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Acute Pseudomembranous Candidiasis in Patients with Hypertension

Lisa Triwardhani[1*], Siti Rusdiana Puspa Dewi[1]

[1]Dentistry Programme, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia

* Correspondence author email: lisatriwardhani@gmail.com

ABSTRACT

Introduction. Oral candidiasis is an opportunistic infection that is often found in the oral cavity caused by the growth of candida fungi. The calcium channel blocker antihypertensive drug, amlodipine, has a side effect that can reduce the amount of salivary flow, the reduced amount of saliva will cause anti-candida components in saliva such as lysozyme, histatin, lactoferrin, and calprotectin are also reduced, so that candida can easily develop in the oral cavity. This research was aimed to determine the management of cases of acute pseudomembranous candidiasis in hypertensive patients.

Case presentation. A woman 16 years old came to the Mohammad Hoesin Hospital in Palembang with a complaint of a yellowish white spot on the upper surface of her tongue which she noticed since 2 weeks ago. The yellowish white patches feel sore when the patient brushes her tongue with a toothbrush. The patient was uncomfortable with the state of her tongue so she wants her tongue to be treated. The patient had a history of hypertension since 1 year ago. The patient was given the drug nystatin drop. In the first control, 1 week after administration of the drug, white lesions on the tongue began to decrease and appear thinner compared to the previous visit. In the next control, the patient's tongue was clean so that the use of nystatin was stopped. The supporting investigation is a microbiological examination with a type of fungal culture against a tongue swab. The results of the examination indicated that the microscopic results of the yeast cell (+) KOH and the results of the germ culture in the form of Candida sp. The patient was diagnosed with acute pseudomembranous candidiasis and was treated with topical antifungals and was referred to an internal medicine specialist for hypertension control.

Conclusion: Management of oral candidiasis is very important to know, and must be followed by controlling hypertension in the patient so that a good oral prognosis is obtained.

Keywords: acute pseudomembranous candidiasis, hypertension, oral candidiasis,

Introduction

Oral candidiasis is an opportunistic infection caused by the fungus *Candida albicans*, which is often found in the oral cavity. Acute pseudomembranous candidiasis, also known as thrush, is the most common form of candidiasis. Clinically this lesion looks like a white, yellowish plaque, can be removed, and leaves a red and painful mark on the mucosa under the area that is removed. The prevalence of candidiasis occurs around 45% in infants, 45-65% in healthy children, 30-45% healthy adults, 50-65% of denture users, 90% in leukemia sufferers, and 95% in AIDS sufferers.

The main cause of this infection is the fungus *Candida (Monilia) albicans*, but other species such as *C. tropicalis*, *C. parapsilosis*, *C. stellatoidea*, *C. krusei*, *C. guilliermondii*, *C.*

dubliniensis, and *C. glabrata* can also be involved in the infection. this.[2.4] Local and systemic factors can predispose to oral candidiasis.[2] Local factors include smoking, use of dentures, use of topical and inhaled steroids, poor oral hygiene, and the quality and quantity of saliva. Systemic factors include immunosuppressive diseases, use of immunosuppressive drugs, chemotherapy, endocrine gland disorders, and hematological deficiency.[2]

Candidiasis is classified into 2 categories, namely acute and chronic. Acute oral candidiasis is divided into acute psudomembranous candidiasis and acute atrophic candidiasis, whereas chronic oral candidiasis is divided into chronic atrophic oral candidiasis and chronic hyperplastic candidiasis.[1.2.3]

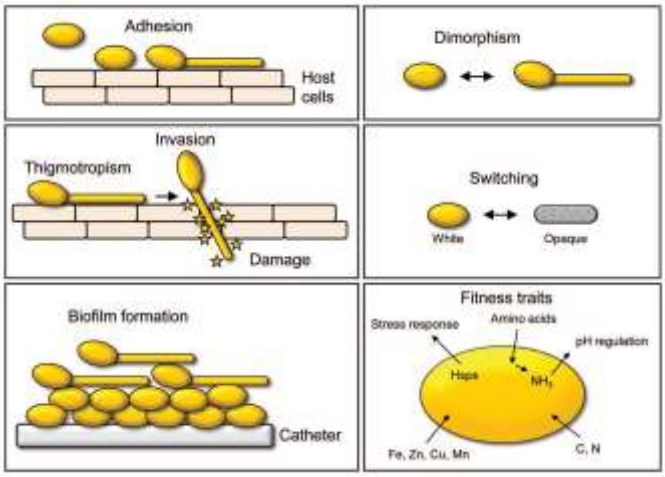

Figure 1. Pathogenesis of candida albicans[10]

The pathogenesis of *Candida albicans* can be explained in Figure 1. Yeast cells carry out adhesion and adhere to the surface of the host cell in the presence of adhesin expression from candida cells.[10] Candida adhesin is in the form of ALS (*Agglutinin-Like Sequence*) and HWP1 (*Hyphal Wall Protein*) genes of cell wall glycoproteins and function in the adhesion of *Candida albicans* to epithelial surfaces. Adhesion between candida and receptors on the host tissue results in a strong adhesion.[6]

Contact with host cells triggers the transition of yeast to hyphal form and directs growth via *thigmotropism.* Adhesion, physical strength, and secretion of extracellular enzyme hydrolases that facilitate the invasion mechanism, namely the active penetration of the fungus into the *host* cell by destroying the host barrier.[6] Candida extracellular hydrolytic enzymes that can damage host cells are *secreted aspartyl proteinase (SAP). Candida albicans* has at least 10 different genes that code for SAP. SAP 1-8 are secreted extracellularly, whereas SAP 9 and 10

are membrane bound. SAP 1 and SAP 3 are particularly expressed during the change in form of *Candida albicans*, while SAP 4-6 is involved in stimulating hyphal growth. *Candida albicans* proteinase has keratinolytic activity which facilitates early penetration of keratinized cells and provides an important nitrogen source during colonization. SAP activity directly induces *host* cell damage, facilitates hyphal growth for tissue invasion, increases adhesion after exposure to receptor sites, and also decreases host immunoglobulins and other defense proteins. Also, the hydrolytic enzyme produced by Candida albicans is phospholipase. Through hydrolysis of phospholipid ester bonds, phospholipase effectively degrades the host cell membrane leading to cell lysis and death. With this process, both the adhesion of *Candida albicans* to the receptors and subsequent penetration into the damaged tissue can be facilitated.[6]

The attachment of yeast cells to the biotic surface of the *host* (in the example of Figure 1 abiotic catheter surface) leads to the formation of biofilms with yeast cells at the bottom and hyphae cells on the top of the biofilm. Phenotypic switching is performed by fungal cells to affect the antigenicity and biofilm formation of *Candida albicans*.[4,6] Fungal cells have several survival properties that can influence the pathogenicity of these fungi, including a strong stress response mediated by heat shock protein (Hsp); auto-induction of hyphae formation through absorption of amino acids, excretion of ammonia (NH_3) and extracellular alkalinization simultaneously, metabolic flexibility and absorption of various compounds as sources of carbon (C) and nitrogen (N), and absorption of metals such as iron (Fe), zinc (Zn), copper (Cu) and manganese (Mn).[4,6]

The survival of fungal cells in the host is in the presence of *haemolysin* activity. *Haemolysin* is a substance that lyss erythrocytes and is produced by *Candida albicans* for survival by increasing the ability to absorb iron.[6]

Case Presentation

Based on the subjective examination, a female patient 16-year-old presented with a complaint of a yellowish-white spot on the upper surface of her tongue which she had noticed since 2 weeks ago. The yellowish-white patches felt sore after brushing her tongue with a toothbrush. On objective examination, it was found that the lesion was in the form of a yellowish-white plaque spread evenly on the dorsal of the tongue from mid 2/3 anterior of the tongue to 1/3 posterior of the tongue, can be scraped off, when scraped leaves a reddish base,

and feels a little sore. Patient's OHI-S examination score was 2.99, indicating poor oral hygiene. Based on subjective and objective examinations, acute pseudomembranous candidiasis can be established as provisional diagnosis. Microbiological investigation was required to make the definitive diagnosis, with the type of fungal culture against tongue swabs. The results showed the microscopic KOH *yeast cell* (+) and the results of the germ culture in the form of *Candida sp.*

Diagnosis in this case was acute pseudomembranous candidiasis, with poor oral hygiene as local predisposing factors. The use of the calcium channel blocker antihypertensive drug, Amlodipine, was acting as a systemic factor that has side effects such as reducing the amount of salivary flow by blocking the work of the parasympathetic nerves through the pathway of the calcium. Calcium ions can not enter the post synapses of the parasympathetic nerve, which is a *chemical messenger* for the parasympathetic nerves to stimulate the salivary glands. Reduced saliva production causes a reduction in salivary anti-candida components such as lysozyme, histatin, lactoferrin, and calprotectin, hence candida can easily develop and become a risk factor for oral candidiasis. The closest differential diagnosis is coated tongue. The clinical features of acute pseudomembranous candidiasis and coated tongue have a similarity, both showing the lesion of white-yellowish plaque that can be removed or scraped on the dorsum of the tongue. However, *the coated tongue* does not leave any red areas after removal, so the most appropriate diagnosis is acute pseudomembranous candidiasis.

Figure 2. Image of the patient's tongue at the initial visit

Management of this case is eliminating predisposing factors by maintaining good oral hygiene. The patient was instructed to maintain good oral hygiene by brushing the teeth and cleaning the tongue. The patient was also given nystatin, an antifungal in the form of a suspension that is used topically by dripping 1ml drops 4 times a day on the dorsal tongue. The patient was asked to control one week afterward. In the first control, subjective examination revealed that the patient had no complaints. The white patches on the tongue had started to decrease and no longer felt pain. Objective examination revealed that the size of the lesion was smaller and thinner. The patient was instructed to maintain oral hygiene, continue using the drug and control 1 week later.

Figure 3. Image of the patient's tongue during the first control

In the second control, the patient had no complaints, the tongue was clean and no longer painful. The objective examination showed that the lesion was completely healed. Acute pseudomembranous candidiasis has been resolved, and treatment is completed. Patients are instructed to stop using antifungal drugs and continue to use antihypertensive drugs and maintain good oral hygiene.

Figure 4. Image of patient's tongue condition on the second control

Discussions

Clinical manifestation of the lesion in this case was yellowish-white plaque that can be removed and leaves a red and painful mark on the mucosa under the area that was removed.[2] These plaques consist of desquamated epithelial cells, aggregates of fungal hyphae, fibrin, and necrotic material.[4] Lesions are commonly seen on the tongue, buccal mucosa, gingiva, palate, floor of the mouth, and oropharynx.[2,4] Lesions can involve the entire oral mucosa or be localized in areas with poor cleaning.[5] Differential diagnosis of acute pseudomembranous candidiasis is coated tongue and leukoplakia.[6,7] Clinical appearance of coated tongue is similar to acute pseudomembranous candidiasis, however, coated tongue does not leave any areas of redness after removal [6.7.8] Leukoplakia is also a differential diagnosis of acute pseudomembranous candidiasis because of its similar appearance of white plaque on the tongue. In leukoplakia, the lesion cannot be removed, shows the appearance of keratosis or dysplasia, and *Candida albicans* is not present on examination of the fungus. The etiology of leukoplakia is associated with tobacco and alcohol.[6,9]

According to WHO, a person is considered hypertensive or has high blood pressure if the systolic pressure exceeds 140 mmHg and the diastolic exceeds 90mmHg based on the average of two or three careful visits while in a resting position in one or two examinations. *Amlodipine* is a antihypertensive drug (calcium channel blocker). This drug is the main choice in hypertension therapy. The mechanism of action of amlodipine is by inhibiting the entry (influx) of calcium ions into heart muscle cells and vascular smooth muscle. It has a smooth muscle relaxing effect resulting in a decrease in blood pressure. One of the side effects of amlodipine that affects the oral cavity is xerostomia.[11,17] In the salivary glands, calcium channel blockers suppress water secretion by blocking Ca^{2+} channels. This mechanism affects the amount of saliva which is 99% water, which in turn causes the dry mouth.[18]

The salivary glands are innervated by both autonomic nerves, sympathetic and parasympathetic nerves. Sympathetic nerves produce thick saliva while parasympathetic produces watery saliva. Amlodipine works to inhibit the action of the parasympathetic nerves in which the calcium pathway at the presynapses is blocked so that calcium ions cannot enter the post synapses of the parasympathetic nerves. In the absence of a supply of calcium which

stimulates the production of acetylcholine, which is a chemical messenger for the parasympathetic nerves to stimulate the production of the salivary glands, it will result in a decrease in salivary gland production.[12,19] The reduced amount of saliva will also decrease the function of the saliva, including the anti-fungal activity by histatins. It has specific anti-fungal activity against *Candida albicans* so that in a state of reduced salivary flow (dry mouth), fungal infections such as candidiasis and *angular cheilitis* are often found. [12,18,19]

Conclusion

Based on the patient's history, clinical examination, and supporting examinations, the diagnosis in this case was acute pseudomembranous candidiasis. The etiology related to poor oral hygiene as a local predisposing factor, and the use of calcium channel blocker antihypertensive drug, amlodipine, as a systemic factor that has a side effect on the oral cavity. The quantity of saliva was decreased so that the salivary anti-candida component is reduced and candida is easy to develop. The treatment given to this patient is to eliminate or control the predisposing factors for candidiasis, with instructions for maintaining oral hygiene and administering anti-fungal drugs in the form of nystatin suspension 12 ml oral drops with a recommendation to use 4 times a day 1 ml applied to the dorsal of the patient's tongue. Patients with hypertension must routinely control their blood pressure and maintain the cleanliness of their oral cavity, and stay away from predictive factors that can worsen their health, such as smoking, consuming alcohol, and taking long-term and excessive antibiotics without a doctor's supervision.

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