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CASE REPORT

The Improvement of Xerostomia and Reduction of Anxiety Score in a Patient with Generalized Anxiety Disorder and Recalcitrant Geographic Tongue: A Case Report and Literature Review

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Introduction: The incidence of post-pandemic psychiatric disorders has increased globally in recent decades. Generalized anxiety disorder (GAD) is one of the psychiatric disorders that are partially associated with emotional factors. It can affect the quantity and quality of saliva, present as xerostomia, and trigger the emergence of the geographic tongue (GT).

Purpose: This case report aims to discuss the management of xerostomia and geographic tongue in a patient with GAD.

Case: A 26-year-old male patient complained of dry and sore mouth for one month after taking medication from the psychiatry department, was diagnosed with GAD, and had already consumed the antidepressant sertraline. Extraoral examination showed dry and exfoliative lips. Intraoral examination showed white plaque with depapilation on the dorsal tongue, frothy saliva, buccal mucosa and dorsal tongue sticking to the dental mirror. The unstimulated salivary flow rate was <0.2 mL/min (sialometry method). The Depression, Anxiety, and Stress Scale-21 (DASS-21) questionnaire was used to estimate the psychological condition and showed an extremely severe level of anxiety (score = 13). The established oral diagnoses were GT with mild xerostomia and exfoliative cheilitis.

Case Management: For two months, patients received hyaluronic acid gel and mouthwash, as well as a non-pharmacological approach to healthy lifestyle counseling. There was an improvement in xerostomia, and the GT became asymptomatic, with a reduction of DASS score in this patient.

Conclusion: Improved psychological conditions will improve xerostomia, but the clinical appearance of the geographic tongue is more difficult to eliminate.

Keywords: anxiety, DASS-21, geographic tongue, salivary flow rate, xerostomia

Introduction

Coronavirus disease 2019 (COVID-19) has spread worldwide, leading to a global pandemic in recent decades.[1] The COVID-19 pandemic resulted not only in acute illnesses but also in long-term consequences. Most COVID-19 survivors still suffer from long-term psychological consequences such as poor sleep quality, anxiety, and depression one year after infection.[2] The prevalence of depression and anxiety in these post-COVID-19 patients was reported to range from 10.4% to 42%.[3] Generalized anxiety disorder (GAD), one of the most common anxiety disorders, is classified in the 5th edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) as chronic (lasting at least six months) excessive anxiety and worry about several events or activities that is difficult to control.[4] GAD is partially associated with emotional factors.[4,5] It can affect the quantity and quality of saliva, present as xerostomia, and trigger the emergence of the geographic tongue (GT).[6–8]

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Xerostomia is the sense of oral dryness, which may or may not be associated with a reduced salivary flow rate.[9–11] The prevalence of xerostomia varies from 10 to 63%.[10–12] Studies propose that psychological disorders and emotional instability may play a role in xerostomia.[8,13] Saliva is a complex physiological and biological fluid that maintains homeostasis of the oral cavity, oral mucosal health, and oral function.[8,14] The reduction in salivary flow rate and its qualitative alteration may lead to various clinical manifestations.[10,14] This can also produce functional manifestations such as impaired speech, chewing, and swallowing.[14]

Geographic tongue (GT), or Benign Migratory Glossitis (BMG), is an inflammatory disorder that is generally asymptomatic and commonly occurs on the dorsum of the tongue.[7,15] The prevalence of GT in general studies varies from 0.5% to 17.2%.[16] The etiology of GT remains unknown, but some patients have shown lesions associated with psychological and emotional factors as well as being significantly associated with anxiety.[15–17] Therefore, it is essential to understand the psychological factors that promote xerostomia and GT to address the underlying condition, alleviate symptoms, and prevent worsening that may reduce the patient's quality of life.

This report presents an improvement of xerostomia and a reduction of Depression, Anxiety, and Stress Scale (DASS) score in a patient with GAD and a recalcitrant GT. This case report aims to discuss the management of xerostomia and GT in a patient with GAD. The presence of uncontrolled psychological disorder and reduction in the DASS score affecting this patient's condition makes this report unique. This report also includes a review of some cases of xerostomia and GT associated with psychological conditions and treatment options.

Case Presentation

A 24-year-old male patient came to the Oral Medicine Clinic, Dental Hospital Universitas Padjadjaran, with the chief complaint of dry and sore mouth for one month after taking medication from the psychiatry department. He was diagnosed with GAD and had been taking a compounded antidepressant from a psychiatrist, namely sertraline 50mg, sulpiride 50mg, and clobazam 10mg. Since three days ago, the patient had stopped taking the drug because he felt his mouth was getting uncomfortable History of recurrent oral ulceration and allergies was denied. He brushed his teeth and tongue twice daily, every morning and night, before bed. He denied the habits of smoking and alcohol consumption.

The patient consulted the psychiatry department because he felt stressed and anxious since being infected with COVID-19 about six months ago. He underwent hemorrhoid surgery in the same year, which intensified his complaint. The patient frequently used internet-based search engines to look for information on his condition and disease, which caused him to feel uncontrollably anxious. The patient worked for a private company with a very high work target at one point. The patient felt quite depressed and unable to self-regulate his psychological condition. He had a poor diet, lacked sleep, and rarely exercised.

This study has received approval and written informed consent from the patient to publish data and images. This study complied with the Declaration of Helsinki. The institution has approved the publication of this study. The extraoral examination showed dry and exfoliative lips. The intraoral examination revealed a depapilation surrounded by a white plaque on the dorsum of the tongue, frothy saliva, and a dental mouth mirror sticking to the tongue and buccal mucosa. The Oral Hygiene Index Simplified (OHI-S) from Green and Vermillion was used as a clinical parameter for evaluating oral hygiene conditions.[18] The patient had plaque and stains in all regions of the teeth and calculus in some regions of the teeth, resulting in moderate oral hygiene with a score of 2.2.

The objective measurement of xerostomia can be done by assessing salivary flow rate (sialometry) or from the patient's clinical condition using the Clinical Oral Dryness Score (CODS).[11] The spitting method was used for salivary flow rate assessment in the unstimulated condition, collected between 8 to 11 am. Navazesh et al, stated that the subjects are required to fast, not smoke, not chew gum, and not perform any oral procedures at least one hour before the examination.[18,19] Saliva is allowed to accumulate on the floor of the mouth and the subject spits it out into the graduated test tube every 60 seconds, for 5 minutes, and is quantified volumetrically using the indicator on the test tube. The salivary flow rate was stated as mL/min (normal = 0.3 to 0.4 mL/min).[18,20–23] The patient's unstimulated salivary flow rate was obtained at 0.28 mL/min.

The objective assessment of xerostomia using CODS obtained a cumulative score of three, categorized as mild xerostomia. The Depression, Anxiety, and Stress Scale-21 items (DASS-21) questionnaire was used to estimate the

psychological condition and screen for common mental disorders.[24] The DASS-21 questionnaire showed an extremely severe level of anxiety (score = 13). Based on anamnesis and clinical examinations, the established oral diagnoses were GT with mild xerostomia and exfoliative cheilitis.

Case Management

Pharmacological and non-pharmacological therapies were conducted to manage this patient. Pharmacological therapy was 0.2% hyaluronic acid gel, 0.025% hyaluronic acid mouthwash, and petroleum jelly 100% given for two months. Oral hygiene instruction and healthy lifestyle counseling were given as non-pharmacological approaches. Oral hygiene instructions include brushing teeth and tongue twice daily, in the morning after breakfast and at night before bed. The patient was also instructed to consume small but frequent amounts of a minimum of 1.5 liters of water daily, eat a nutritionally balanced diet, get enough rest, and exercise regularly. Patients were also referred back to psychiatrists regarding complaints and management of the patient's GAD condition, however, he did not follow our instructions. He felt his mouth was getting uncomfortable due to the psychiatric medication.

The periodic treatment visits in this patient showed encouraging results at each control visit. This article reports three follow-up visits: two weeks after the first visit (first follow-up), four weeks after the second visit (second follow-up), and three months and ten days after the third visit (third follow-up). Figure 1 summarizes patient cases and treatments received at each visit.

At the first follow-up visit (two weeks after the first visit), the patient still had a sore tongue, and the oral cavity and lips were still dry. The patient has used the medication as instructed, the mouthwash has run out, and the gel medication remains in stock. The objective examination is shown in Figure 2A–E). There were dry and exfoliated lips, frothy saliva, dental mirror sticks on the buccal mucosa and dorsum of the tongue, and depapilation surrounded by a white plaque on the dorsum of the tongue. CODS and salivary flow rate as the supporting examinations can only be carried out at this visit. The CODS assessment resulted in a score of three, which is mild xerostomia, and the unstimulated salivary flow rate was 0.28 mL/min, which is hyposalivation. The DASS-21 questionnaire obtained a score of 29 with an anxiety score of 13, described as extremely severe anxiety.

After four weeks, the patient visited for a second follow-up. The patient felt that the appearance of islands on the tongue remained but with a reduced level of pain, however, the dryness of the lips and mouth had improved. The patient has used mouthwash and topical medication as instructed. The objective examination revealed depapilation surrounded by a white plaque on the dorsum of the tongue, as shown in Figure 3A–F). The CODS assessment resulted in a value of zero, which is normal, and the unstimulated salivary flow rate was 0.34 mL/min, which has reached normal values. The DASS-21 questionnaire obtained a score of 28 with an anxiety score of 10, described as severe anxiety.

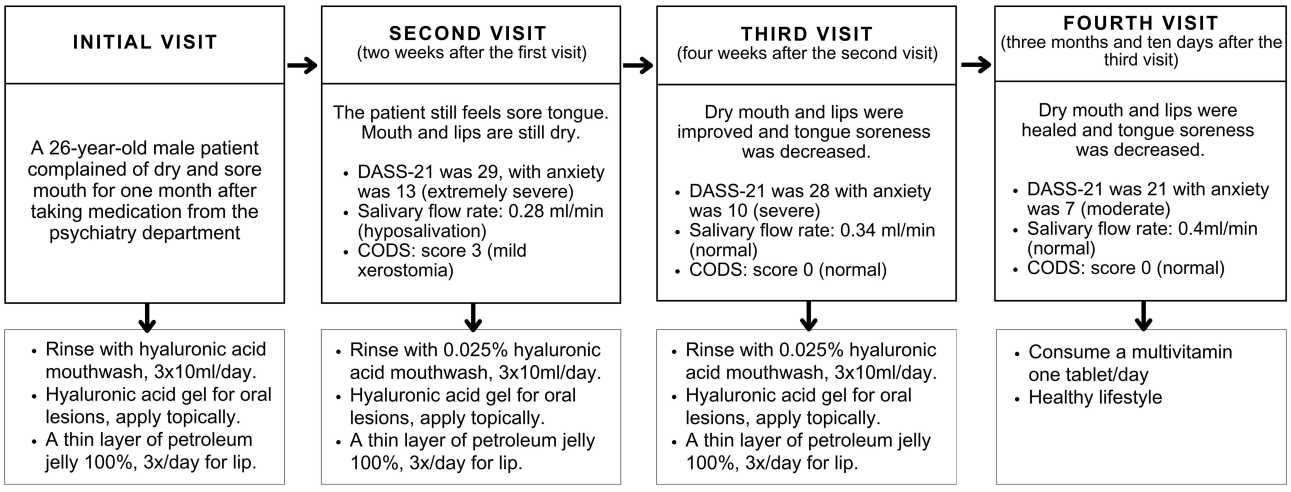

Figure 1 A summary of patient cases and treatments received at each visit.

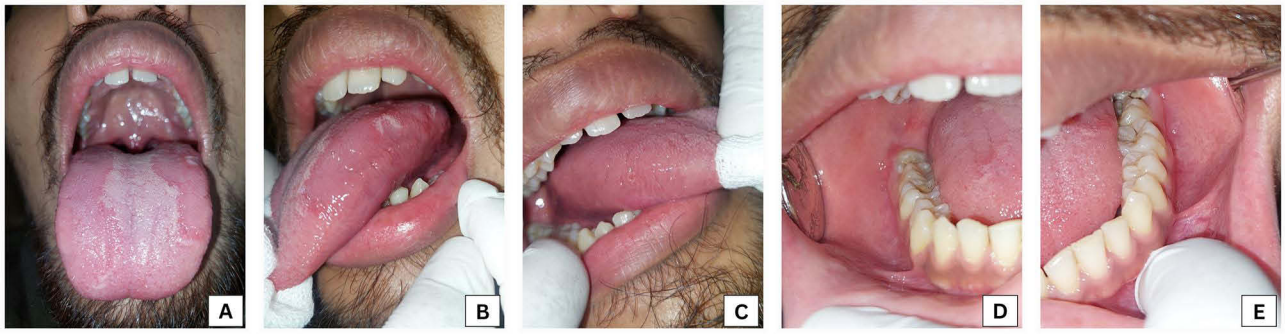

Figure 2 (**A**–**E**) The clinical appearance of intraoral condition on the second visit follow-up (two weeks after the first visit).

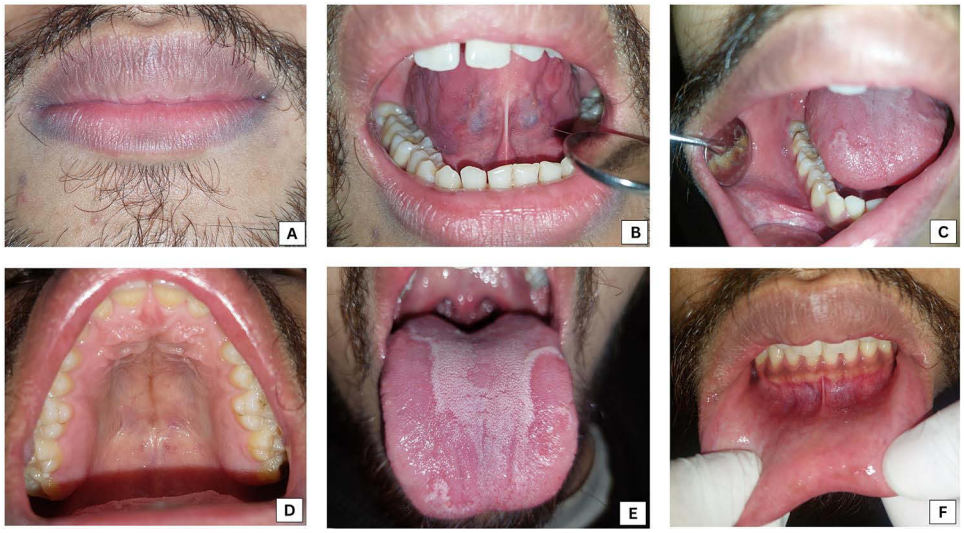

Figure 3 (**A**) shows dry lips; (**B**–**F**) The clinical appearance of intra-oral condition on the third visit follow-up (four weeks after the second visit).

After three months and ten days, the patient no longer complained of oral dryness, the CODS was decreased to zero, and the unstimulated salivary flow rate increased to more than 0.3 mL/min. There was an improvement in xerostomia, and the GT became asymptomatic, with a greater reduction of the DASS in this patient. The DASS questionnaire obtained a score of 7 for anxiety, described as moderate anxiety. Until this fourth visit, the patient had not visited a psychiatrist and did not continue taking antidepressant medication. DASS assessment in this patient showed favorable progress in reducing anxiety scores at every visit. Supplementary extra-oral and intra-oral documentation taken during the third follow-up visit (three months and ten days) is presented in Figure 4A–J). Furthermore, we educated the patients

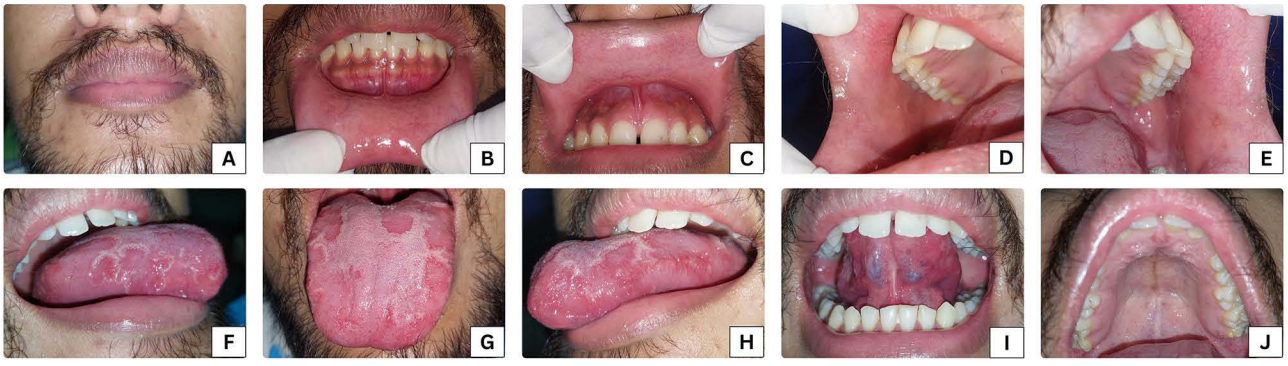

Figure 4 (**A**–**J**) The clinical appearance of extraoral and intraoral condition on the fourth visit follow-up (three months and ten days after the third visit).

to consume one tablet of multivitamins daily, maintain oral hygiene, maintain a healthy lifestyle, and consult a mental health expert about their psychological condition.

Discussion

Generalized anxiety disorder (GAD) is a medical condition that can cause substantial dysfunction affecting daily physical, psychological, and social functioning.[25] The patient complained of feeling very anxious when infected with COVID-19, which persisted for more than six months, so the patient decided to consult the psychiatry department and was diagnosed with GAD. Based on previous studies, SARS-CoV-2 penetrates the blood-brain barrier and can directly infect nerve tissue, leading to the development of neurological and psychiatric symptoms. At the same time, quarantine, social distancing, uncertainty about disease status, and socioeconomic losses can be risk factors for signs of mental disorders, in particular anxiety.[2,26,27]

Treatments for anxiety disorders might include psychological interventions, pharmacological interventions, or a combination of these modalities.[25,28–31] First-line psychopharmacologic treatments for adults with GAD are selective serotonin reuptake inhibitors (SSRIs) and selective norepinephrine reuptake inhibitors (SNRIs). Second-line treatments include buspirone, benzodiazepines, second-generation antipsychotics (SGAs), pregabalin, and tricyclic antidepressants (TCAs).[25,28–30] Several types of psychological treatments have been developed, such as cognitive behavioral therapies (CBT), psychodynamic therapies, non-directive supportive therapy, and spiritual therapy.[31] The commonly used psychotropic medications such as SSRIs, TCAs antidepressants, and benzodiazepines exhibit several oral manifestations. In addition, long-term use of these drugs seems to cause changes in the mouth.[13,32,33]

The patient received compound medication containing sertraline 50mg, sulpiride 50mg, and clobazam 10mg from the psychiatrist, and his anxiety was reduced. However, the patient complained of dry and sore mouth for one month after taking these drugs. These conditions are in line with a study about oral manifestation in patients diagnosed with psychiatric illness and under psychotropic medication. It has been reported that the majority of the oral manifestations including xerostomia (21.7%), sialorrhea (17.4%), GT (13.0%), periodontitis (10.9%), candidiasis (8.7%), and burning mouth syndrome (8.7%).[32,33]

Psychiatric disorders are characterized by physical and physiological changes originating partially from emotional factors.[8,33,34] It has the potential to influence the body, cause pathological changes or subjective symptoms in normal oral mucosa, and procreate the development and worsening of oral diseases.[33] The oral tissues are highly reactive to psychological influences. Psychological factors result in the alteration in the nervous system markers (catecholamines, adrenaline, noradrenaline, and dopamine); endocrine system markers (cortical and aldosterone); immune system (T cells, B cells, natural killer cells, and Immunoglobulin); vascular and muscular function, resulting in the initiation or pathogenesis of the oral disease. It can also lead to decreased salivation and dryness of oral mucosa.[8,33,34]

Xerostomia is a fairly common finding and is classified as "true" xerostomia when inadequate saliva is secreted due to abnormal salivary gland function; however, most xerostomia patients do not exhibit objective indications of hyposalivation. Oral dryness, despite normal salivary gland function, is referred to as "symptomati" or "pseudo" xerostomia. Despite normal salivary gland function, oral dryness is referred to as "symptomatic" or "pseudo" xerostomia.[35,36] Xerostomia in patients with mental illness may be related to psychological effects directly affecting salivation and the side effects of a wide variety of psychiatric medications.[8,37] More than 400 medications are estimated to affect the salivary gland function and lead to hyposalivation.[8] Xerostomia was seen among the patients who were under antipsychotics (80.0%), antidepressants (44.4%), benzodiazepine (1.1%), and SSRI (11.1%).[32] This statement explains that the patient in this case report was found to have a dry mouth, which may be related to his mental illness and the use of a single or polypharmacy of drugs.

The frequency of xerostomia in emotionally altered patients may be explained by a variety of neurophysiologic, neurochemical, and neurobiological changes associated with psychosocial disorders. Since the autonomic nervous system neurobiologically regulates salivary glands, processes influencing the levels of transmitter substances in this system affect salivary gland function. The alterations in cerebral blood flow and metabolism lead to the stimulation of lateral and paraventricular nuclei by the amygdala.[8] The result is autonomic arousal and increased plasma cortisol levels, leading to

altered salivary secretion and flow. Also, endocrinal changes like hyperactivity of the hypophysis pituitary adrenal axis result in increased the cortisol levels, which in turn have xerogenic effects.[8,37]

The patient was diagnosed with mild xerostomia along with exfoliative cheilitis. Diagnosis of xerostomia requires careful evaluation of signs and symptoms, with clinical extraoral and intraoral examinations, assessment of salivary gland function by measurement of resting and stimulated flow rates, and, in some cases, biopsy of minor salivary glands.[35,38] A review of the patient's medications, medical history, and social history are all needed to determine the underlying causes of dry mouth. After that, examining the entire oral cavity is an essential part of the assessment.[38]

The CODS has been developed and shown to be reliable and easy to use as a clinical sign for routine assessment of the severity of dry mouth (hyposalivation).[11,36,39] The CODS assessment consists of a 10-point scale, each point representing a feature of dryness in the mouth. The ten features are sticking of a dental mouth mirror to the tongue or buccal mucosa, foamy saliva, no or minimal salivary accumulation in the floor of the mouth, more than two cervical caries, mucosal debris on the oral palate, fissured or lobulated tongue, smoothed gingiva, loss of papillae of the dorsal tongue and glassy oral mucosa. Each feature has a score of one point, and the total is interpreted to reflect the approximate severity scale of oral dryness, ie, scores 1–3 are mild, 4–6 are moderate, and 7–10 are severe.[11,39] The CODS examination results in the patient, showed three abnormalities in clinical features. Therefore, the score was 3 (first visit) and continued to decrease with each visit until it reached zero at the last visit.

Another clinical method often employed for diagnosing salivary dysfunction is the sialometry test (salivary flow rate measurement). These are relatively easy to perform, reproducible, and quantitatively assess salivary production (objective measurement). The reduced flow rate of the saliva usually correlates with complaints of dryness.[35] Sialometry test measures the stimulated or unstimulated salivary flow rates, as well as parotid and palatal secretion. The normal stimulated salivary flow rate is 1.5 to 2.0 mL/min, while the normal unstimulated salivary flow rate is 0.3 to 0.4 mL/min.[11,38]

Establishing the correct diagnosis is considered the most crucial step in managing patients with xerostomia since it encompasses distinguishing patients with subjective complaints from those presenting salivary gland hypofunction. Once a diagnosis is established and an underlying etiology is identified, a stepwise management approach can be implemented to institute preventive measures, alleviate symptoms, treat oral manifestations, and improve salivary function.[36]

Preventative measures are crucial to managing xerostomia. Patients should be counseled on maintaining hydration with adequate water consumption, increasing humidity in the evening, avoiding crunchy, spicy, sour, or hard foods, and lifestyle modifications. Good oral hygiene is necessary to identify signs of xerostomia and prevent dental caries.[11,38] Specifically, diligent oral hygiene and regular dental care with examinations every 4–6 months are essential.[36] Medical management of the underlying disease may improve clinical manifestations. Discontinuing medications that cause dry mouth or replacing them with alternative medications should be considered if it is safe and necessary for the patient, which must be discussed with the psychiatrist.[38]

The clinical manifestations of xerostomia can be treated with systemic sialogogues and topical agents.[36,38,40,41] Topical medications are the first-line treatments recommended for xerostomia. These include chewing gums, saliva stimulants, and substitutes.[38,41] Sugar-free chewing gum can often stimulate salivary secretion and reduce friction on the oral mucosa.[35,38] Salivary stimulants and substitutes, such as toothpaste, mouthwashes, and gels, can help to increase salivary gland function. Saliva substitutes resemble natural saliva and increase its viscosity. Saliva substitutes commonly contain carboxymethylcellulose, xanthan gum, mucins, hydroxyethylcellulose, polyethylene oxide, or linseed oil. Other topical products containing xylitol, betaine, and olive oil have also been effective against medication-induced dry mouth.[35,36,38]

The United States Food and Drug Administration (US FDA) has approved two systemic agents for xerostomia: oral pilocarpine and cevimeline.[35,38,41] Their effect depends on the presence of functional glandular tissue. Oral pilocarpine is a parasympathomimetic medication with muscarinic action.[38,42] Other systemic sialogogues include bethanechol, anethole trithione, and yohimbine. Yohimbine, an α2-adrenoceptor antagonist, may be beneficial for xerostomia in people on psychiatric medicines, according to one small study.[35,38] Other reported treatments for xerostomia include acupuncture, lip trainer appliances, and intraoral electrostimulation.[38]

After more than three months, the patient no longer complained of oral dryness, decreased CODS score to zero, and increased unstimulated salivary flow rate of more than 3 mL/min, reaching normal values. Patients improved in the condition of xerostomia, along with a decrease in anxiety scores on the DASS-21 assessment. Considering the different functions of saliva in the oral cavity, any change in volume or composition can lead to malfunction. The results of Gholami et al showed that stress, depression, and anxiety have a significant relationship with unstimulated saliva flow rate and xerostomia. Previous studies applied the importance of applying the DASS-21 questionnaire in xerostomia patients. By using this reliable, brief, and comprehensive psychological scale, three different major psychological disorders (stress, anxiety, and depression) can be assessed simultaneously.[37]

The patient in this case report also had a complaint on his tongue, which was diagnosed by an oral medicine specialist as Geographic tongue (GT). The habit of the patient to search for information independently using the internet made him even more anxious, and he considered his GT to be a dangerous thing. Furthermore, the patient even suspected that his GT was an oral cancer. There is some information found in various internet-based sources that GT also referred to as Covid Tongue.[43] However, the GT in this patient was observed as a normal variation of the oral mucosa, which has no known cause but may triggered by a decrease in immunity.[7,15,44]

GT is characterized by migratory erythematous patches, representing atrophy of the filiform papillae that sometimes include raised whitish peripheral margins that recover spontaneously, resembling a map-like appearance.[7,15,44] It is a dynamic lesion that presents morphology changes, can heal spontaneously periodically and has a recurrent character in different moments. The lesion is often found in people with immunological disorders, inside the presence of stress and anxiety, and may be related to allergic conditions.[15] GT was also reported in patients receiving psychiatric medications and was the second most common oral manifestation seen in patients under SSRIs (66.7%) and TCAs (13.7%).[32]

The etiology of GT could not be established in our patient; he denied allergy to any medication or food. Various studies support the role of emotional stress as a causative agent in the development and exacerbation of GT. Alikhani et al, investigated the immunological and psychological factors in GT patients. They found high levels of tumor necrosis factor-alpha (TNF-α), IL6, salivary cortisol, and anxiety. Their studies revealed that levels of anxiety and cortisol were significantly higher in people with GT.[7] The GT is usually diagnosed based on its unique clinical features, so histopathological confirmation or biopsy is rarely needed.[39,45]

Since the etiology is unknown, no causal treatment strategy is available.[39] If GT is asymptomatic, no treatment is indicated, and patients should be provided information and reassurance.[39,45] It is important to emphasize that it is not a pathologic lesion but a morphologic variation of generally healthy mucosa.[39] Symptomatic GT lesions may be managed with topical anesthetics to obtain temporary relief. Other suggested treatment strategies include antihistamines, anxiolytic drugs, or steroids, but these have yet to be systematically evaluated.[39,45] The topical factors that exacerbate a patient's symptoms, such as hot, spicy, or acidic food and dried salty nuts, should be avoided.[46] GT may regress, but it is impossible to predict when and to which patient this will occur. The disease's prevalence diminishes with age, supporting spontaneous regression over time.[39] The patient in this case report received topical non-steroidal anti-inflammatory therapy in two dosage forms: gel and mouthwash. The administration of drugs in line with the patient's cooperation in carrying out the therapy given showed satisfactory results.

Patients with mental illness take various psychotropic medications, so it is crucial to understand their effects on managing their oral conditions. Most psychiatric medications cause adverse reactions that can affect the oral environment and trigger oral diseases. Therefore, dental practitioners must be aware of and carefully understand the potential oral health risks involved in treating psychiatric patients. Dental practitioners play a role in the management of oral manifestations of mental illness through routine examinations, early diagnosis, early intervention, multidisciplinary management, and prevention of the condition from getting worse.[32,33]

Mental health experts should also consider oral health as part of the patient assessment. Awareness among psychiatric specialists about oral changes associated with the use of psychotropic medication will assist them in making necessary modifications to the prescriptions. Dental practitioners and mental health experts often need collaboration to help improve the patient's condition.[32,33]

This case report has limitations due to short-term follow-up, whereas observation of oral diseases triggered by psychological conditions requires long-term monitoring. More cases with long-term follow-up are needed to observe further psychological conditions and their therapy affecting oral diseases such as xerostomia and GT.

Conclusion

Oral health is essential for patients with special needs, such as psychiatric patients. The results of the present report provide improvements in the psychological conditions that will improve xerostomia despite the clinical appearance of the GT being more challenging to eliminate. Oral manifestations in patients with mental illness can reduce the patient's quality of life, and the mental condition may even worsen due to anxiety in the presence of oral complaints. Multidisciplinary management is needed between mental health experts and dental practitioners to manage psychiatric patients with oral complaints. In the future, we need to explore the relationship between psychological disorders, their treatments, and oral health so that patients can efficiently obtain the most direct guidance and effective treatment.

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Disclosure

The authors declare no conflicts of interest in this work. The patients have approved and written informed consent for the publication of this case report, including the images, by prioritizing the confidentiality of patient identity. The institution has also approved the publication of this report. The drug formula we wrote about in the case management is the commercial preparation of Gengigel® gel and Gengigel® mouthwash. However, there is no conflict of interest.

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