Clinical and epidemiological features of complex approaches in the treatment of osteoporosis in systemic scleroderma

Tuychiyev Sardor Azamatovich

Karshi State University, Faculty of Medicine
e-mail:tuychiyev_9292@gmail.ru
+998908765007

ABSTRACT

Systemic sclerodermia is a disease of the connective tissue with an unknown etiology, clinical manifestations of heterogeneity and chronic progressive disease. It is based on 3 pathological processes: vasculopathy, cellular and humoral autoimmune conditions and progressive visceral and vascular fibrosis in many organs. In the United States alone, there are between 9 and 19 cases of disease per 1 million people.

According to the National Osteoporosis Foundation (NOF), in the United States in 2010 more than 10 million adults age 50 years and older had osteoporosis and more than 43 million had low bone mineral density (BMD). In the United States in 2015, as many as 2 million Medicare beneficiaries sustained 2.3 million osteoporotic fractures. Within 12 months of experiencing a new osteoporotic fracture, approximately 15% of patients suffered one or more subsequent fractures and nearly 20% died. Mortality was highest in those with hip fracture, with 30% dying within 12 months.

Keywords: Systemic scleroderma (SS), diffuse systemic scleroderma (DSS), limited systemic scleroderma (LSS), gastric antral, anemia.

Systemic scleroderma is an autoimmune inflammation of connective tissue of unknown etiology, with heterogeneous clinical course and often progressive, which is fibrosis of the skin and internal organs and vascular damage (vasculopathy). [14,15]

Systemic scleroderma is a decrease in the synthesis and accumulation of collagen in the connective tissue of the skin (scleroderma) and other internal organs, especially the lungs, gastrointestinal tract (gastrointestinal), heart and kidneys. In the early stages of the disease is manifested in combination with obvious signs of inflammation. Over time, patients show signs of developing structural and production of blood production and internal organs due to fibrosis. In addition, patients suffering from pulmonary fibrosis, arterial pulmonary hypertension, heart failure, and especially malnutrition, depression, osteoporosis, late-stage treatment failure [10]

Systemic scleroderma is sporadically prevalent worldwide and present in all races. Every year in Uzbekistan, more than a thousand people face 9-19 new cases. Systemic scleroderma rates in the United Kingdom, Australia, and Japan are lower than in the United States. [15,16]

Systemic scleroderma, like other connective tissue diseases, is more common in women, especially during childbirth and after menopause. [5]

According to a study conducted in Poland, 3653 out of 9049 first-time visitors to the hospital in 4 years were diagnosed with systemic scleroderma. Their average age is 53 years, 84% women and 16% men. [14]

This means 1.9 cases per 100,000 population per year, and the most observed age is 55 years.

A cohort study in Uzbekistan also found that out of 185 systemic scleroderma patients from 16 medical centers, 167 were women and 18 were men.

For unknown reasons, systemic scleroderma is as common in women as systemic disease of other connective tissue. [5]

Clinical signs - Systemic scleroderma affects almost every organ. It is divided into 2 subgroups due to the high variability of clinical signs. [12]

Japanese scientists emphasize that Limited systemic scleroderma and Diffuse systemic scleroderma are separate diseases and do not pass each other during their development. However, they have a number of common symptoms, including endothelial cell dysfunction, Th2-dominant immune activation, and the development of excess fibrous tissue in the skin. [5,8]

Limited Systemic scleroderma often persists with Raynaud's syndrome. Diffuse systemic scleroderma, of course, is accompanied by damage to internal organs. Systemic scleroderma Limited form occurs at all ages (20-50). According to the study, it is 0.4-2.7 per 100,000 individuals and the ratio of females to males is 2.4-4.2: 1, respectively. The diffuse form of SD develops at the age of 35-55 years and rarely in children and in boys under 35 years of age. A limited form of systemic scleroderma is also common in young people. [9]

The initial clinical signs are very different in these two forms. In patients with diffuse systemic scleroderma, the interval between Raynaud's phenomenon and other clinical signs is usually short (from weeks to months). [4]

In the early edematous inflammatory phase of diffuse systemic scleroderma, the fingers, the distal parts of the limbs, and the face are first affected. Edematosis is a phase of fibrosis within the inflammatory phase, in which the ability to sweat is reduced by induration of the skin, hair loss in the body, and a decrease in the production of sebaceous glands in the skin. [8]

In the first 4 years, the risk of systemic damage, kidney and lung injury is very high. The development of cardiac injury and isolated pulmonary artery hypertension in patients is 10-15%. [7]

There are three cardinal signs in systemic scleroderma: vasculopathy, cellular and humoral autoimmune processes, and vascular and visceral fibrosis in many organs. Autoimmune processes and vascular disorders appear earlier. [13]

The clinical manifestations of systemic scleroderma are mainly due to damage to the vascular endothelium by immune cells. Circulating CD4 + T cells have high levels of chemokine receptors and alpha 1 -integrin adhesion molecules and the ability of these cells to bind to vascular endothelium and fibroblasts. [14]

Antibodies produced by B cells that provide humoral immunity work against antinuclear and intracellular proteins, as well as antigens or proteins on the cell surface. These antibodies increase blood titers with disease activation. Multiple antibodies show anti-single-stranded DNA, anti-histone, and anti-topoisomerase II alpha antibodies in limited scleroderma. These antibodies are found in very small amounts in systemic scleroderma. In the general form of systemic scleroderma, anti-topoisomerase I antibody, antisentromer antibody and anti-RNA polymerase III antibody are detected. [6,8]

A study in France found that 133 SSD patients were tested for RNA-P III and 6-9% of these patients were diagnosed. The prevalence of anti-RNA-P III in this population is highly variable (0-41%). The overall prevalence of anti-RNA-P III was 11%. But heterogeneity was high in the studies. Geographical factors partially explain this heterogeneity. Other primary systemic scleroderma indications were significantly associated with anti-RNA-P III proliferation. [8]

According to Kagort's research and meta-analysis, the prevalence of anti-RNA polymerase-III antibody in patients with systemic scleroderma depends on geographical, genetic background, and environmental factors. However, the nature of heterogeneity remains largely unclear. [10,]

Some scientists believe that LSD is a systemic scleroderma disease associated with skin injury. Although LSD is a rare disease, TSD is present in approximately 4% of cases. In contrast, others do not consider LSD Systemic scleroderma to be a skin injury. Because systemic scleroderma and LSD progression are not the same. [9]

However, a study in Japan found that patients diagnosed with systemic scleroderma were

followed for 5 years. During this period, LSD symptoms appeared before or after a patient, and autoantibodies associated with systemic scleroderma were detected in almost all patients. This confirms that LSD is a skin injury form of systemic scleroderma. [5]

In the pathogenesis of the development of dermal fibrosis in SD patients, the transition of endothelial tissue to mesenchymal tissue occurs. As a result, endothelial dysfunction and dermal fibrosis develop.

In systemic scleroderma, Reynaud's syndrome occurs in 99% to 100% of cases in the form of LSD and systemic scleroderma. Raynaud's syndrome In patients with systemic scleroderma, episodic vasoconstriction of the blood vessels of the fingers and toes, as well as in the ear and nose. Cold exposure, hypothermia, emotional stress, and vibration are triggers for this syndrome. [12]

Reynaud's syndrome affects 3-5% of the general population, and the majority of this figure is in women. Primary and secondary forms of Raynaud's syndrome are secondary to systemic scleroderma and other connective tissue diseases, hematological, endocrine, and occupational diseases, as well as to drug-related beta-blockers and anticancer drugs. [11]

In the pathogenesis of Raynaud's syndrome, the balance in the functioning of several mechanisms (nerve, vascular, mediators and the immune system) is disturbed. In its pathogenesis, reperfusion, free oxygen radicals, as well as ischemia develop. Antibodies to the antioxidant enzyme are detected in the blood of patients with systemic scleroderma. [9]

IgG and IgM anticardiolipin (aCL), IgG and IgM anti-beta-2-glycoprotein-I (ab2GPI) antibodies Systemic scleroderma is higher in patients. [12]

Gastro-antral vascular ectosis in systemic sclerosis Gastric antral vascular ectasia (Gastric antral vascular ectasia-GAVE) also continues to be difficult to diagnose and treat. GAVE can be associated with a variety of disease groups: cirrhosis, chronic renal failure, and autoimmune connective tissue disease. [9]

Anemia and telangiectasia may be the first striking manifestations of systemic sclerosis. Renal artery stenosis, aortic stenosis, widespread skin and mucosal teleinjection, and hypertension are associated with a poor prognosis and require prompt intervention and careful monitoring. [4]

In the diagnosis of systemic scleroderma, laboratory tests are usually of relative diagnostic importance. Anti-Scl-70 (specificity 81-98%, sensitivity 28-70%), antisentromer antibody (positive result-60-90%) and anti-nuclear antibody (40-90% in patients) considered specific for SSD. [2, 8] Morphological examinations (skin, synovial membrane and muscle, fibrous tissue and vascular biopsies) play a key role in the diagnosis of the disease. [4] Positive anti-citrulline peptide antibody (ACPA) increases the risk of developing erosive arthritis, pulmonary fibrosis, esophageal injury, and diffuse changes in the skin. ACPA is found in 9.2% of patients with systemic scleroderma. Met-analyzes suggest that ACPA detection should be included in the screening plan to assess disease progression. [8] To determine the importance of the primary method as a prognostic factor in systemic sclerosis, data were collected in the Spanish Scleroderma Register (RESCLE), a national-scale retrospective multicenter database created in 2006. Raynaud’s phenomenon (RP), skin sclerosis, arthralgia / arthritis, pulmonary artery disease, interstitial lung disease (ILD), pulmonary arterial hypertension (PAH), and gastric hypomotorism were taken as the first symptom. A total of 1625 patients were admitted. One thousand three hundred and forty-two patients (83%) with RP as the first sign, and 283 patients (17%) did not show this. The survival time of patients who present as the first symptom of RP is higher than that of patients with SSD who present as the first symptom of other symptoms. 97% and 90% were 5 years old, 93% and 82% were 10 years old, 83% and 62% were 20 years old, and children aged 71 to 50 years were 30 years old ($p < 0.001$). According to the analysis, the factors associated with death were age, male sex, dcSSc type, ILD (interstitial lung disesea), PAH (pulmonary arterial hypertension), sclerodermic renal crisis, the process did not begin with heart and Raynaud's phenomenon, in particular, injuries to the arms of the lungs or the lungs were also included. It was also found that the prognosis was worse in cases not associated with Reynaud's syndrome in the early stages. [5]

Meta-analysis of the effect of vitamin D deficiency on the prognosis of systemic

scleroderma concluded that a decrease in the amount of vitamin D in the body in the diffuse form does not affect the acceleration of the disease. [11]

Systemic scleroderma shows a higher mortality rate than the general population (SMR = 2.72). Total survival from diagnosis was estimated at 74.9% in 5 years and 62.5% in 10 years. Stomach involvement is the leading cause of death. [13]

If patients with systemic scleroderma have pulmonary artery hypertension, their life expectancy is 3 years. [6]

Treatment of systemic scleroderma is currently carried out depending on its pathogenesis.

- Immunosuppressants against autoimmune process
- Anti-fibrotic therapy
- Drugs are selected depending on the vascular therapy and the affected organs.

In cases where systemic scleroderma comes with Raynaud's syndrome, the following medications are recommended based on meta-analyzes. Calcium channel blockers, prostanoids, tadalafil and bosentan received the highest recommended levels in terms of their effectiveness. including Class A for nifedipine, nicardipine, kinnapril, IV iloprost, bosentan, tadalafil, and MQx-503; B grade for beraprost, cicaprost, DMSO, cyclophenyl, and atorvastatin; C-level drugs for misoprostol, prazosin, OPC-2826, enalapril, sildenafil, antioxidant, and stanazolol were tested and obtained these levels. [3]

References

1. Antonelli A, Ferri C, Fallahi P, Cazzato M, Ferrari SM, Sebastiani M/Clinical and subclinical autoimmune thyroid disorders in systemic sclerosis//Eur J Endocrinol - 2007. Vol.156- P.431–437
2. Akesson A, Fiori G, Krieg T, van den Hoogen FHJ, Seibold JR/Assessment of skin, joint, tendon and muscle involvement//Clin Exp Rheumatol-2003. Vol.29-P.5–8
3. Atteritano M, Sorbara S, Bagnato G, Miceli G, Sangari D, Morgante S/Bone mineral density, bone turnover markers and fractures in patients with systemic sclerosis//a case control study.-2015. PLoS One
4. Avouac J, Koumakis E, Toth E, Meunier M, Maury E, Kahan A/Increased risk of osteoporosis and fracture in women with systemic sclerosis: a comparative study with rheumatoid arthritis//Arthritis Care Res (Hoboken)-2012.Vol.64-P.1871–1878
5. Arnson Y, Amital H, Agmon-Levin N, Alon D, Sa´nchez-Casta-n˜o´nM,Lo´pez-Hoyos M/Serum 25-OH vitamin D concentrations are linked with various clinical aspects in patients with systemic sclerosis// a retrospective cohort study and review of the literature. Autoimmun Rev - 2011.Vol.10-P.490–494
6. Antico A, Tampoia M, Tozzoli R, Bizzaro N/Can supplementation with vitamin D reduce the risk or modify the course of autoimmune diseases//A systematic review of the literature. Autoimm Rev-2012.Vol.12-P.127–136
7. Agmon-Levin N, Theodor E, Segal RM, Shoenfeld Y/Vitamin D in systemic and organspecific autoimmune diseases//Clin Rev Allergy Immunol-2013.Vol.45-P.256–266
8. Amital H, Szekanecz Z, Szucs G/Serum concentrations of 25-OH vitamin D in patients with systemic lupus erythematosus (SLE) are inversely related to disease activity: is it time to routinely supplement patients with SLEwith vitaminD//Ann Rheum Dis-2010.Vol.69-P.1155–1157
9. Arnson Y, Amital H, Agmon-Levin N/Serum 25-OH vitamin D concentrations are linked with various clinical aspects in patients with systemic sclerosis//a retrospective cohort study and review of the literature. Autoimmun Rev-2011.Vol.10-P.490–494
10. Atteritano M, Sorbara S, Bagnato G/Bone mineral density, bone turnover markers and fractures in patients with systemic sclerosis: a case control study//PLoS One-2013. 8:e66991Corrado
11. Artaza JN, Norris KC/Vitamin D reduces the expression of collagen and key profibrotic factors by inducing an antifibrotic phenotype in mesenchymal

multipotent cells//J Endocrinol-2009.Vol.200-P.207–221
12. Avouac J, Koumakis E, Toth E / Increased risk of osteoporosis and fracture in women with systemic sclerosis // a comparative study with rheumatoid arthritis. Arthritis Care Res (Hoboken)-2012.Vol.64-P.1871–1878.
13. Atteritano M, Sorbara S, Bagnato G / Bone mineral density, bone turnover markers and fractures in patients with systemic sclerosis: a case control study // PLoS ONE8,-2013.
14. Al-Dhaher FF, Pope JE, Ouimet JM / Determinants of morbidity and mortality of systemic sclerosis in Canada // Semin Arthritis Rheum-2010.Vol.39-P.269-277.
15. Asano Y, Sato H // Vasculopathy in scleroderma // Seminars in Immunopathology-2015.Vol.35-P.489–500.
16. Asano Y, / Epigenetic suppression of Fli1, a potential predisposing factor in the pathogenesis of systemic sclerosis // International Journal of Biochemistry &Cell Biology-2015.Vol.67-P.86–91.