Acute pseudomembranous candidiasis accompanied with oral malignant lesions in HIV-Infected Patient

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Abstract

Objective: Oral candidiasis is the most opportunistic infection in HIV/AIDS patient. Neoplasms may also frequently be found in the oral cavity of HIV/AIDS patient and may indicate the progression of HIV infection.

Methods: A 56-year-old complaint of yellowish-white spots in oral cavity and swelling in the palate accompanied with shortness of breath and difficulty in eating and swallowing. Various medication was used to relieve the complaints but there were no improvements. He claimed a weight loss of 10 kg in last three months. Physically showed pale and weakness. Intraorally, diffuse pseudomembranous was found throughout the oral cavity to pharynx, and an exophytic mass with red color at the palate area extending to oropharynx. Direct mycology test, complete blood count examination and HIV rapid test were conducted.

Results: Topical antifungal and antiseptic mouthwash was prescribed after direct mycology test result was positive for Candida albicans, a reactive anti-HIV examination with immunochromatography confirmed the patients was HIV and referral to head and neck oncologist for the Kaposis's sarcoma. In second visit, two days after therapy, the pseudomembrane slightly reduced, but complaints of tightness still felt. Unfortunately, the patients passed away after second visit and have not yet received therapy from head and neck oncologist.

Conclusion: Oral candidiasis may be the oral manifestation of HIV/AIDS which may accompanied by oral malignant lesions. Due to the late management of the oral candidiasis and oral malignant lesion, may result in poor prognosis for the treatment of the patient.

Keywords: Candida albicans, HIV/AIDS, Oral candidiasis, Oral malignant lesions DOI: 10.15562/jdmfs.v8i1.1594

Introduction

HIV (Human Immunodeficiency Virus) is an RNA retrovirus that causes infection and death. This virus is transmitted through blood and body fluids. HIV comes from the term 'human T lymphotropic virus III' (HTL-III) which results in HIV infection by destroying a subset of T lymphocyte cells, specifically CD4 +. Severe damage to T helper immune cells, resulting in HIV disease and ultimately causing acquired immunodeficiency syndrome (AIDS). The emergence of symptomatic symptoms of HIV infection shows the number of CD4 T cells that decreases progressively and occurs within a period of 5-15 years or more with manifestations that can occur in the form of infection and malignancy. The most common infectious disease is candidiasis which is experienced by more than 90% of AIDS patients during the phase of HIV infection and can be an important sign of disease progression towards AIDS. One of the most common forms of candidiasis in the oral cavity is acute pseudomembranous candidiasis and associated with a low CD4 cell count of <200 cells/mL. Other candidiasis that can also be found including erythematous candidiasis, angular cheilitis, median rhomboid glossitis and hyperplastic candidiasis.

In addition to infectious diseases, most people with HIV / AIDS also experience malignancy and the most common case is Kaposis's sarcoma. This malignancy is caused by Human Herpesvirus 8 (HHV8), also known as Kaposis Sarcoma Herpes Virus (KSHV). Kaposis's sarcoma usually occurs in the later stages of HIV infection and is characterized by a very aggressive clinical course.

This case report will discuss the oral manifestations of patients infected with HIV in the form of acute pseudomembranous candidiasis and Kaposis's sarcoma. At first, the patient came because of complaints in the form of yellowish-white spots that arise in large quantities in the oral cavity, also complaints of shortness of breath accompanied with difficulty in swallowing and eating. From the results of examinations that have been carried out, it was found positive patients infected with HIV.

Case Report

A 56-year-old male patient who works as a personal driver came to the Universitas Airlangga Dental Hospital with a chief complaint of the appearance of a white coating on the tongue and swelling in the palate and shortness of breath. White coating felt since about 2 months ago; initially, only a little but over time it grew more and spread to the cheeks, lips, and palate. Swelling appeared since about 2 months ago; initially,
The white coating that arises previously has been checked by a doctor and given a prescription of nystatin which has been used as many as two bottles but no change was felt so that the use was stopped. Furthermore, patients took herbal medicine Ganoni to date. Swelling and complaints of cough that were felt since + 2 months ago have also been examined by a doctor and given drugs Ciprofloxacinc, Prednisone and Quantidex®. However, shortness of breath and cough complaints is still felt to date.

The patient lost 12 kg in the last 3 months. There was a history of smoking half a pack per day for 20 years. The patient worked as a bottled water factory employee for 25 years until finally retiring and then working again as the personal driver of the head of the factory to date.

Extraoral examination, the face was not symmetrical and there was swelling on the left cheek. In the upper extremity, there were diffuse macules. At the corners of the left and right lips there is a white pseudomembrane, clear border, irregular edge, could be scraped off figure 1. Intra oral examination, there was diffuse white pseudomembrane, clear border, irregular edge, could be scraped on the palate to the oropharynx, on the tongue, on the gingiva and labial mucosa of the lower jaw on the buccal mucosa and on the maxillary gingival and labial mucosa. There was also swelling on the palate, solid and painless figure 2.

Based on anamnesis, clinical and supportive examination diagnosis acute pseudomembranous candidiasis accompanied by Kaposi’s sarcoma was made with a differential diagnosis of Kaposi sarcoma and treatment was started. Patients were given symptomatic therapy with 1% povidone-iodine gargle, chlorine dioxide mouthwash and mycostatin 100.00 IU. Instructed to use povidone-iodine first before using mycostatin and chlorine dioxide 30 minutes later after using mycostatin. The patient was referred for complete blood tests, anti-HIV, and fungal examination and referred to a head and neck oncologist for further examination of suspected Kaposi’s sarcoma.

Two days later the patient came for control. The patient felt better, the white spots on the mouth began to change, the swelling also seems to have shrunk, shortness of breath was still felt but has slightly reduced figure 3.

At the same day, the patient visited head and neck oncologist and the results of the examination on the oncology unit diagnosed patients with suspected palatal abscesses and suggest some examination but not yet done. The patient
Table 1. Result of laboratory investigations

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Unit</th>
<th>Normal value</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>12.7 g/dL</td>
<td></td>
<td>13.2 – 17.3</td>
<td>Low</td>
</tr>
<tr>
<td>WBC</td>
<td>5.4 x 10^3/uL</td>
<td></td>
<td>3.8 – 10.6</td>
<td>Normal</td>
</tr>
<tr>
<td>Platelets</td>
<td>350 x 10^3/uL</td>
<td></td>
<td>150 - 440</td>
<td>Normal</td>
</tr>
<tr>
<td>Differential count</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Eosinophil</td>
<td>1 %</td>
<td></td>
<td>2 - 4</td>
<td>Low</td>
</tr>
<tr>
<td>Basophil</td>
<td>1 %</td>
<td></td>
<td>0 - 1</td>
<td>Normal</td>
</tr>
<tr>
<td>Neutrophil</td>
<td>61 %</td>
<td></td>
<td>55 - 65</td>
<td>Normal</td>
</tr>
<tr>
<td>Lymphocyte</td>
<td>17 %</td>
<td></td>
<td>25 - 35</td>
<td>Low</td>
</tr>
<tr>
<td>Monocyte</td>
<td>20 %</td>
<td></td>
<td>3 - 6</td>
<td>High</td>
</tr>
<tr>
<td>Erythrocyte Sedimentation Rate</td>
<td>88 mm</td>
<td></td>
<td>1 - 30</td>
<td>High</td>
</tr>
<tr>
<td>Ferritin</td>
<td>4.8 x 10^6/uL</td>
<td></td>
<td>4.4 - 5.9</td>
<td>Normal</td>
</tr>
<tr>
<td>Retikulosit</td>
<td>0.5 %</td>
<td></td>
<td>0.5 - 1.5</td>
<td>Normal</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>39 %</td>
<td></td>
<td>40 - 52</td>
<td>Low</td>
</tr>
<tr>
<td>Eosinophil Count</td>
<td>80 /uL</td>
<td></td>
<td>80 - 360</td>
<td>Normal</td>
</tr>
</tbody>
</table>

Table 1. Result of immunological investigations

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anti HIV</td>
<td></td>
</tr>
<tr>
<td>1. Immunochromatography</td>
<td>Reaktif</td>
</tr>
<tr>
<td>2. Immunochromatography</td>
<td>Reaktif</td>
</tr>
<tr>
<td>3. Elisa</td>
<td>Reaktif</td>
</tr>
<tr>
<td>Cut off</td>
<td>0.192</td>
</tr>
<tr>
<td>Abs</td>
<td>3.758</td>
</tr>
</tbody>
</table>

Discussion

Oral candidiasis is the most common fungal infection of the oral cavity and occurs in 90% of people with HIV with high morbidity. The presence of cross-infection between HIV and Candida species can influence the severity and progression of HIV disease and its manifestations are related to progression towards AIDS. The most common form of candidiasis is pseudomembranous candidiasis which has a yellowish-white appearance, especially on the tongue and palate. In about 85-90% of patients infected with HIV, there is fungal colonization of the oral cavity and Candida albicans is the most common species. Reduction of CD4 lymphocytes in cellular infiltration from candida lesions in HIV patients results in significantly lower salivary histatin-5 concentrations so that Candida albicans which is a dimorphic fungus and is usually present in the oral cavity in a non-pathogenic state can cause fungus-5 and can turn into pathogenic hyphae. However, this species can also be found in healthy individuals in controlled amounts in saliva that beneficial for the immune system and prevent infection in the innate and adaptive immune system.

Intraoral clinical examination results obtained pseudomembranous scattered through the patient’s oral cavity to the pharynx. The suspect is acute pseudomembranous candidiasis. Therapy with antifungal drugs can overcome the condition and is temporary so that recurrent infections often occur. Further development of chronic pseudomembranous candidosis is an infection involving the esophagus which can cause difficulty in swallowing and chest pain.

Complaints of shortness of breath and difficulty in swallowing that are felt by the patient indicate that the candida infection experienced may have involved the esophagus. The patient also complained about a cough that did not heal despite treatment. These complaints have been felt since about 3 months that made him forced to stop working because he always felt weak. A weight loss of around 12 kg has also been experienced in the past three months. Pseudomembranous candidiasis and esophageal candidiasis have a similar depiction in the presence of white patches that resemble cheese. About 64-88% of patients with oral candidiasis also experience esophageal candidiasis. In HIV infection, candidiasis occurs as angular cheilitis in stage 2, pseudomembranous/erythematous candidiasis in the oral cavity and esophageal candidiasis in stage 4. Oropharyngeal candidiasis occurs when CD4 cell counts range from 200 to 500 cell / mm3 and when CD4 cell count decreases to <200 cell / mm3 patients will experience oesophageal candidiasis.

The development of candida infections begins with the formation of colonization on the surface of mucocutaneous HIV infection is associated with an increase in colonic candida which also has a relationship with the development of the disease. During the course of the disease the rate of candida infection is inversely proportional to CD4+ count and is strongly influenced by anti-retroviral treatment. Patients only find out if they are infected with HIV after an anti-HIV immunological examination and the results are reactive by immunochromatography and ELISA and have never received antiretroviral therapy before.

HIV is a retrovirus that mainly affects T cells and other CD4 expressing cells such as macrophages, dendritic cells, and lymph nodes. Early in the course of the disease or two weeks after infection, there is a decrease in CD4 cells associated with primary clinical infection and then partial recovery happens. At 3-4 weeks after infection, there is an increase in CD4 T cells but then it will slowly decrease again during the latent period and more quickly in the final stages and is subject to immune deficiency with CD4 <500 cells/mm3. Based on this, the percentage of CD4 T lymphocytes and the presence of opportunistic infections can determine the stage of...
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HIV infection and become a guide for therapy. The percentage of CD4 T lymphocytes is a biological and immunological reference for HIV infection and AIDS control markers and are a predictor of mortality. The determination is based on the results of three stages of laboratory examination, namely the number of leukocytes, lymphocyte count and percentage of CD4 lymphocytes. In a study by Rodriguez (2013) which explained one method of determining an estimate of CD4 lymphocyte counts based on leukocyte values and lymphocyte counts on a complete blood count. The results showed the effectiveness in the prediction of 81.4% for the range of leukocytes 4000-4999, 91.89% for the range of leukocytes 3000 to 3999 and 100% for leukocyte values below 3000. This method can be performed to determine the number of CD4 difficult flow cytometry and can reduce costs in determining the level of HIV/AIDS in the suffering.9

On patients with CD4 examinations that yet to be done, the results of complete blood tests obtained the number of lymphocytes which decreased to 17% of the normal value that should be 25-35% and the number of leukocytes at 5400 µL with normal values 3800 - 10600 µL. If this value is adjusted can be predicted that the CD4 cell count is around 200 cells/mm3. This is what causes opportunistic infections to develop easily as well as the malignancy experienced by patients.

CD4 cell count that is less than 200 cells/mL is one factor that can describe the clinical development of HIV disease so that antiretroviral treatment must be started immediately without delay. Untreated HIV infection will develop into AIDS characterized by opportunistic infections and malignancies due to a drastic decline in the immune system and can cause death. The development of untreated HIV into AIDS mostly lasts for about 10 years and is related to viruses, host, and environmental factors. With antiretroviral therapy, one can increase life expectancy from one year to five years.10 However, the patient died before being referred to UPIPI and given anti-retroviral treatment.

Since the introduction of antiretroviral therapy, especially Highly Activated Antiretroviral Therapy (HAART), the prevalence of oral candidiasis in HIV-infected patients has decreased significantly. Based on research it was found that antiretroviral therapy can improve the body’s immune system and has anti-fungal effects. HAART can increase CD4 T lymphocyte levels so that the body’s immune system becomes better, and the protease inhibitors contained in the HAART cocktail can disrupt SAPs, the main protein produced by Candida albicans by inhibiting fungal proliferation and pathogenicity.4 In this case, the patient died before receiving antiretroviral therapy.

Not only in pseudomemranous, but an enlargement was also found in the palate to the oropharynx which was suspected to be a malignancy namely Kaposi’s sarcoma caused by the HHV-8 or KSHV virus. Primary KSHV infections are usually asymptomatic in immunocompetent hosts, but in conditions of immune deficiency, such as in HIV sufferers, KSHV can cause lymphoproliferative abnormalities such as Kaposi’s sarcoma.2 The presence of fungal infections and malignancies in the oral cavity of the patient are suspected to be the cause of hard to breathe and difficulty in swallowing while eating. Fungal infections appear to have spread to the esophagus and malignancy has spread to the oropharynx. From this condition, the patient has experienced a significant CD4 cell decline, possibly by <200 cells/mL.

Based on mycological examination, positive results of the fungal for staining KOH and Candida albicans species after fungal culture. So that the patient is prescribed mycostatin and antiseptic mouthwash, povidone iodine 1 % and chlorine dioxide mouthwash. In developing countries, topical therapies such as nystatin are still the choice of treatment because of the rapid therapeutic effect at a more economical price and few side effects. A study in Jordan found that nystatin is the most prescribed antifungal agent.11 Based on the guidelines of the Infectious Diseases Society of America, oropharyngeal candidiasis can be treated with nystatin suspension with a concentration of 100,000 IU / mL, 4-6 mL four times a day or 1 to 2 nystatin tablets with a concentration of 200,000 IU/tablet four times a day for 7-14 days. Based on WHO recommendations, topical therapy for nystatin suspension can be replaced with fluconazole for the treatment of oropharyngeal candidiasis in HIV patients in children and adults.11

Patients treated with nystatin drops 100,000 IU as much as 4 ml four times a day. Oral drop nystatin (polyene group) for patients aims to kill the fungus by binding to ergosterol sterols contained in the fungal membrane cell walls, causing leakage in the cytoplasmic wall which will cause fungal death. By inhibiting the cytochrome p450 enzyme will bind to lanosterol which is an enzyme involved in ergosterol synthesis. Inhibition of these enzymes will cause damage to cell membranes and impaired cell membrane structure-function, thereby inhibiting cell growth and fungal death.12 Patients are also given povidone-iodine mouthwash and
chlorine dioxide mouthwash. Povidone-iodine has antifungal activity and prevents the attachment of Candida and oral mucosal cells thereby eliminating the ability of C. albicans to penetrate the oral epithelial cells.\textsuperscript{1–3} The clinical and microbiological efficacy of chlorine dioxide as a topical antiseptic and a disinfecting agent has been used to treat chronic atrophic candidiasis in geriatric patients.\textsuperscript{1–3}

Unfortunately, patient treatment is not completed because of the delay in the examination, so that the spread of the disease becomes severe. A low CD4 lymphocyte number and a high viral load are associated with disease progression that can develop rapidly and increase the risk of death if no treatment is taken.

**Conclusion**

One of the manifestations of HIV AIDS in the oral cavity is acute pseudomembranous candidiasis and is often one of the first indications that a person is infected with HIV which can show the progression of the disease. When CD4 cell drops and is very low there is an increased risk of morbidity and mortality. For this reason, prompt and appropriate therapy must be carried out immediately to improve the patient’s quality of life.

**Acknowledgment**

None

**Conflict of Interest**

The authors report no conflict of interest.

**References**


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