Advances in Pharmacology and Therapeutics Journal
Shahid Sadoughi University of Medical Sciences, Yazd, Iran

SHAHID SADOUGHI UNIVERSITY OF MEDICAL SCIENCES

Case study

A Limited Systemic Scleroderma Patient with Social Behavior Change and Role of Gut Microbiome: a Case Report

Running Title: Systemic Scleroderma and Gut Microbiome

Reza Bidaki[1], Mahsa Motamed[2], Sina Taherzadeh Boroujeni[3], Narjes Sadat Farizani Gohari[4], Maryam Sadeh[5*]

[1]MD, Professor of Psychiatry Department, Research Center of Addiction and Behavioral Sciences, School of Medicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
[2]MD, Resident of Psychiatry, Department of Psychiatry, Tehran University of Medical Sciences, Tehran, Iran.
[3]MD, Psychiatrist, Department of Psychiatry, Tehran University of Medical Sciences, Tehran, Iran.
[4]Student Research Committee, Faculty of Medicine, Yazd University of Medical Sciences, Yazd, Iran, Interest Group of Corona Virus 2019 (IGCV-19), Universal Scientific Education and Research Network (USERN), Yazd, Iran, USERN Office, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.
[5]Assistant Professor of Bacteriology, Department of Laboratory Sciences, School of Paramedicine, Shahid Sadoughi University of Medical Sciences, Yazd, Iran.

ARTICLEINFO

Received: 05/15/2022

Accepted: 07/19/2022

Corresponding author
Department of Laboratory Sciences, School of Paramedicine, Emam Reza complex, Daneshjoo Blvd, Yazd, Iran.
Postal Code: 8916188635
Tel/Fax: 0098-9132527679/0098-3536238561
E-mail
sadeh_m20@yahoo.com

Abstract

The role of the gut microbiome in influencing immune function and homeostasis is being investigated. A 56-years-old female patient was referred due to nightmares, insomnia, pain, and redness in all her fingers. At first, Zolpidem was prescribed by a psychiatrist, but it induced a stuffy nose, change in behavior, drugged feeling, and tiredness. Previously she had been referred to a rheumatologist, and after some visits, atypical scleroderma had been diagnosed. She received psychiatric treatment with quetiapine and melatonin and was prescribed a probiotic diet. The patient was followed up and showed an excellent therapeutic response after augmentation with diet therapy. The treatment based on gut or fecal microbiome transplantation (FMT) may affect the patient's behavior and sleep disturbance. Thus the key point is the role of gut microbiota and FMT-based therapy in chronic rheumatic patients with resistance and refractory psychiatric symptoms, which improves the quality of life and acceptance of treatment.

Keywords: Systemic sclerosis, Gastrointestinal involvement, Gut microbiome, Immune system

Citation: Bidaki R, Motamed M, Taherzadeh Boroujeni S, Farizani Gohari N, Sadeh M. A Limited Systemic Scleroderma Patient with Social Behavior Change and Role of Gut Microbiome; a Case Report. Adv Pharmacol Ther J. 2022;2(1): 14-18.

Introduction

Systemic sclerosis (SSc) is an autoimmune disease. The role of the gut microbiome in influencing immune function and homeostasis is being investigated. Therefore, microbiome changes in inflammation and fibrosis in SSc are possible (1). Depression is a common psychiatric manifestation in SSc (2). Some studies assert that patients with SSc with gastrointestinal involvement (GI) usually show a more severe disease than the patients without GI involvement. In this case, SSc patients with GI involvement may experience more psychological disturbances, in which the Gut microbiome plays a significant role (3, 4). Subsequently, SSC patients with GI experience lower social functioning and less well-being (4). Considering the therapeutic effect of commensal microorganisms in this disease (5), it was raised whether the use of pre/probiotic supplementation (Lactobacillus and Bifidobacterium) can also affect sleep and depression of patients. However, a decrease in beneficial microbial populations (genera of Faecalibacterium, Clostridium, and Bacteroides) and an increase in pathobionts such as (Fusobacterium, Prevotella, Erwinia) in SSC patients have been identified, and research has been done on how gut microbiome changes can be effective in causing fibrosis, inflammation, and clinical disease in SSc patients (6). Therefore, interventional studies with diet modification, use of pro/ pre-biotic supplements, and fecal microbiome transplantation (FMT) to change the gut microbiome are recommended to evaluate the recovery process in SSc patients. Some studies have shown that gut microbiota can affect disease progression, response to treatment, and prognosis (6). The relationship among gut microbiome, scleroderma, psychiatric disorders, and medications is shown in **Figure 1**. Therefore, the question arises whether the role of the gut microbiome is effective in the occurrence of depression, behavioral and sleep-related disorders, and adverse responses to Zolpidem? Here, it was presented a patient who experienced a chronic stage of atypical SSc with only hand involvement (**Figure 2, 3**); the patient also suffered from psychiatric disorders which were not initially managed and caused the patient not to respond adequately to common chronic disease medications.

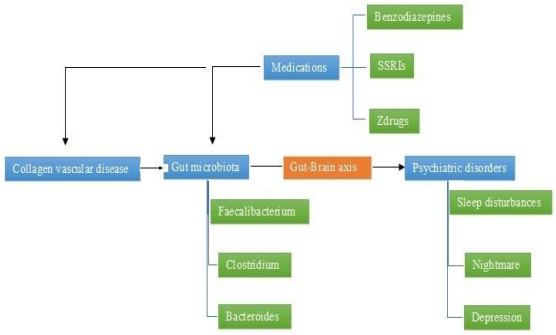

Figure 1. The relationship between gut microbiome, scleroderma, psychiatric disorders and medications

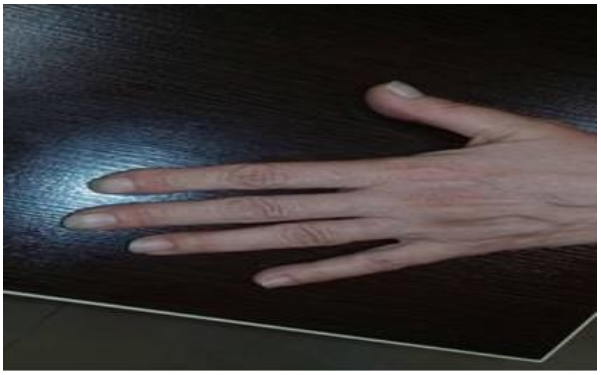

Figure 2. Atypical, limited scleroderma, dorsum the patient's hand

 DOI: https://doi.org/10.18502/aptj.v2i1.10653

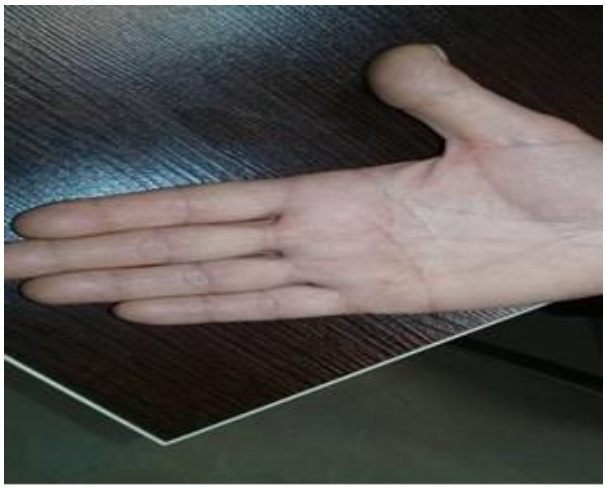

Figure 3. Atypical, limited scleroderma, palm region

Case report

The right-handed, married, 56-years-old female patient was referred to clinc Imam Ali (Yazd, Iran) with a history of pain and redness in whole fingers (**Figure 2, 3**) since 11 years ago; she still had nightmares and insomnia since two years ago. She had also suffered from uncontrollable hand and leg tremors (postural tremors) and restlessness at night for the past two years. In the past, the patient was diagnosed with mild anxiety and no depression, but after the illness, a behavior change became apparent, and she became socially isolated. The drugs and medications prescribed are listed in **Table 1**. There was no history of movement disorders. She also complained about recent hyperphagia and was obsessed with weight gain and obesity. No lung, cardiovascular system, or skin involvement was reported. she was previously referred to a rheumatologist, and after some visits, she was diagnosed with atypical scleroderma. She was prescribed anti-inflammatory treatments and finally referred to a psychiatrist due to a lack of acceptable therapeutic response, especially despite the anxiety and sleep disorders based on The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, Text Revision (DSM-5-TR), nightmares, and severe pain. The patient had low libido for a long time. At first, Zolpidem induced a stuffy nose, change in behavior, drugged feeling, and tiredness; the patient discontinued the tab. Nortriptyline because of constipation. She was in menopause with no history of hypothyroidism, sleep apnoea, or other medical conditions; no past personal and family psychiatric history of her were reported. She was treated psychiatrically with nortriptyline and quetiapine along with psychotherapy. But she had no suitable therapeutic response. After a probiotic diet prescription, she was followed up and showed a significant therapeutic response to insomnia, anxiety, and quality of life.

TABLE 1. The drugs and medications prescribed for the patient in various durations

	Dosage
Ropixon	10 mg or 5 mg daily
Angiopars	2 capsules after meals and usage of cream twice a day
Tab. Methotrexate	3 to 4 tabs (each 2.5 mg) once a day
Folic acid	1 mg daily
Methylprednisolone	40 mg IM monthly
Magnesium	4 mg is the maximum daily dose
Selenium	60 µg (0.75 µmol) daily
Tab.Trazodone	50 mg at night
Tab. Nortriptyline	25 mg at night
Tab. Melatonin	3 mg/ sublingual at night
Tab. Zolpidem	5 mg at night worsened REM behavioral sleep disorder (RSBD)
Tab. Quetiapine	25 mg improved the patient's sleep disorder

Discussion

Psychiatric disorders are commonly comorbid with chronic organic diseases such as mucocutaneous and rheumatoid (7). Psychiatric comorbidity can decrease the patient's quality of life and cause non-efficient treatment responses (2). Although it is misdiagnosed, selective serotonin reuptake inhibitors (SSRIs) can improve itching, Raynaud's phenomenon, and depression in Scleroderma patients (8). As SSRIs effect on inflammation, these medications can improve depression and scleroderma if the depression is inflammatory (9). Since the SSc can involve the esophagus and intestine, affecting the gastrointestinal function and peristaltic movements may affect the gut microbiome, therefore, this condition may affect sleep (10). A systematic review reported that Zolpidem is an effective therapeutic agent for sleep disturbance, but complex behavior change rarely accured (11). Because the serum concentration of Zolpidem is higher in women, side effects are more common. Poly pharmacy is other factor for this phenomenon (11).

Suitable psychopharmacotherapy about depression and insomnia caused improvement in drug compliance and quality of life in these patients. There are hypotheses that depression is considered as an inflammatory disease. The question is whether the nature of depression in inflammatory diseases is different from other diseases or major depressive disorder. Besides, considering that the gut microbiome plays a key role in social behavior, treatment based on the gut microbiome or fecal microbiome transplantation (FMT) may cause a change in the patient's behavior (12). After a clinical interview and psychiatric education, the psychiatrist prescribed medication and the probiotic diet. The patient showed a good therapeutic response after follow-up. Therefore, it seems that a teamwork among rheumatologists, psychiatrists, nutritionists, and gastroenterologists can play a key role in these patients' therapeutic response and increasing quality of life.

Conclusion

Since systemic sclerosis (SSc) is an autoimmune disease, and gut microbiota influences the immune system, it is recommended caution in prescribing drugs, especially Z drugs and benzodiazepines, for these patients. Some medications may cause behavioral changes that physicians should consider. Furthermore, evaluation of psychiatric disorders, especially depressive disorders and sleep problems are recommended. In addition, assessment of dietary status and gut microbiota is essential. Besides, treatment based on gut or fecal microbiome transplantation (FMT) may affect the patient's behavior.

Conflict of interests: The authors declare that they have no competing interests.

Funding: Not applicable

Acknowledgments: We would like to thank the patient for her cooperation in this study and for her consent.

 DOI: https://doi.org/10.18502/aptj.v2i1.10653

Ethical considerations: This manuscript is presented and accepted by the Ethical Committee of Shahid Sadoughi University of Medical Sciences. Its ethical code number is IR.SSU.REC.1400.155. The manuscript was published with written consent from the patient.

Authors' contributions: RB contributed to the conception and design of the work, visited the patient and its follow-up, and wrote the initial draft; MS and STB contributed to drafting the work; MM contributed to revising the draft and submitting it; NF revised the draft again.

References

1. Volkmann ER. Intestinal microbiome in scleroderma: recent progress. Curr Opin Rheumatol. 2017;29(6):553-60.
2. Mura G, Bhat KM, Pisano A, Licci G, Carta M. Psychiatric symptoms and quality of life in systemic sclerosis. Clin Pract Epidemiol Ment Health. 2012;8:30-5.
3. Patrone V, Puglisi E, Cardinali M, Schnitzler TS, Svegliati S, Festa A, et al. Gut microbiota profile in systemic sclerosis patients with and without clinical evidence of gastrointestinal involvement. Scientific Reports. 2017;7.
4. Volkmann ER, Hoffmann-Vold A-M, Chang Y-L, Jacobs JP, Tillisch K, Mayer EA, et al. Systemic Sclerosis Is Associated With Specific Alterations in Gastrointestinal Microbiota in Two Independent Cohorts. 2017;4(1):e000134.
5. Volkmann E, Chang Y, Barroso N, Furst D, Clements P, Tong M, et al. OP0213 Systemic Sclerosis is Associated with a Unique Colonic Microbial Consortium. 2015;74:151.
6. Bellocchi C, Volkmann ER. Update on the Gastrointestinal Microbiome in Systemic Sclerosis. Curr Rheumatol Rep. 2018;20(8):49.
7. Marrie RA, Hitchon CA, Walld R, Patten SB, Bolton JM, Sareen J, et al. Increased Burden of Psychiatric Disorders in Rheumatoid Arthritis. Arthritis Care Res (Hoboken). 2018;70(7):970-8.
8. Gayraud M. Raynaud's phenomenon. Joint Bone Spine. 2007;74(1):e1-8.
9. Dionisie V, Filip GA, Manea MC, Manea M, Riga S. The anti-inflammatory role of SSRI and SNRI in the treatment of depression: a review of human and rodent research studies. Inflammopharmacology. 2021;29(1):75-90.
10. Figueiredo FP, Aires GD, Nisihara R, Skare TL. Sleep Disturbance in Scleroderma. J Clin Rheumatol. 2020.
11. Inagaki, T., Miyaoka, T., Tsuji, S., Inami, Y., Nishida, A., & Horiguchi, J. (2010). Adverse reactions to Zolpidem: case reports and a review of the literature. Primary Care Companion to the Journal of Clinical Psychiatry, 12(6), PCC.09r00849. https://doi.org/10.4088/PCC.09r00849bro
12. Münger E, Montiel-Castro AJ, Langhans W, Pacheco-López G. Reciprocal Interactions Between Gut Microbiota and Host Social Behavior. Front Integr Neurosci. 2018;12:21-.