Chapter 6
Mood Problems and Depression in Systemic Sclerosis

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Introduction

Systemic sclerosis (SSc) is a severe disease with skin and internal organ fibrosis. A progressive course, complications, functional limitations, multiple visits to the clinic, hospitalizations, an uncertain prognosis often lead to mood disorders, such as depression and anxiety. Pain, chronicity, compromised physical health, disfigurement, limited treatment options, and disability negatively affect Health Related Quality of Life (HRQoL) [1]. Mood disorders and depression may overlap with SSc.

Depression is characterized as sad mood, loss of interest or pleasure, feelings of guilt, low self-esteem, poor concentration, disturbed sleep and/or appetite, loss of energy, and psychomotor dysfunction for more than 2 weeks [2]. A diagnosis of depression is based on patient interview, documented use of antidepressants or psychiatric consultation.

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The relative risk of depression in SSc patients is 3.3–6.9 [3]; depression comprised 73.2% and anxiety 23.9% of all mood disorders in SSc [4]. About 18.1% of SSc patients hospitalizations were due to depression and about 4.4% to psychosis [5]. SSc patients have a higher incidence of depression than patients with other rheumatic diseases [6–8]. SSc was an independent risk factor for depression [9]. SSc patients may develop adjustment disorders (dysthymia or alexithymia), or a mild, moderate or major depressive disorder (MDD). Mild depression was reported in 36–69%, moderate in 20%, MDD in 5% of patients [10–12]. Lifetime MDD was reported in 22.9%, current MDD (30 days) in 3.8% and 12 months MDD in 10.7% of patients; MDD is associated with low vitality and suicidal ideation [13, 14]. Depression correlated with poor indexes of FACIT-Fatigue score, Health Assessment Questionnaire-Disability Index, and Center for Epidemiologic Studies Depression. Patients with SSc have a reduced capacity to perform previous duties, they are absent from work, lose social position and income [15]. Depression correlated with all case mortality in SSc patients [9]. Depression and psychosis increased the risk of in-hospital mortality among SSc patients [5].

Anxiety is an exaggerated reaction to stress, pain, disability, and uncertainty, presenting with fear, anger, or panic disorder; it often complements depression [16]. The prevalence of anxiety is 35–80% [1, 10, 17, 18]. Patients fear SSc complications, assessments, hospitalization, limited number of specialists specializing in scleroderma, SSc progress, disfigurement, disability and early death [19].

We report on a severe case of MDD. A 42-year-old female school teacher was diagnosed with SSc and myositis 3 years ago. She presented with Raynaud's phenomenon, arthralgia, muscle weakness, dyspepsia, digital ulcers, interstitial lung disease, diffuse skin thickening (DcSSc), severe interstitial cystitis which required self-catheterizations, elevated creatine

kinase levels and positive anti-topoisomerase antibodies. The patient was treated with corticosteroids, omeprazole, iloprost, mycophenolate mofetil, elatrol, and intravenous immunoglobulins. She was strongly supported by family members but developed a reduced mood, disturbed sleep and feelings of guilt. Serial psychological interventions, occupational and physical therapy were started; pregabalin was added by a psychiatrist. Later, the patient was admitted for MDD with suicidal ideation; escitalopram and brotizolam were started; pregabalin was changed to duloxetine. Gradually, her condition improved; on her last visit to the clinic, she was physically and mentally stable. *One may learn, that early diagnosis of depression, recruitment of psychologist and psychiatrist, organizing of "supporting circle" could help in stabilization of patient's mental health*.

Contributory Factors Related to Mood Disorders

Pains and pruritus significantly contribute to depression; 75% of patients reported pain; pain impairs sleep, induces fatigue, functional limitation, and disability. *Sleep disorders* aggravate depression, pain, and vice versa [20, 21]; 76% of SSc patients have sleep disturbances [22]. Dyspnea, fatigue, digestive problems, digital ulcers, pruritus, and depression have a major influence on sleep [21, 23–25]. *Fatigue* is described as persistent exhaustion, inability to perform, and a need to invest additional effort; 89% of SSc patients reported fatigue [23]. Fatigue is associated with digestive and respiratory problems, pain, depression, impaired coping capacity, and reduced HRQoL [26–28]. Fatigue in SSc patients was significantly worse than in cancer patients in remission, and was compatible with cancer patients on active treatment [29]. The negative effect of fatigue progresses with life-time [30].

Scleroderma-Related Features and Mood Disorders

Hand stiffness, Raynaud's phenomenon, digital ulcers, early SSc, DcSSc, dyspnea, reflux, fecal incontinence, malnutrition, renal crisis, sexual dysfunction, and urinary tract abnormalities are associated with depression and/or anxiety [11, 31–37]. Disfigurement with facial and hand changes and telangiectasia correlated with depression, anxiety, and impaired HRQoL [12, 16, 27, 38–40]. Low Appearance Self-Esteem score in SSc patients correlated with depression, anxiety and disability [19].

Possible Pathogenic Mechanisms of Mood Disorders in SSc

Inability of the immune system may lead to insufficient physical and psychological defense mechanisms; long-lasting psychological and physical distress predisposes to mood disorders. Possible mechanisms for the development of depression were proposed: dysfunction of microvasculature in central nervous system [41], impaired cortisol response to stress [42], dysregulation of serotonin synthesis [43], and excessive production of Interleukin-1, Tumor Necrosis Factor-alpha and Interleukin-6; their levels correlate with active inflammation and fibrosis and induce fatigue and sleep disturbances in patients with inflammatory diseases and correlated with depression.

Patients' Perspectives

A patient's perception of SSc has a major impact on mental scores [44]; patients with "illness identity" had reduced functional capacity and ineffective coping with scleroderma [45]. Patients wish to participate in support groups with emphasis on education, including family members, information on centers specializing in SSc [46]; 78.6% indicated "education"

as a major need with an accent on information about SSc, medications, alternative medicine, relaxing strategies and exercise programs, coping with pain, fatigue, stress and changes in appearance, information on social services, disability and prognosis.

Patients' associations are helpful in providing balanced information and sharing coping styles, such as "think positive"; media and the internet can be additional channels to learn about scleroderma [47].

Case 2. A 34-year-old patient has suffered from scleroderma for 4 years; her main problems include skin involvement, digital ulcers, esophageal reflux, and mild interstitial lung disease. The patient was very anxious about her pulmonary condition; in recent months, she arrived at the emergency room several times with severe attacks of cough and dyspnea. Repeated imaging, respiratory function, and oxygen saturation tests showed no worsening of lung condition. In repeated conversations it became clear that the patient had been suffering from esophageal reflux with probable micro-aspirations. She had received a detailed explanation from a rheumatologist, had been evaluated by a gastroenterologist. A detailed explanation of eating arrangements, prevention of food before lying down, lifting of a pillow, conversation with clinical psychologists, and acupuncture treatment resulted in an improvement in respiratory condition. *Symptoms of SSc and anxiety may overlap; patient' education and advices how to manage disease complication may help to both, scleroderma and mood disorder.*

How to Provide Better Health Care to SSc Patients with Mood Disorders

Severe emotional distress in early DcSSc or exhaustion in long-standing disease leads to cognitive impairment, poor compliance with treatment, loss of interest and energy, and progression to MDD; psychosis and delirium are rare in scleroderma. It is crucial to diagnose mood disorders early.

The approach to SSc patients includes proper attention to mood disorders, building a relationship with the patient on the basis of deep empathy and trust, providing available access for help, construction of "supportive circle" with family members and care-providers, and simultaneous treatment of scleroderma symptoms and mood disorders. Physicians should make an effort to understand the patient's feeling to indicate the problem. Detailed anamnesis should include the patient's description of symptoms (pains, pruritus, sleep quality, fatigue, and organ specific problems), family history of autoimmune and mental diseases, smoking, alcohol, and drugs. Compliance with medications and probable adverse events need to be checked. Functional disability, mouth and hand handicap, disfigurement, disability, social aspects (input, role in the family and society, meetings, pleasure) should be appreciated; it is useful to meet family members and informal care-givers. Identification of mood disorder, especially moderate and severe depression, is an indication to assessment by psychologist and psychiatrist and prescription of medications (selective serotonin reuptake inhibitors, selective serotonin and norepinephrine reuptake inhibitors, pregabalin). Treatment of mood disorders should include psychological support, providing the way to "positive" thinking, behavior therapy aimed at restoring a positive attitude, helping in understanding the situation, learning to adapt demands and expectations to new conditions, priorities, and construction problem-solving plans. Patients should be taught how to avoid stressing or challenging situations and how to balance between functioning and disease, how to cope with Raynaud's phenomenon and digital ulcers, how to prevent cough and aspiration caused by reflux, how to keep joint range of movement and muscle strength. Patients need an explanation on the importance of regular blood tests and cardiac and pulmonary assessments, measurement of blood pressure and weight, and treatments options; they need to be sensitive to changes in their body and soul. Providing online support by a nurse, psychologist and the treating rheumatologist with problem-oriented and real-life information is of great importance.

Case 3. A 35-year-old woman developed progressive SSc with joint contractures and digital ucers. She had pain, itching, evere fatigue and could not sleep. Difficulties at work and at home made her sad. We advised her to stop working and adjust activities to her new situation. She was treated with cyclophosphamide, bosentan, and abatacept; there was gradual improvement of skin and joints condition and digital ulcers. In addition, she was putted on multidisciplinary program with contemporary care by nurse, psychologist, occupational therapist and "drama-therapy". Patient' high motivation and "positive attitude", family and care-providers support were fruitful: after 2 years of fighting, she could return to half-time work and some of her regular activities, including social gatherings and trips abroad. During her last visit to the department, she said, "I learned to accept my illness with dignity, to give it a place in my life, I do not like my illness, but I think it changed me and gave me strength to be an another person. I did not realized, how strong I could be!". *It is very important to recruit patient' positive attitude and teach to choose the right priorities and to look for positive side in every situation, be motivated and try to bring life back to normal. Multidisciplinary approach can certainly provide an answer.*

Conclusion

Patients with SSc often have mood disorders; they correlate with more severe skin and joint problems, functional limitation, and disability. SSc is characterized by a variety of organ involvement with a diverse course and severe prognosis; absence of radical treatment makes patients insecure and hopeless. Dyspnea, Raynaud's phenomenon, pain, fatigue, sleep disturbances, gastro-intestinal tract dysmotility and disfigurement induce impaired patients' HRQoL. Mental disorders often run subtle and underdiagnosed; patients with scleroderma receive less or late treatment in this regard. Mood disorders aggravate SSc symptoms, cause poor disease perception and compliance, social isolation and work disabil-

ity; they have an adverse effect on treatment outcomes and survival of patients with SSc. Building of a multidisciplinary team in centers specializing in the treatment of SSc are of great importance in physicians' and patients' perspectives; they provide advanced support which includes a spectrum of physicians' sub-specialties (rheumatologists, pulmonologists, cardiologists, gastroenterologists, etc.) and health-care providers (nurses, psychologist, occupational therapists, physiotherapists, etc.). Empathic relationships between the patient and treating team, accessebility and personalized care are the best way to achieve patients trust and compliance. Use of various formats for patients' education, such as formal lectures, patients' meetings or support groups; media and on-line facilities will provide better eligibility of information, understanding of SSc features, and treatment modalities. Recruitment of a psychologist and social worker to a multidisciplinary team will contribute to the early recognition of mood disorders and treatment with a positive effect on a feeling of secure, improved compliance, better coping with SSc, and improvement in HRQoL.

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