune inflammation of the exocrine glands and the obligatory involvement of the salivary and lacrimal glands [3].

In pathogenesis of the disease the genetic and especially, immunogenetic factors most probably play an important role. However, only a number of genes have been identified to be associated with Sjogren's disease. HLA genes associations are the most studied in this syndrome, varying widely between the countries. In USA mostly the HLA-DRB1*0301-DRB3*0101-DQA1*0501-DQB1*0201 haplotype was shown to play a major role, in Japan — HLA-DRB1*0405-DRB4*0101-DQA1*0301-DQB1*0401, in China — DRB1*0803-DQA1*0103-DQB1*0601. HLA B8, DW3, DW2 alleles are also often registered in such patients [1; 4]. Other potential pathogenic genes include genes, associated

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with B and T cell function, interferon production and several others [4]. Also the role of a viral infection is assumed, e.g., retroviruses, that cause via interferon response the aberrant expression of HLA DR antigens. The autoimmune nature of the disease is confirmed also by extensive lymphoid infiltration of the affected glands, as well as the detection of not only organ-specific (against lacrimal and salivary glands), but also non-specific autoantibodies (rheumatoid factors, antinuclear antibodies, antibodies to SS-A/Ro and SS-B/La antigens) [5; 6].

Clinically, the lesions of the lacrimal glands, cornea, and conjunctiva are described, as well as the xerophthalmia, photophobia, burning and redness of the eyes, lack of tears, and erosion of the cornea. Damage to the salivary glands is also typical with the occurrence of the pseudo-mumps with a decrease in saliva secretion and dry mouth (xerostomia). The parotid, submandibular glands dysfunction leads to the development of cheilitis, glossitis, dental caries, and stomatitis [1–3]. Damage to other exocrine glands is manifested by dry skin, as well as dysfunctions of reproductive, respiratory systems, and gastrointestinal tract. Systemic manifestations include fever, lymphadenopathy, vasculitis, myositis, kidney damage, Raynaud syndrome.

Clinical observation

Female patient A., 60 years old, was admitted to the Rheumatology center with complaints on knee pain, constant dry mouth, dry eyes, feeling of “sand in the eyes”, general weakness, constant headaches, and dizziness. The symptoms were first described at 1985 (at the age of 33), when the diagnosis was first established of primary Sjogren’s syndrome. The diagnosis was verified in 1993 after a pathomorphological study of the salivary gland. The disease debuted with symptoms such as dry mouth, dry eyes and vagina. Prescribed therapy: during 1993-1994 — delagil, 250 mg, in 1994 — delagil, 250 mg + prednisolone 10 mg per day for 7 months, later in 1994 — prednisone 10 mg per day + chlorobutin 2 mg per day for a year — all without positive effect. During 1995-2000 she used prednisone 10 mg per day and cyclophosphamide — 400 mg per week, with some positive effect. Since 2000, she completely stopped taking basic therapy. Progressive deterioration since December 2006 was noted with severe pain appeared in the right half of the chest. The basic therapy was immediately prescribed again (15 mg of prednisone per day and cyclosporin A 75 mg per day), and marked improvement was observed with a normalization of X-ray picture, as well as other clinical and immunological parameters. Until November, 2011, the patient was feeling relatively well with periods of the articular pain, with a positive effect while taking NSAIDs. After cold exposure and episode of hypothermia, at November 23, 2011, severe pains appeared in all joints with brutal stiffness, and patient was hospitalized to Rheumatology center. Anamnesis vitae: menopause occurred at 45, 4 pregnancies, 2 childbirths. The patient’s mother has an oncological disease, her monozygotic twin sister (identical) also has primary Sjögren’s syndrome, the disease debuted in sister earlier by 3-4 years and was more aggressive, mainly displaying with myalgic syndrome.

Comorbid diagnoses in patient A. included arterial hypertension, chronic pyelonephritis and erosive antral gastritis. At the time of the examination, the condition of the patient was satisfactory. The skin is pale, dry. Visible mucous membranes are pale pink, clean, dry. Peripheral lymph nodes are not enlarged, painless. Muscle tonus is reduced,

muscles are painless on palpation. Joints are without visual inflammatory changes. Active and passive movements are normal. Auscultation of the lungs: breathing is normal, no wheezing. Heart sounds are rhythmic, clear. Blood pressure — 140/80 mm Hg. Pulse rate — 82 beats per minute. The abdomen is not swollen, soft, and painless on palpation. Slight pain in the epigastric region, in the projection of the pancreas is felt. The liver has elastic consistency, palpatory painless. No peripheral oedema is observed.

Laboratory and instrumental data

Blood analysis — anemia (Hb = 90 g/l, erythrocytes — $3.74 \cdot 10^{12}/l$), an increase in ESR up to 45 mm per hour. Glucose blood level — 6.3 mmol / L. Immunological tests: antibodies to SS- A, SS-B, CENT-B were detected (SS-A = 44.3 U/ml, SS-B = 71.2 U/ml, CENT-B = 83.6 U/ml with a normal upper range below 35 U/ml). RF < 30 IU/ ml, CRP < 6 mg/L. Thyroid status check revealed a moderate increase in TSH (6.1 mU/l). ECG documented sinus rhythm with a heart rate of 85 beats per minute. Left ventricular hypertrophy noted. On echocardiography: calcification of the base of the posterior mitral valve, fibrosis of the aortic valves, mitral valves and chords of the left ventricle matched. Any dysfunctions of contractility were not detected. On X-ray examination of lungs: lung tissue without focal and infiltrative changes, pneumofibrosis. On oesophagogastroduodenoscopy: reflux-oesophagitis and erosive antral gastritis.

Clinical diagnosis

Main disease — chronic primary Sjogren's syndrome (arthralgia, dry rhinitis, xerobronchitis, lung involvement, anemia). Concomitant diseases: arterial hypertension. Urolithiasis. Chronic pyelonephritis. Erosive antral gastritis.

In the hospital, the patient underwent glucocorticoid therapy (prednisone — 5 mg, 2 tablets in the morning, metipred — 250 mg), antihypertensive (moxonidine — 0.2 mg, 1 tablet once a day, metoprolol — 25 mg, 1 tablet 2 times a day, fosinopril — 10 mg in the morning), gastroprotective (omeprozole — 20 mg, 1 tab per night), antiproteolytic (aprotinine — 10 thousand units), antibacterial (norfloxacin — 400 mg, 1 tab. 2 times a day), anti-osteopenic therapy (Ca²⁺+D³ — 1 tablet per day).

Discussion

The concordant cases of Sjögren's syndrome in identical twins suggest the genetic determination of the disease. But, recently a discordant case of congenital heart block was described in twins begot from a mother with anti-Ro-positive Sjogren's syndrome, which witness for some role of epigenetic factors also [7]. Early diagnosis of the disease and initiation of immunosuppressive therapy in this patient prevented the serious complications. The effect of treatment was clearly visible with cancellation of the basic therapy for the patients for almost 6 years, after which the general condition worsened, and a joint pain developed. Long-term therapy with small doses of alkylating cytostatics and glucocorticosteroids positively affects systemic manifestations of the disease, and significantly improves the survival of patients. The presence of complications caused by glucocorticosteroid therapy should be taken into account. In this case it may cause gastric ulcers and

disorders of adrenocortical function, which requires regular examination and prescription of the appropriate treatment.

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