CASE REPORT

Recurrent Intraoral Herpes Simplex Infection Exacerbated by Cytomegalovirus and Toxoplasma With Under-weight Condition: A Case Report

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ABSTRACT

Oral ulcer has many etiological factors, the most common are infections, condition related to the immune system, traumatic or neoplastic. A 23-year-old woman complained of sore throat and painful in swallowing accompanied by poor diet causing weight loss of 2-3 kg since a month ago. Body Mass Index (BMI) examination showed under-weight. Intraorally there were irregular multiple ulcers surrounded by halo-erythematous, varying in size, yellowish base, 1-2 mm depth on the soft palate to the tonsils. Laboratory examinations showed positive anti-HSV-1 IgG, reactive anti-CMV IgG, reactive anti-Toxoplasma IgG, increased ESR, and non-reactive HIV. The diagnosis was recurrent intraoral herpes simplex infection aggravated by the presence of cytomegalovirus, toxoplasma, and under-weight condition. The treatment including pharmacological therapies and non-pharmacological therapies and referring to internal medicine and nutritionist. The oral ulcers improved in eight weeks. Cytomegalovirus (CMV), toxoplasma, and under-weight condition can worsen and delaying the healing of recurrent intraoral herpes ulcers.

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INTRODUCTION

Oral ulcerative lesions have many underlying etiological factors. One of the trigger factors that often appear is infection, especially herpes simplex virus-1 (HSV-1). HSV-1 infection is transmitted by contact with saliva of infected person. Globally, the prevalence of HSV infection in the human population is 40-80% and those under 50 years of age was 67%. (1)

There are three clinical manifestations of HSV-1 infection in oral cavity including herpes labialis infection, primary herpetic stomatitis, and recurrent intra-oral herpes ulceration. HSV-1 infection can recur at varying locations, interval, and duration, take longer time to heal. HSV infection patients react confirmed by the rise of IgG and IgM antibodies. However, only IgG is typically found throughout the HSV reactivation process. Serological testing for recurrent oral infections may use serum IgG examination.(1,2)

The prevalence of Citomegalovirus (CMV) in adults is between 60% and 70% in developed countries and almost 100% in developing countries. Of all herpes viruses, CMV has the largest number of genes dedicated to evading innate and adaptive immunity in the host. CMV represents a lifelong burden of antigenic T cell surveillance and immune dysfunction. Clinical manifestation in oral cavity of CMV mimiking lession of HSV-1 infection. The opportunistic organism Toxoplasma gondii has become a global concern due to its impact on public health and socioeconomics, infecting a variety of immune cells and using them to migrate and infiltrate the brain, where it employs various strategies to overcome the complex cellular structure of the blood-brain barrier.(3) Nutritional Conditions like under-weight or over-weight is a known risk factor for metabolic and endocrine disorders. Recent research shows that decreased food intake also result in reduced immune function and increase risk of infection. Nutritional Conditions like under-weight or over-weight

can affect delay healing in HSV-1 infaction in oral cavity. (4) The purpose of this case report is to describe the factors that can cause an HSV-1 infection in the oral cavity to recover more slowly than it should.

CASE REPORT

A 23-year-old women complaining of canker sores in her throat since one month ago, accompanied by discomfort when eating and swallowing which led to weight loss of 2-3 kg for a month. The patient had a history of recurrent canker sores for seven years, which was reccurent frequently and delyed wound healing. Canker sores got worse, especially during on first pregnancy until giving birth about seven months ago and using injectable birth control since six months ago, since then menstruation has become irregular. Canker sores were not preceded by fever, cough or runny nose, occurred in different locations, but now in the throat. She had a poor eating habit, didn't like eating rice, vegetables and doesn't eat enough fruit she prefer snacks, fried foods and fast food. A history of injuries to other bodies including genitals and food and drug allergies were denied. History of systemic disease also denied.

An analysis of BMI revealed underweight (12.67 kg/m2). Additionally, we performed a Complete Blood Count (CBC), and the results came within normal limits. Intraorally there were multiple irregular ulcers surrounded by halo-erythematous, varying in size, yellowish base, 1-2 mm depth on the soft palate until the tonsils. The laboratory result showed in Table I. The diagnosis was recurrent intraoral herpes simplex infection with co-infection of cytomegalovirus, toxoplasma, and under-weight condition. We perform toxoplasma tests since the patient has three cats at home and there is evidence in the literature that toxoplasma infections can impair the immune system.

The patient received non-pharmacological therapy including instructions to avoiding spicy, hot and spicy foods, had to drink at least eight glasses of water a day, enough rest and avoiding possible trigger factors as well as eliminating predisposing factors, one of which is the possibility of nutritional deficiency to reduce recurrence. Pharmacological therapy including 500 mg systemic valacyclovir twice a day, a 10 ml compounded mouthwash consists of 25 mg diphenhydramine HCl, 500 mg sulphate, 100 ml of magnesium hidroxyda susp which were dissolved in 50 ml distilled water for one minute gargling and then swallow it three times a day to coat the oral mucosa can reduce pain during the patients daily eating and replaced it with 0.025% hyaluronic acid to aid in healing, however the next visit resulted in severe pain, therefore it was replaced with tetracycline mouthwash diluted in distilled water. Complaints improved, and 0.025% hyaluronic acid was administered to aid the healing process. In addition, we recommend taking a multivitamin once every day.

Table I : Serologi Examinations - Result of serological test on first visit and after ten days

Examination	First Visit	Second Visit	Unit	Normal
IgG HSV 1	120,4	105,6	AU/mL Reactive	<20 negative, 20-25 borderline, >25 positive
Anti CMV IgG	>250	>250	AU/mL Reactive	Normal < 6
ESR	-	29	mm/ H	Normal < 20
Anti-toxo-plasma IgG	-	11,8	IU/mL	Non-reactive <1.6, Gray zone 1.6 - <3, >=3 reactive

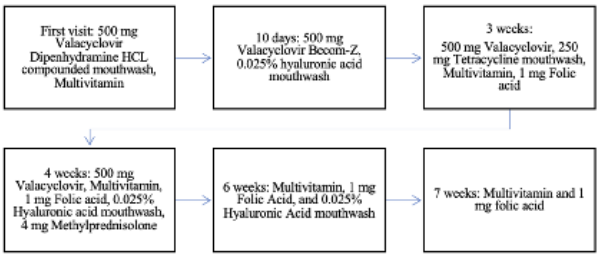

Fig. 1: The flow of therapeutic changes given to the patient.

Fig. 2: Intraoral lesion of the oropharynx. (A) first visit the lesions appeared to be inflammed (B) Follow up ten days: The lesions still pain (C) Three weeks later: the lesion began to improve but still hurts when eating (D) Follow up four weeks: the lesions spreading, inflammed and painful (E) Six weeks later with methylprednisolone therapy, the inflammation reduced (F) Seven weeks later: no more complaints.

Ten days later the cancer sore still remain accompanied by pain in the area around the right ear and the lesion seemed inflammatory we do Visual Analoq Scale (VAS) to meassured pain score and the result is eight. Three weeks later, the lesions began to improve, but she still experienced pain when eating. She was referred to the internal medicine policlinic for TB and HIV screening to seek for linked systemic disorders, and the results were negative. Four weeks later, the lesions did not show any significant changes, she still complaining about the pain and referred her to a nutritionist and was advised to increase consumption of high protein foods such as eggs, fish and beans, we added priscribeing methylprednisolone. After six weeks, the complaints of pain had already subsided VAS is five, the patient was asked to taking multivitamins, folic acid, and

methylprednisolone was stop. The next visit (one week later), there was a significant improvement, no pain anymore and no new lesions were found, but scar tissue was seen at the tonsils VAS is two. The therapy showed at Fig. 1.

DISCUSSION

Herpes simplex virus types 1 and 2 (HSV-1) are members of the human herpes virus family. Both viruses produce similar ulcerations, although HSV-1 is more common on the oral mucosa. In healthy people, intraoral recurrence consists of minimal ulceration of the attached gingiva and palate.(2)

Cytomegalovirus (CMV) is another member of the human herpesvirus family. Oral manifestations are relatively uncommon. This non-specific ulceration occurs in immunocompromised patients and most usually affects the tongue, floor of the mouth, and palate. CMV ulcers can last longer from weeks to months. Good hydration and dietary modifications are required.(5)

Toxoplasma gondii is an obligate intracellular parasite found worldwide in warm-blooded species, including humans, with a varying incidence based on climatic circumstances, being more abundant in tropical locations than in cold or dry areas. Infection can occur by ingesting tissue cysts present in uncooked meat or oocysts that contaminate water or food and that come from a definitive host environment, such as cats releasing their feces. T. gondii can attenuate CD4-mediated immune responses through inhibition of MHC II transactivator, contributing to its long-term survival in the brain.(3)

The diagnosis of HSV-1 is made based on anamnesis and clinical picture so we add supportive examination like anti HSV IgG for HSV-1. We suspected another infection due to the location of the lesion and we dug deeper due to the slow healing process.We carry out further examinations to look for possible involvement of systemic diseases that can hinder the healing process, So we ask the patient for more examination like CMV, toxoplasma because the patient has cats as a pet that are probably the source of toxoplasma, and TB because the patient has underweight condition and a history of TB when she was younger.

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Nutrients play an important role in the optimal regulation of the immune response in sufficient concentrations for immune cells and for tissue repairing and regeneration. The immune system has the ability to build up an effective defence against infections. Chronic inflammation can be avoided by taking nutrients derived from food, that might have a significant impact on providing an immune response.

In our bodies, macrophages are antigen presenting cells (APCs) and can be found in the bloodstream and tissues. It has the ability to phagocytize and create various inflammatory mediators and plays a key role in the immune response. Consumption of proteins containing L-arginine can produce genes responsible for the inhibition and stimulation of macrophages whose capacity to maintain cell membrane stability and DNA homeostasis, thus stimulating cell proliferation.(4)

This patient was in an under-weight condition due to nutritional disorders causing a decrease in the immune system; therefore, she was susceptible to infection by microorganisms (viruses, bacteria, fungi and parasites). Those infections can heal faster if the immune system is good, but the patient's immune system is very low due to inadequate nutrition. We advise patients to consume high protein L-arginine like meets, fish, nuts and others. HSV-1 infection has a variety of treatment options. Causative therapy, which comprises antivirals as well as analgesics, antipyretics, and antibiotics, are used to treat individuals with HSV-1 infection. Antivirals are used to prevent viral DNA synthesis and outbreaks. Antipyretics and analgesics are used to alleviate the clinical symptoms caused by the lesions, whereas antibiotics are utilized for patients with lesions that have spread widely. Supportive therapy works in tandem with causative therapy. Mouthwash, multivitamins, and liquid diets high in calories and protein are the examples of supportive therapy.(1)

The functions of antiviral drugs for HSV include inhibiting HSV reactivation and viral proliferation, pain and patient's symptoms reduction. Several types of antiviral agents, including acyclovir, famciclovir, penciclovir, and valacyclovir, have been recommended for the treatment and/or prevention of HSV- 1related infections. This medication is available in oral dosage, but only acyclovir is available in parenteral and topical formulations. Acyclovir requires more frequent dosing due to its low bioavailability (estimated at 20%) and three-hour plasma half-life. Valacyclovir and famciclovir have high oral bioavailability, hence that dosing is less frequent. Drugs used to treat or prevent HSV have a broad margin of safety since they are activated by viral thymidine kinases only in infected cells. (2) Valacyclovir was prescribed for this patient because it had a higher bioavailability than acyclovir. It is thought that by administering valacyclovir twice daily, the patient will have better rest intervals and their adherence to medicine consumption will be easier to control.

The use of corticosteroids as an anti-inflammatory medicine is solely considered to manage and minimize the severity of the condition. Previous case show that a combination of antiviral medications and corticosteroids can be a successful therapeutic choice.

(1) The administration of systemic corticosteroid therapy in the form of methyl prednisone in this patient was intended to help reducing the inflammation as well as pain complaints.

Mouthwash as the supportive therapy was administered for the patient: 0.025% hyaluronic acid mouthwash to reduce the inflammation replaced with 250 mg tetracycline dissolved in 10 ml aquadest to prevent secondary infection, then replaced with 0.025% hyaluronic acid, it has anti-inflammatory properties, to reduce pain, and could help in the healing process.(1)

Multivitamins were given to patients in an effort to strengthen their ability to recover. They may also function as an immunomodulator to support the patient's immune system, which would shorten recovery times and reduce the likelihood of recurrences. We prescribe folic acid for patients because it promotes in the healing process and plays an important part in DNA and RNA synthesis, including red blood cells. Nutritionists advised this patient to boost the protein diet to promotes in her healing process. Protein plays an important role in wound healing by influencing RNA and DNA synthesis, collagen and elastic tissue creation, immune system function, epidermal growth, and keratinization processes.(4) The main reasons this case management is limited are the patient's disobedience for our instructions, her preference for high-calorie, low-nutrient foods, and the fact that she has a baby and doesn't get sufficient rest.

CONCLUSION

Cytomegalovirus, infection T. Gondii can aggravate and delay healing of recurrent intraoral herpetic ulcers. Management of oral ulcers is quite challenging, especially if there is involvement of co-infection because it will weaken the body's immune system therefore adequate pharmacological and non-pharmacological management is needed.

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