Pharmacogn J. 2024; 16(5): 1143-1149
A Multifaceted Journal in the field of Natural Products and Pharmacognosy
www.phcogj.com

Research Article

# Atypical Manifestation of Oral Candidiasis in Patient with Aplastic Anemia

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## ABSTRACT

Candidiasis is an opportunistic fungal infection predominantly caused by Candida species, which can manifest in immunocompromised individuals such as those with aplastic anemia. Aplastic anemia, characterized by bone marrow failure, significantly increases susceptibility to infections, with fungal infections being a leading cause of mortality. Oral candidiasis is one of the most common manifestations, and it typically presents as white pseudomembranes. However, atypical presentations can occur.

We report a case of a 26-year-old male with aplastic anemia who presented with general weakness, fever, and painful swallowing. On examination, a blackish plaque was observed on his palate. Laboratory tests, including palatal tissue smear, histological examination, and culture, confirmed an infection of Candida tropicalis. This unusual blackish manifestation of oral candidiasis, resembling mucormycosis, has not been previously described in the literature. The patient was treated with intravenous fluconazole, leading to complete resolution of the oral lesions within 11 days.

Through this case, we underscore the importance of recognizing atypical presentations of common infections, particularly in immunocompromised patients, and highlight the need for thorough diagnostic evaluation to guide appropriate antifungal therapy.

**Keywords:** Oral candidiasis, Aplastic anemia, Candida tropicalis, Black oral thrush, Atypical presentation.

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**History**

- Submission Date: 02-08-2024;
- Review completed: 14-09-2024;
- Accepted Date: 30-09-2024.

**DOI : 10.5530/pj.2024.16.187**

**Article Available online**

http://www.phcogj.com/v16/i5



## INTRODUCTION

Candidiasis is an opportunistic infection caused by a type of fungi referred to as Candida. Candida, a specific variety of yeast, thrives within the oral cavity, gastrointestinal tract, genitalia, and other regions. It remains largely benign unless circumstances conducive to its pathogenicity emerge. This condition predominantly emerges as a secondary infection among individuals with compromised immune systems. It has the potential to impact not only localized areas like the oral cavity and urogenital but also can extend systemically, affecting the bloodstream and deep-seated organs like the lungs and gastrointestinal tract.[1–3]

Aplastic anemia is an illness that compromises the immune system of patients. It is characterized by the failure of the bone marrow and a significant reduction in all marrow components. Most individuals afflicted with aplastic anemia encounter recurrent instances of infection throughout their lives. The primary culprits of these infections are gram-positive bacteria, particularly gram-positive cocci, and gram-negative microorganisms, especially multi-drug-resistant (MDR) negative bacilli. However, fungal infections remain the leading cause of death and mortality among aplastic anemia patients. A retrospective study conducted at a single center in Brazil revealed that the occurrence of fungal infections among individuals with hematological malignancies stood at 6.4%.[4]

Oral candidiasis is one of the most common fungal infections affecting the oral mucosa. The primary agent responsible for this condition is Candida albicans, and it exhibits various clinical manifestations. Pseudomembranous candidiasis, referred to as oral thrush, appears as amalgamated white patches resembling curdled milk and is generally asymptomatic. Erythematous candidiasis, on the other hand, manifests as localized redness within the oral mucosa, sometimes accompanied by symptoms or occurring without them. Atypical presentations of oral candidiasis have been reported in a number of cases.[5–9] However, oral candidiasis presenting with a blackish pseudomembrane has not been previously described. Here, we report a case of aplastic anemia patient with oral candidiasis that manifested as an atypical blackish oral thrush.

## CASE REPORT

A 26-year-old male patient presented to the Emergency Room at Dr. Soetomo General Academic Hospital, Surabaya, on October 12, 2022, with a chief complaint of general weakness.

### Anamnesis

Chief complaint: general weakness

History of present illness:

The patient was referred from Ibnu Sina Hospital, Gresik, after a week of hospitalization with no improvement in his condition. He had been experiencing weakness and had a fever for three days prior to admission. He also reported mouth pain, especially when swallowing, for one month before admission and had lost his appetite, and his family noted the presence of a blackish plaque on his palate seven days before admission. He had also lost 5 kg in the past month.

Past medical history:

The patient denied any history of hypertension or diabetes. He was diagnosed with aplastic anemia on October 6, 2022, but had not yet received any therapy.

**Cite this article:** Nahlalogi P, Bramantono. Atypical Manifestation of Oral Candidiasis in Patient with Aplastic Anemia. Pharmacogn J. 2024;16(5): 1143-1149.

Social history:

The patient is unmarried. He denied smoking and alcohol consumption. He works as an employee. He denied any drug use and having multiple sexual partners.

Family medical history: No family members had similar symptoms.

## Physical Examination

The patient's general condition was weak, with a Glasgow Coma Scale (GCS) score of E4V5M6, a pressure of 90/50 mmHg on NE 100 nano, a pulse rate of 113 beats per minute, a respiratory rate of 24 breaths per minute, an axillary temperature of 38 °C, and a peripheral oxygen saturation of 98% on a nasal cannula at 4 liters per minute. Examination revealed anemic conjunctiva, no icteric sclera, no cyanosis, no dyspnea, and no enlargement of the cervical lymph nodes. Heart sounds were characterized by a single S1 and S2 without murmur, gallop, or extrasystole. Breath sounds were vesicular on both sides without rhonchi or wheezing. The abdomen was flexible (no distention) with normal bowel sounds; the liver and spleen were not palpable. The acral extremities were warm, dry, and pale, with a capillary refill time of less than 2 seconds. There was no edema.

## Additional examination (October 12, 2022)

Laboratory examination results included: Hemoglobin (Hb) 8.8 g/dL; leukocytes 870/mm$^3$; neutrophils 36.8%; lymphocytes 32.2%; absolute neutrophil count (ANC) 320; platelet count 31,000/mm$^3$; sodium 138 mmol/L; potassium 6.6 mmol/L; chloride 105 mmol/L; blood urea nitrogen (BUN) 79 mg/dL; creatinine 3.3 mg/dL; albumin 2.42 g/dL; alanine aminotransferase (ALT) 40 U/L; aspartate aminotransferase (AST) 37 U/L; total bilirubin 8.4 mg/dL; direct bilirubin 6.6 mg/dL; CRP 25.36 mg/L; prothrombin time (PT) 12.5 seconds; activated partial thromboplastin time (APTT) 30.6 seconds; non-reactive HBsAg; and negative anti-HIV. Blood gas analysis (BGA) results included: pH 7.27; $pCO_2$ 24 mmHg; $pO_2$ 158 mmHg; $HCO_3$ 11 mmol/L; and BE -15.9; $SaO_2$ 99%. Complete urine examination results included: pH 5.5; specific gravity 1.021; ketones -; proteins 1+; bilirubin 2+; normal urobilinogen; erythrocytes -; leukocytes -; nitrite -; cloudy yellow color; ACR ≥ 300; and PCR ≥ 0.5. COVID-19 antigen and PCR swab results were negative. Chest X-ray results demonstrated no abnormalities in the lungs or heart.

Peripheral Blood Smear: Erythrocytes: Normocytic normochromic anisopoikilocytosis (microcytic, ovalocytes), polychromasia cells (+), normoblasts (-). Leukocytes: Normal count, dominated by segmented neutrophils, immature granulocytes (+) (myelocytes, metamyelocytes), atypical lymphocytes (+) (plasmacytoid, monocytoid), and blasts (-). Thrombocytes: Decreased count, giant platelets (+). Conclusion: Normocytic normochromic anemia with anisopoikilocytosis, leukocytes with immature granulocytes (+) and atypical lymphocytes (+), and thrombocytopenia suggesting pancytopenia.

## Initial Diagnosis

Based on the history, physical examination, and additional/supporting examination, the patient was diagnosed with febrile neutropenia, septic shock, sepsis suspected to be due to fungal infection with a differential diagnosis of bacterial infection (SOFA score 12), multiple organ dysfunction syndrome (MODS), including acute kidney injury and hyperbilirubinemia, pancytopenia due to aplastic anemia (Hb 8.8, platelet count 31,000, WBC 870), metabolic acidosis, hyperkalemia (6.6 mmol/L), and hypoalbuminemia (2.42 g/dL).

## Therapy Plan

- $O_2$ nasal cannula (NC) 4 L/min

- Fine porridge, high-calorie, low-protein diet of 2,100 kcal/24 hours

- Syringe pump with NE 100 nano

- Infusion of D10 500 cc and rapid-acting insulin 10 units/24 hours

- Infusion of sodium bicarbonate 100 meq/NaCl 0.9% 400 ml/24 hours

- PRC transfusion 1 bag/day until Hb >10 g/dL if $K^+ < 5$

- Infusion of albumin 20% 100 ml over 4 hours

- Injection of ceftriaxone 1 gram IV/12 hours (Day 1)

- Injection of calcium gluconate 500 mg/8 hours

- Per oral administration of nystatin drops 4 ml/6 hours

- Per oral administration of paracetamol 500 mg/8 hours

- Aseptic gargle/12 hours

Admission to HCU

## Disease Progression

## October 13, 2022 (Day 1) (HCU)

The patient felt weak.

His vital signs were as follows: Glasgow Coma Scale (GCS) 4-5-6, blood pressure (BP) 100/60 mmHg on norepinephrine (NE) at 100 nanograms, heart rate (HR) 105 beats per minute, respiratory rate (RR) 22 breaths per minute, and oxygen saturation (SpO2) 98% on nasal cannula at 3 liters per minute (nc 3 lpm). Procalcitonin was elevated at 45.91 ng/mL.

Advice from an Infection and Tropical Disease Consultant:

- Injection of gentamycin 280 mg/48 hours (Day 1)

- Injection of fluconazole 200 mg/24 hours (Day 1)

- Blood culture test

## October 17, 2022 (Day 5) (HCU)

The patient continued to feel weak, his fever had improved, and he reported persistent pain when swallowing.

**Table 1. Culture and antifungal sensitivity of palatal scrap specimen.**

| Culture | Candida Tropicalis |
|---|---|
| **Sensitivity Test** | |
| Fluconazole | Sensitive |
| Voriconazole | Resistant |
| Amphotericin B | Sensitive |
| Flucytosine | Resistant |
| Caspofungin | Resistant |
| Micafungin | Resistant |

**Table 2. Systemic or local host factors predisposing to oral candidiasis.[10,11]**

| Systemic Host Factors | Local Host Factors |
|---|---|
| **Altered physiological status** | **Mucosal barrier alterations** |
| Infancy/old age | Exogenous epithelial change |
| **Altered hormonal status** | Trauma |
| Diabetes | Loss of occlusion |
| Hypothyroidism/Hypoparathyroidism | Maceration |
| Cushing's syndrome | Endogenous epithelial changes |
| **Altered hematinic or nutritional status** | Atrophy |
| Iron deficiency | Hyperplasia |
| Hypovitaminosis, Vit B12, folic acid | Dysplasia/Oral cancer |
| Malnutrition | **Saliva quantitative changes** |
| **Altered immune status** | Xerostomia |
| Defects in cell-mediated immunity | Sjogren's syndrome |
| Reduced numbers of phagocytes | Radiotherapy/Cytotoxic therapy |
| Lymphopenia or leukopenia | **Saliva qualitative changes** |
| Decreased CD4 count | pH/glucose concentration |
| Due to infective states/ HIV | **Poor oral or denture hygiene** |
| **Blood dyscrasias/ malignancies** | **High carbohydrate diet** |
| **Immunosuppressant/ chemotherapy** | **Heavy smoking/ Betel nut chewing** |
| **Broad spectrum antibiotics** | **Inhaled steroid** |

**Table 3. Criteria for proven invasive fungal diseases.**

| Fungus | Microscopic Analysis: Sterile Material | Culture: Sterile Material | Blood | Serology | Tissue Nucleic Acid Diagnosis |
|---|---|---|---|---|---|
| Molds[a] | Histopathologic, cytopathologic, or direct microscopic examination[b] of a specimen obtained by needle aspiration or biopsy in which hyphae or melanized yeast-like forms are seen accompanied by evidence of associated tissue damage | Recovery of a hyaline or pigmented mold by culture of a specimen obtained by a sterile procedure from a normally sterile and clinically or radiologically abnormal site consistent with an infectious disease process, excluding BAL fluid, a paranasal or mastoid sinus cavity specimen, and urine | Blood culture that yields a mold[c] (eg, *Fusarium* species) in the context of a compatible infectious disease process | Not applicable | Amplification of fungal DNA by PCR combined with DNA sequencing when molds are seen in formalin-fixed paraffin-embedded tissue |
| Yeasts[a] | Histopathologic, cytopathologic, or direct microscopic examination of a specimen obtained by needle aspiration or biopsy from a normally sterile site (other than mucous membranes) showing yeast cells, for example, *Cryptococcus* species indicating encapsulated budding yeasts or *Candida* species showing pseudohyphae or true hyphae[d] | Recovery of a yeast by culture of a sample obtained by a sterile procedure (including a freshly placed [<24 hours ago] drain) from a normally sterile site showing a clinical or radiological abnormality consistent with an infectious disease process | Blood culture that yields yeast (eg, *Cryptococcus* or *Candida* species) or yeast-like fungi (eg, *Trichosporon* species) | Cryptococcal antigen in cerebrospinal fluid or blood confirms cryptococcosis | Amplification of fungal DNA by PCR combined with DNA sequencing when yeasts are seen in formalin-fixed paraffin-embedded tissue |
| Pneumocystis | Detection of the organism microscopically in tissue, BAL fluid, expectorated sputum using conventional or immunofluorescence staining | Not applicable | Not applicable | Not applicable | Not applicable |
| Endemic mycoses | Histopathology or direct microscopy of specimens obtained from an affected site showing the distinctive form of the fungus | Recovery by culture of the fungus from specimens from an affected site | Blood culture that yields the fungus | Not applicable | Not applicable |

**Table 4. Criteria for probable invasive fungal diseases.**

| **Candidiasis** |
|---|
| *Host factors* |
| Recent history of neutropenia <0.5 × $10^9$ neutrophils/L (<500 neutrophils/$mm^3$ for >10 days) temporally related to the onset of invasive fungal disease |
| Hematologic malignancy |
| Receipt of an allogeneic stem cell transplant |
| Solid organ transplant recipient |
| Prolonged use of corticosteroids (excluding among patients with allergic bronchopulmonary aspergillosis) at a therapeutic dose of ≥0.3 mg/kg corticosteroids for ≥3 weeks in the past 60 days |
| Treatment with other recognized T-cell immunosuppressants, such as calcineurin inhibitors, tumor necrosis factor-a blockers, lymphocyte-specific monoclonal antibodies, immunosuppressive nucleoside analogues during the past 90 days |
| Inherited severe immunodeficiency (such as chronic granulomatous disease, STAT 3 deficiency, CARD9 deficiency, STAT-1 gain of function, or severe combined immunodeficiency) |
| Acute graft-versus-host disease grade III or IV involving the gut, lungs, or liver that is refractory to first-line treatment with steroids |
| *Clinical features* |
| At least 1 of the following 2 entities after an episode of candidemia within the previous 2 weeks: |
| Small, target-like abscesses in liver or spleen (bull's-eye lesions) or in the brain, or, meningeal enhancement |
| Progressive retinal exudates or vitreal opacities on ophthalmologic examination |
| *Mycological evidence* |
| ß-D-glucan (Fungitell) ≥80 ng/L (pg/mL) detected in at least 2 consecutive serum samples provided that other etiologies have been excluded |
| Positive T2Candida[a] |

**Table 5. Treatment of oropharyngeal candidiasis (Patil et al., 2015).**

| Severity | Antifungal drug | Dosage/ Duration |
|---|---|---|
| **First-line agents** | | |
| | Fluconazole (PO or IV) | 100–200 mg/7–14 days |
| | Clotrimazole troches | 10 mg five times/7–14 days |
| | Nystatin suspension (100,000 U/mL) | 4–6 ml four times/7–14 days |
| | Nystatin pastilles (200,000 U each) | 1–2 pastilles four times/7–14 days |
| **Second-line agents** | | |
| | Itraconazole solution (PO) | 200 mg/28 days |
| | Posaconazole (PO) | 400 mg daily in divided doses |
| | Voriconazole (PO or IV) | 200 mg twice daily |
| **Agents used in refractory case of OPC** | | |
| | Caspofungin (IV) | 70 mg loading dose followed by 50 mg daily |
| | Micafungin (IV) | 100-150 mg daily |
| | Anidulafungin (IV) | 100 mg loading dose followed by 50 mg daily |
| | Amphotericin B oral suspension | 500 mg every 6 h |
| | Amphotericin B deoxycholate (IV) | 0.3 mg/kg once |

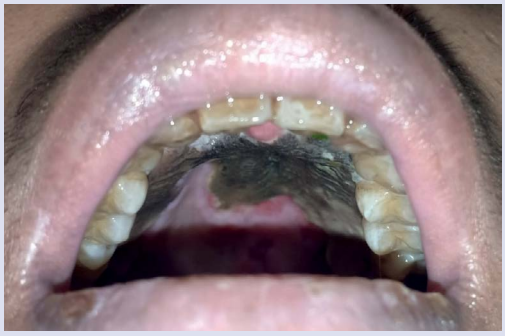

**Figure 1.** Blackish plaque on the patient's palate.

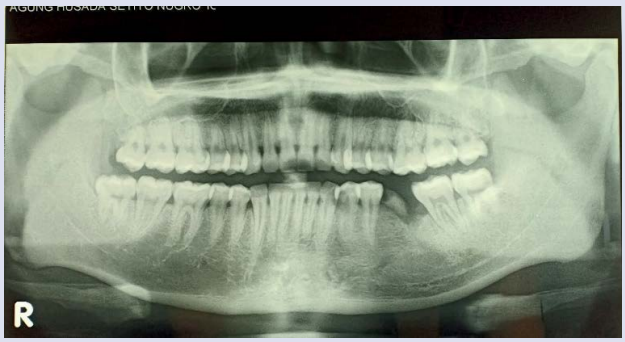


**Figure 2.** Panoramic photo displaying no deep infiltration of fungal infection.

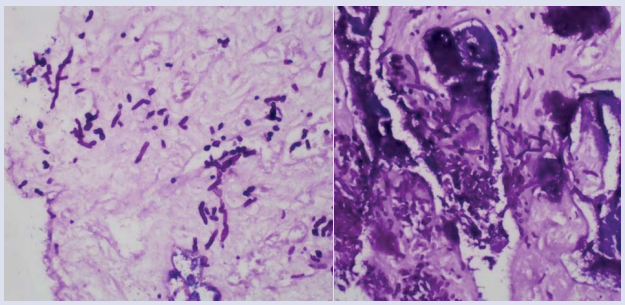

**Figure 3.** Palatal tissue smear with PAS staining displaying yeast and aseptate fungal hyphae. Histological examination of the palatal biopsy revealed pieces of tissue in the form of large areas of necrosis with an accumulation of inflammatory cells, including lymphocytes, histiocytes, and neutrophils. No signs of malignancy were identified.

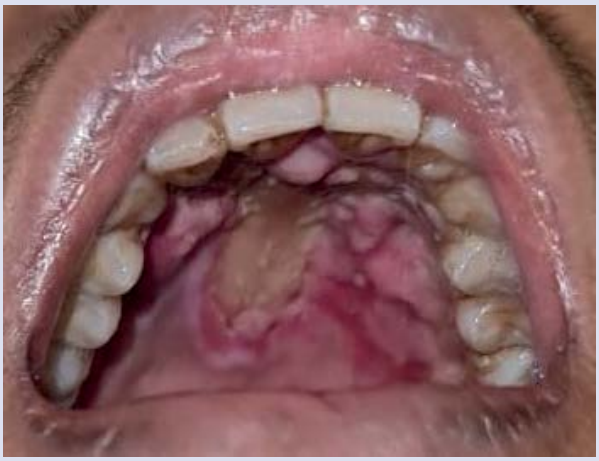

**Figure 4.** Clinical resolution after 11 days of fluconazole injection.

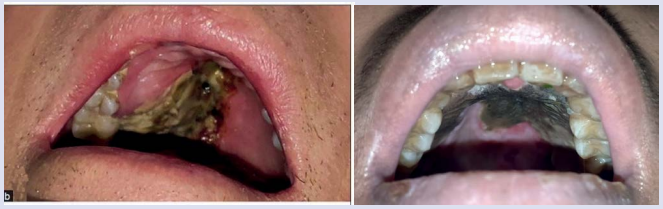

**Figure 5.** A mucormycosis infection as a comparison (left)[18] and a blackish plaque on the patient's palate (right).

Vital signs: GCS 4-5-6, BP 110/70 mmHg without support, HR 98 beats per minute, RR 20 breaths per minute, and SpO2 98% on free air.

Blood Culture Results: Staphylococcus hominis sensitive to gentamycin, linezolid, and vancomycin was identified. No fungal growth was identified.

Diagnosis: Sepsis (improved), pancytopenia due to aplastic anemia (Hb 8.3, WBC 3370, platelet count 56,000), and oral candidiasis with a differential diagnosis of mucormycosis.

Therapy:

- Ceftriaxone injection was stopped.

- Injection of gentamycin 280 mg/48 hours (Day 5)

- Injection of fluconazole 200 mg/24 hours (Day 5)

- Other therapy was continued.

- Transferred to a low-care ward (RIK5A)

### October 18, 2022 (Day 6) (RIK5A)

The patient was still feeling weak but much better. The blackish plaque remained, but there was no fever.

Vital signs: GCS 4-5-6, BP 130/70 mmHg, HR 88 beats per minute, RR 20 breaths per minute, and SpO2 98% on free air.

Laboratory examination results: Hb 9.4, Wbc 5,790, platelet count 129,000, albumin 2.69, BUN 34, Serum creatinine 1.9.

Diagnosis: Oral candidiasis, with a differential diagnosis of mucormycosis, and aplastic anemia.

Diagnosis Plan:

Smear palatal swab, palatal swab culture, palatal biopsy, and panoramic photo

Therapy:

- Gentamicin injection was stopped.

- Injection of fluconazole 200 mg/24 hours (Day 6)

- Per oral administration of aseptic gargle/12 hours

- Other therapy was continued.

### October 23, 2022 (Day 6) (RIK5A)

The patient had no complaints. The blackish plaque on the palate had peeled off and was painless.

Vital signs: GCS 4-5-6, BP 130/70 mmHg, HR 80 beats per minute, RR 20 breaths per minute, and SpO2 98% on free air.

Diagnosis: Oral candidiasis due to candida tropicalis and aplastic anemia.

Therapy:

- Injection of fluconazole 200 mg/24 hours (Day 10)

- Per oral administration of aseptic gargle/12 hours

The patient was planned for discharge and fluconazole injection was switched to oral fluconazole 200 mg/24 hours.

## DISCUSSION

Candida infections exhibit a clinical spectrum ranging from mild infections, such as oral candidiasis, to more severe infections, such as invasive fungal infections (IFIs), which can pose life-threatening risks, particularly in individuals with compromised immune systems. The occurrence of candidiasis is typically linked to an underlying cause, earning it the label "disease of the diseased." In the pathogenesis of Candida infection, systemic host factors are deemed important, and Candida species are categorized as opportunistic pathogens that cause disease when the host's defenses are compromised. These species are remarkably adaptable commensal organisms, finely attuned to the human host. Changes in the host's microenvironment that promote their growth provide ideal conditions for these pathogens to invade various sites.[10]

The transition of Candida from a benign commensal state to a pathogenic one depends on numerous predisposing factors (refer to Table 2). This transition involves an intricate interplay between the virulent attributes of the Candida species and the host's defense mechanisms. A pivotal stage in Candida colonization and infection is its attachment to the oral mucosa. This adhesion process is intricate and influenced by multiple factors, including complex interactions among the yeast itself, the host, and environmental elements such as pH, saliva, and sugars. Candida can alter its physiology and structure, transitioning from yeast to hyphal or pseudo-hyphal forms, thereby facilitating penetration to the epithelial layer. Hyphal cells possess a distinctive trait called thigmotropism, characterized by directional growth, enabling the fungus to actively infiltrate intercellular junctions. Additionally, Candida cells have a fibrillar layer on their outermost cell wall, enhancing adherence by providing resistance against dislodgment and protecting against the flushing action of saliva and phagocytosis by immune cells.[10]

This patient had predisposing systemic host factors, such as aplastic anemia, and local factors, such as poor oral hygiene. Altered immune functions, such as a significant decrease in white blood cells (leukopenia) or lymphocytes (lymphopenia), are frequently the primary reasons that make individuals more susceptible to fungal infections. Neutrophils have been demonstrated to provide protection against fungal infection. Profound and persistent neutropenia is the

primary factor that increases the risk of bacterial and invasive fungal infections in individuals with aplastic anemia.[4,12,13]

Pseudomembranous candidiasis, commonly referred to as oral thrush, stands as the most prevalent form of oral candidiasis. The surface of the oral mucosa in this condition manifests as creamy white to whitish-yellow patches, resembling cottage cheese or curdled milk. These patches primarily consist of fibrin, necrotic substances, intricate masses of fungal hyphae, and desquamated epithelial cells.[14]

The diagnosis of any kind of oral candidiasis mostly relies on clinical assessment and the accurate identification of the lesion, together with the patient's medical history. Additional adjunctive diagnostic methods, including direct smear examination, culture, and biopsy, are required to confirm the diagnosis if there are any diagnostic uncertainties.[5] From the direct examination of smears, hyphae, and yeast can be observed. Another diagnostic option for establishing superficial Candida infection is a culture examination. If there is suspicion of deep fungal infection, diagnostic options include blood culture examination and biopsy.[15] Diagnosing IFIs poses its own challenges, particularly in patients with hematologic malignancies, where symptoms are commonly nonspecific, and fever may be the sole clinical sign. The European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group (EORTC) and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (MSG) have published criteria that define IFIs within the spectrum of proven, probable, and possible categories. These criteria were last updated in 2020. Proven IFIs involve the identification of fungal elements with associated tissue damage through histopathological examination or the growth of fungi from a sterile source (e.g., blood, cerebrospinal fluid (CSF), or sinus samples). Probable IFIs are established when three elements are present: host risk factors, clinical symptoms, and mycological evidence, such as fungal antigens. The diagnosis of possible IFIs is made based on the identification of clinical criteria and host risk factors without mycological evidence. The complete criteria for diagnosing IFIs, along with host risk factors, clinical symptoms, and supporting examinations based on the consensus of EORTC and MSG, are outlined in Tables 3 and 4.[16,17]

In this case, the blackish oral thrush manifestations resembled a black fungus infection (mucormycosis); thereby, adjunctive examinations were conducted to confirm the diagnosis. Histological examination of palatal tissue scrapings, palatal scraping culture, and blood culture were performed. A panoramic X-ray examination was also conducted to assess the depth of the fungal infection. However, the patient did not meet the criteria for an invasive fungal infection.

The presentation of the fungal infection in this patient closely resembled that of mucormycosis. Mucormycosis stands as the predominant form of mold infection among individuals with aplastic anemia. The most prevalent and fatal form of this infection is rhino-cerebral/sino-orbital/rhinosinusitis. Mucor, a group of molds, primarily targets individuals with compromised immune systems, particularly those with diabetes mellitus, organ transplants, or hematological malignancies. Notably, angioinvasion followed by thrombosis is a distinctive clinical characteristic of mucormycosis. Symptoms indicative of mucor infection include periorbital facial discomfort, swelling of the eyelids, protrusion of the eyeball (proptosis), bilateral inflammation of the maxillary sinuses, headaches, tooth pain in the anterior region of the upper jaw, and, in severe cases, sudden loss of vision. Additionally, other common signs include the presence of black nasal discharge and black lesions in the palatal region of the maxilla, extending toward the soft palate.[19]

Clinically, the patient did not exhibit the symptoms of mucormycosis infection, but the appearance of black plaque on the palate strongly resembled mucormycosis, necessitating further examination to establish the diagnosis. The diagnosis of Candida infection was established after all examinations were consistent with the description of Candida despite the black coloration of the palate. Oral candidiasis with a black color, as observed in this case, has not been previously described. It could have a multifactorial cause, such as alcohol and smoking, poor oral hygiene, metabolic disorders, multiplication of saprophytic bacteria and fungi, and the accumulation of necrotic material due to a lack of normal desquamation.[20] The dark coloration observed in oral thrush may be attributed to the presence of other microorganisms' colonies within the biofilm created by Candida. It is known that Candida forms biofilm when infecting the human body. Recent studies have demonstrated that Candida infections, such as oral candidiasis, rarely occur as mono-infections. Candida synergizes with other microbes, including bacteria and fungi, to form a biofilm known as a polymicrobial biofilm infection. Some bacteria, like *Porphyromonas gingivalis* and *Streptococcus mutans*, are known to collaborate with Candida in oral diseases. These bacteria can produce black-colored pigments due to their chromogenic nature. However, this possibility is still speculative and requires further examination through RT-PCR (real-time Polymerase Chain Reaction) and bacterial culture.[21–23]

The treatment approach for candidiasis falls within three primary categories of antifungal agents: polyenes (including amphotericin B and nystatin); ergosterol biosynthesis inhibitors (azoles [such as fluconazole, miconazole, clotrimazole, ketoconazole, and itraconazole], allylamines-thiocarbamates, and morpholines); as well as the DNA analog 5-fluorocytosine, and newer options, including echinocandins (caspofungins). The selection of the appropriate antifungal treatment depends on the specific lesion and the immunological condition of the patient. For healthy individuals with superficial oral candidiasis, topical treatment is often sufficient, while immunocompromised patients with oral candidiasis may require a combination of systemic and topical therapies. The drugs of choice for oropharyngeal candidiasis are presented in Table 5.[11,15,24]

In this case, the patient was considered immunocompromised and was therefore given intravenous fluconazole, 200 mg/24 hours. The oral candidiasis clinically resolved after 11 days of therapy.

## SUMMARY

A case of a patient with oral candidiasis with an atypical manifestation of blackish color has been reported. The patient's predisposing factors included aplastic anemia, which caused neutropenia, and poor oral hygiene. Blood culture results revealed no fungal growth, but a palatal scrape culture revealed an infection of Candida tropicalis that was sensitive to fluconazole and amphotericin B. After 11 days of fluconazole administration, the patient's oral candidiasis resolved, and the patient was discharged.

## ACKNOWLEDGEMENTS

The authors would like to express their gratitude to the staff of the Department of Internal Medicine, Faculty of Medicine, Universitas Airlangga; and the Division of Tropical and Infectious Disease, Department of Internal Medicine, Dr. Soetomo General Academic Hospital Surabaya, for their support during this study.

## CONFLICTS OF INTEREST

The authors have stated that they do not have any conflict of interest regarding this study.

## FUNDING SOURCE

There was no specific funding from governmental, commercial, or non-profit entities for this study.

## AUTHORS' CONTRIBUTION

All authors contributed to article preparation and paper revision and have collectively assumed responsibility for all aspects of this study.

## DATA AVAILABILITY

The article contains all the necessary data to support the results, and no supplementary source data is needed.

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**Cite this article:** Nahlalogi P, Bramantono. Atypical Manifestation of Oral Candidiasis in Patient with Aplastic Anemia. Pharmacogn J. 2024;16(5): 1143-1149.