



MULTIPLE ETIOLOGIES OF XEROSTOMIA IN AN HIV POSITIVE PATIENT: A CASE REPORT

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Abstract

Xerostomia is commonly reported as an oral complaint among dental patients. Many factors contribute to its presence, including medication use, chronic diseases, and psychogenic conditions. Strong association to extensive dental caries and oral infections has been discussed in several studies. Here we report a case of xerostomia related to various medical issues in a patient who was currently undergoing 6-month rehabilitation program. **Case Presentation:** A 45-year-old male patient with histories of multiple substance abuse, HIV positive, Hepatitis C, and schizoaffective disorder came with a chief complaint of excessive dry mouth in last two months. At clinical examination, poor oral hygiene with debris-coated on tongue, fissures in lip corners, little saliva amount, shiny oral mucosa, multiple carious lesions and missing teeth were revealed. Patient was given education how to maintain oral hygiene, asked to increase fluid intake, use 0.9% sodium chloride mouthwash every two hours daily, and scheduled weekly to receive dental treatments. **Discussion:** Proliferation HIV-infected CD8+ cells and infiltration of HCV to salivary glands, drug-induced vasoconstriction, and consuming numerous medications that inhibit salivary production are suspiciously associated to the occurrence of Xerostomia. **Conclusion:** Comprehensive treatment that requires teamwork between dentist, physicians, and patient is strongly needed to obtain good result.

Keywords: xerostomia, HIV, drug abuse

INTRODUCTION

Xerostomia can be defined as “dry mouth” condition.(A. Cherian & Jeftha, 2017) It is relatively distinct to hyposalivation since xerostomia is established only based on subjectivity of patient’s feeling, in contrast to hyposalivation evaluated objectively by using sialometry.(S. Article et al., 2011) However, both cannot be separated because xerostomia reflects the condition of low salivary flow rates, especially of unstimulated saliva.(Nittayananta et al., 2013)

As one of the most essential fluid in oral cavity, saliva plays numerous critical roles(Hugo et al., 2008), including coating and lubricating during mastication, swallowing, and speaking; maintaining moisture; removing residue and microbes; and providing innate immunity in oral cavity.(Nizamuddin et al., 2018; Turner, 2016) It is primarily secreted by three major glands (parotid, submandibular, and sublingual glands) and numerous minor glands with its activity is under controlled by autonomic nervous system (ANS) and normally produced between 800 and 1500 mL per day in healthy adults.(Putri et al., 2018)

The process of saliva production can be stimulated by two pathways: sympathetic input by adrenergic signaling and parasympathetic input by cholinergic signaling. Parasympathetic stimulation induces the release of high-flow, low protein serous fluids, while sympathetic stimulation leads to the release of low-flow, high protein

mucinous fluids.(Nizamuddin et al., 2018) Thus, the disruption of both pathways can decrease salivary production, leading to the occurrence of Xerostomia.

There are many factors contributing to Xerostomia among dental patients, mainly medication use in which its severity will be increased following the increasing of duration, number, and dosage; uncontrolled chronic diseases that pathologically attacks salivary gland cells, such as diabetes mellitus, hepatitis, and immunodeficiencies; and psychogenic conditions.(S. Article et al., 2011) Delayed to identify xerostomia in patients with these conditions may rise other oral complaint, such as halitosis, dysgeusia, burning sensation, difficulty in mastication and speech, extensive dental caries, and infections. As a consequence, the quality of life may be reduced.(Nizamuddin et al., 2018; Veerabhadrapa et al., 2016)

Here we report a challenging case of xerostomia predisposed by various medical issues in a patient who was currently undergoing drug rehabilitation program.

CASE REPORT

A 45-year-old male patient who was currently undergoing 6-month inward rehabilitation program came to dental clinic in Drug Rehabilitation Center, National Narcotics Board, Republic of Indonesia, with a chief complaint of excessive dry mouth resulting discomforts in eating and cracks at both corner of lips. Some questions were asked verbally to describe more detailed about his complaint. (Table 1.)

Items	Answer (Yes/No)
Do you feel dryness in your mouth?	Yes
Do you feel dryness in your throat?	Yes
Do you feel dryness in your lips?	Yes
Do you feel dryness in your tongue?	Yes
Do you feel difficult to speak due to dryness?	No
Do you feel difficult to swallow due to dryness?	Yes
Do you feel thirsty throughout the day?	Yes

Table 1. Questions related to oral dryness

The history of smoking cigarettes, drinking alcoholic beverages, and multiple drug dependency has been reported from the assessment by physician. The drug dependency was started from heroin with sharing needles for 1 year, cannabis for 2

years, and methamphetamine for 5 years. Oral dryness had been noticed when methamphetamines was still being consumed routinely six months ago, but it gradually increased during these two months.

	5 months before visiting dentist	4 months before visiting dentist	2 weeks before visiting dentist
Absolute CD4	554	514	347
Absolute CD8	871	734	528
CD4:CD8 ratio	0.64 ↓	0.7	0.66 ↓

Table 2. CD4 count, CD8 count, and CD4:CD8 ratio

From the anamnesis, multiple systemic diseases have also been revealed, including HIV, Schizoaffective disorder, and Hepatitis C. The diagnosis of HIV was established four years ago and Tenofovir and Lamivudine, as Antiretroviral Therapy (ART), were prescribed by internist once daily. Before visiting dentist, CD4 and CD8

counts, as well as Hemoglobin (Hb), Erythrocyte (Er), Hematocrit (Hct), were reported slightly decreased. The ratio of CD4:CD8, as well as ALT, were also unstably normal (Table 2. and 3.). Cotrimoxazole 960 mg was also added once daily due to suspicion to bacterial infection.

	4 months before visiting dentist	3 months before visiting dentist	A month before visiting dentist
Hemoglobin (Hb)	13.5 g% ↓	12.8 g% ↓	13.3 g% ↓
Leukocyte	5000 /m ³	5400 /m ³	4900 /m ³
Erythrocyte (Er)	4,37 mil/mm ³ ↓	4.08 mil/mm ³ ↓	4.36 mil/mm ³ ↓
Erythrocyte Sedimentation Rate (ESR)	10 mm/hr	6 mm/hr	5 mm/hr
Hematocrit	36 % ↓	35 % ↓	39 % ↓
Thrombocyte	192000 /mm ³	217000 /mm ³	179000 /mm ³
AST	34 U/L	58 U/L	38 U/L
ALT	46 U/L	66 U/L ↓	27 U/L
HBsAg	Non-reactive	-	-
Anti-HCV	Reactive	-	-

Table 3. Blood Test Results

The diagnosis of Schizoaffective disorder was established by psychiatrist according to psychosis symptoms he experienced, including difficulty in concentrating, feeling unhappy and guilty, hearing small voices, becoming more emotional, tendency to act aggressive, and sleep deprivation. Various psychiatric drugs (Risperidone 4 mg, Divalproex sodium 250 mg, Escitalopram oxalate 10 mg, and Clozapine 25 mg) had been given daily in the last five months. Hepatitis C was known from blood test result a month after and HP Pro (Fructus Schisandra 7.5 mg) was given twice a day.

Extraoral examination highlighted tenderness in right parotid gland and cervical

lymph nodes, desquamation and hyperpigmentation on upper and lower lips, and fissures at both corner of lips. Intraoral examination revealed poor oral hygiene with great amount of calculus and stain on the lingual area of mandibular teeth, localized attrition, multiple carious and missing teeth. The oral mucosa was generally shiny and sticky. The tongue was extremely dry and some debris were seen on middle part of dorsum area. The macroscopic salivary qualitative examination was only showed from the thick consistency of saliva since there was limited equipment available in dental clinic.



Figure 1. The Oral Condition

The condition of Xerostomia was concluded based on anamnesis, clinical and additional examinations. For treatment, the patient was given basic education about oral health maintenance, including how to brush teeth properly, the impact of multiple drug dependency to oral health, and the relation between chronic diseases and its manifestation in oral cavity. He was also asked to use 0.9% sodium chloride mouthwash every two hours per day, increase fluid intake up to 10 glass a day, and advised to stop smoking cigarettes and drinking alcoholic beverages. To recover his teeth condition, he was scheduled every week to dental clinic to obtain various dental treatments, including dental scaling, teeth fillings, and teeth extractions during his rehabilitation period so the oral health status could be improved.

DISCUSSION

In the present case, several factors that contribute to the appearance of xerostomia in this client were identified: multiple drug dependences, numerous medications used to psychogenic condition, HIV, and Hepatitis C.

Xerostomia is known as a popular oral complaint among drugs dependent population. This complaint becomes more distressing after taking drugs more often with gradual dosage. A study in USA revealed that of 459 users in Los Angeles, MA users were 4.4 times more likely to report having too little saliva, 7.2 times experiencing dry mouth, and 3 times having altered taste. In this case, the patient has been used MA for five years and it became more routine in the last six months, simultaneously to when the complaint of dry mouth was noticed. Many possible mechanisms can be considered to MA-induced xerostomia. As sympathomimetic amines, MA is able to stimulate the sympathetic nervous system, inhibitory α_2 -adrenoreceptors in salivatory nuclei, and α -adrenoreceptors within the salivary gland vasculature to make vasoconstriction and all these lead to reduction of salivary flow and amount. Besides that, the elevation of metabolism and increase in physical activity induced by MA contributes to the occurrence of dehydration. PACAP (pituitary adenylate cyclase-activating polypeptide)-DBI (diazepam-binding inhibitor) pathway in salivary glands can also be activated by MA withdrawal

stress, resulting the inhibition of salivary secretion.(Sun et al., 2018)

Numerous medications prescribed six months ago to control his psychogenic condition are also considered to be factors that induces xerostomia. Risperidone and Clozapine are both antipsychotics used for schizophrenia. Based on its inhibiting effect on dopamine, antipsychotic is divided into two groups: typical and atypical. Typical antipsychotic is given to obtain strong inhibiting effects on dopamine D₁- and D₂-receptors. Atypical antipsychotic is to exert less robust, selective dopamine D₂-combined with serotonin 5HT₂-receptors blockade. Unfortunately, the antagonist effects on secretion of both drugs inhibits muscarinic M₃ and alpha 1 adrenergic receptor, two essentials receptors to receive stimuli in salivary glands, so the reduction of parasympathetically- and sympathetically-stimulated flow cannot be abandoned.(R. Article, 2018) In addition, escitalopram and divalproex sodium that had similar effects on saliva was also given. Divalproex sodium is an anti-epileptic drug indicated to patients with manic episodes associated to bipolar disorder. It marks saliva amount by reducing excitability of salivary gland nerves by inhibiting sodium ions inflow.(Wolff et al., 2017) Escitalopram that belongs to a group of antidepressant is used to treat his major depressive episodes. Thus, dry mouth caused by inhibition in selective 5-HT reuptake occurs as one of common side effects, resulting saliva reduction.(Polychroniou et al., 2018)

Xerostomia was also common among HIV positive patients. It can be seen from the estimation that varies between 1.2% and 40%

in different study groups and geographic locations.(Mortazavi et al., 2014) The perception was mostly related to minor palatal glands secretion rate, suggested that xerostomia is perceived when mucosal wetting is insufficient. Another study considers that this subjective oral dryness might be resulted from salivary gland hypofunction.(Nittayananta et al., 2013) It occurs as side effects of medication as well as the proliferation of CD8⁺ cells in the major salivary glands, particularly parotid glands. Therefore, in HIV positive patient, salivary gland hypertrophy is often found as its compensative reaction.(Mortazavi et al., 2014) Besides that, some HAART also cause dry mouth as their adverse effect, including Didanosine (DDI), Emtricitabine (FTC), Lamivudine (3TC), Nevirapine (NVP), Indinavir (IDV), and Ritonavir (RTV).(A. P. Cherian, 2014) In this case, the patient was consumed Tenofovir and Lamivudine since the diagnosis of HIV has been made five years ago. Lamivudine synthetically derived from cytosine is usually used as part of combination therapy. Although minor adverse effects have been reported in >30% of patients, including diarrhea, malaise, migraine, hair loss, nausea, lipodystrophy, and xerostomia, but this relationship is still difficult to be found.(Dios & Scully, 2002)

Xerostomia in patients with chronic Hepatitis C ranges from 10 to 20%.(Ramos-Casals et al., 2001) There are various mechanisms that may contribute to the reduced salivary flow rate, including direct infection and proliferation of HCV in salivary gland, molecular mimicry between HCV and salivary glands, and formation of immune complexes containing HCV.(Ramos-Casals

et al., 2001) Some treatment of HCV, particularly interferon and ribavirin, were also reported to have oral side effects, including gingival swelling, periodontitis, dental caries, cheilitis, altered taste, oral lichen planus, and dry mouth.(Ramos-Casals et al., 2001) However, in this case, the patient has not received these therapy since the diagnosis of HCV infection was established, so the association between both of them can be neglected.

From above, we can conclude that two most prominent factors that contributes to xerostomia in this HIV positive patient are methamphetamine and numerous psychogenic medications use. Several strategies can be done to recover xerostomia with the basic principal are to reduce patient's complaints and/or increase salivary flow rate, with or without medication. Therapy with medication is by using mucosal lubricant, saliva substitutes, or saliva stimulant. Therapy without medication includes giving suggestions to increase hydration, avoid using mouthwash or toothpaste containing irritative agents, and chew non-sugar gums.(Villa et al., 2015) In this case, suggestions to use 0.9% sodium chloride mouthwash every 2 hours, increase fluid intake, stop smoking cigarettes and drinking alcoholic beverages was done to reduce his discomfort. Sodium chloride functions as mucosal lubricant as well as enable to increase pH balance temporarily in oral cavity. Avoidance using mouthwash or toothpaste and chewing non-sugar gums could not be done since he was still undertaking rehabilitation program. Education about basic dental knowledge and dental treatments are also necessary to

receive because to have good oral hygiene behaviors is more important determinants of xerostomia than blaming the type of illicit drug used.(Clague et al., 2017)

CONCLUSION

The occurrence of xerostomia in HIV positive patient can be predisposing by various factors. Comprehensive treatment that requires teamwork between dentist, physicians, and patient is strongly needed to obtain good result and increase the quality of life.

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