

Colitis as a clinical manifestation of disseminated histoplasmosis in HIV-positive patient: a case report

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Abstract

Introduction: Disseminated histoplasmosis is a systemic fungal infection resulting from co-infection in severely immunosuppressed patients, such as those with human immunodeficiency virus (HIV) or acquired immunodeficiency syndrome.

Case report: In this case report, a 49-year-old female HIV-positive patient, with complaints of black stool with fresh blood since two months was presented. Hemorrhoidectomy, followed by colonoscopy and biopsy were performed, confirming histoplasmosis infection diagnosis.

Conclusions: The spectrum of clinical manifestations of disseminated histoplasmosis in HIV-infected patients are non-specific. Most disseminated histoplasmosis patients suffer from gastrointestinal problems. Anti-fungal therapy in histoplasmosis shows a good clinical response.

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Key words: colitis, disseminated histoplasmosis, HIV.

Introduction

Disseminated histoplasmosis (DH) is a systemic fungal infection resulting from co-infection in severely immunosuppressed patients, such as those with human immunodeficiency virus (HIV) or acquired immunodeficiency syndrome (AIDS) [1, 2]. Frequently, DH infection is also co-infected with tuberculosis (TB), causing atypically severe clinical presentation and requiring comprehensive treatment [2-4].

There are no worldwide data on histoplasmosis. However, in Southeast Asia, 233 cases in Thailand, 76 in Malaysia,

48 in Indonesia, 21 in Singapore, and several cases in other countries were reported [5, 6]. Most of the histoplasmosis cases reported are DH [5, 7].

In general, limited access to appropriate anti-fungal therapy, lack of effective diagnostic methods for rapid detection, and co-infection with infectious diseases, especially TB, can affect clinical outcomes leading to high mortality of DH patients co-infected with HIV infection [8, 9].

This case report aimed to provide an overview of the difficulties in establishing the diagnosis of DH in patients with immunodeficiency.

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Case report

An unmarried 49-year-old woman presented to emergency department with a complaint of black stool with blood. This condition has been irregular since two months, and associated with around 10 kg weight loss in the past two months. The patient had a history of hemorrhoids, and had a surgery two months ago. She previously worked as a cafe employee in a tourist area, and had a history of more than one sexual partner.

The patient had pale conjunctiva, and oral plaque was found in the mouth. On physical examination, she was alert and conscious, with vital signs within normal ranges. On rectal examination, stool mixed with red blood was found. Complete blood count showed lymphopenia, normocytic

normochromic anemia (hemoglobin, 9.1 g/dl), hypoalbuminemia (albumin, 2.34 g/dl) with an inverse globulin ratio (globulin, 4.27), hyponatremia (serum sodium, 129 mmol/l), prolonged hemostasis with partial thromboplastin time (PPT) = 14.5 seconds and activated partial thromboplastin time (APTT) = 50.9 seconds, and reactive anti-HIV antibody test, with HIV RNA viral load of 2.82×10^5 copies/ml. Chest X-ray showed bilateral nodules in the lung, suspicious of nodular-type lung metastases (Figure 1). Colonoscopy results revealed internal hemorrhoids, rectal polypsis, and colitis in the transverse and ascending colon (Figure 2). Biopsy and examination histopathology confirmed histoplasmosis (Figure 3).

The patient was diagnosed with the transverse and descending colon colitis due to histoplasmosis, pre-antiretroviral (ARV) therapy stage IV HIV infection (WHO), oral candidiasis, malnutrition, and hypoalbuminemia. Moreover, 0.9% NaCl infusion therapy (20 drops per minute), and high calorie and high protein diet were administered, with 400 mg fluconazole every 24 hours intravenously and 960 mg co-trimoxazole every 24 hours. ARV therapy was planned to initiate after resolving the acute phase of fungal infection.

Discussion

DH can appear after acute lung infection or may be latent for several years after histoplasmosis infection, because there are no initial significant symptoms, which only appear when the patient is immunocompromised [9-11]. Patients with immunodeficiencies, newborns (< 1 year old), and elderly (> 50 years) are those with increased risk of developing DH. Moreover, environmental factors, such as living in endemic area, are considered a risk factor as well [9, 11]. In the

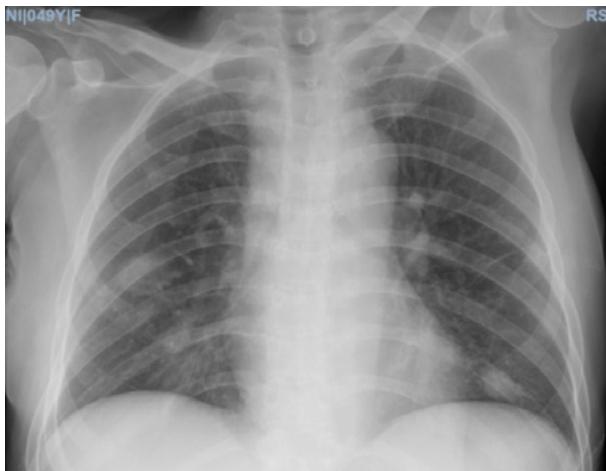


Figure 1. Chest X-ray with suspected nodular-type pulmonary metastases

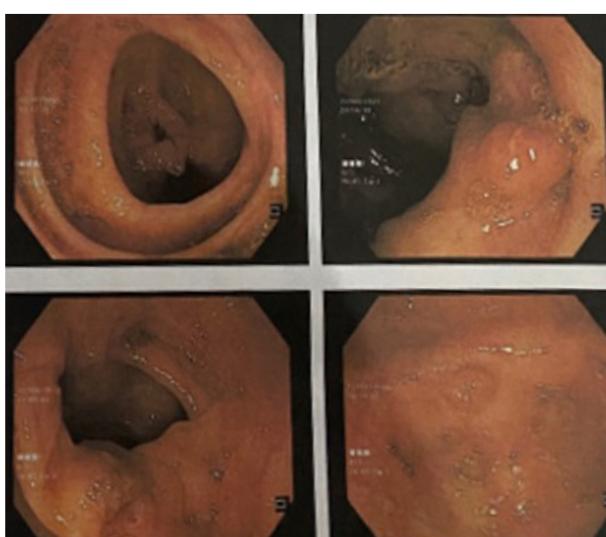


Figure 2. Colonoscopy with internal hemorrhoids, rectal polypsis, and colitis in the transverse and ascending colon

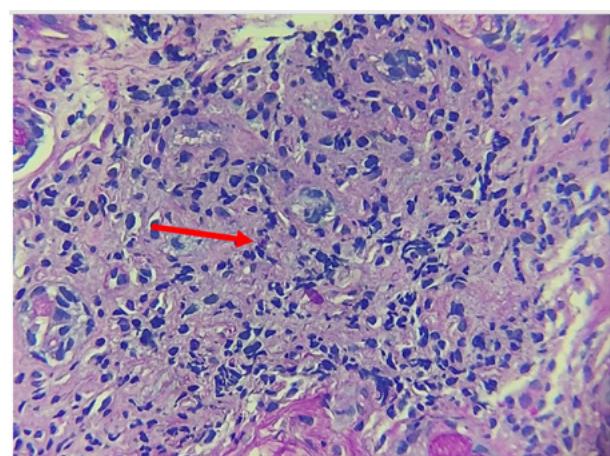


Figure 3. Small-sized micro-organisms (parasites) seen between the connective tissue stroma and inflammatory cells, with round oval morphology and clear area around it. Some of the nucleus are located eccentrically (red arrow), suggesting histoplasmosis

current case, the patient was diagnosed with HIV, which is considered a high-risk for histoplasma infection.

In general, DH patients complain of clinical manifestations, such as fever, weight loss, night sweats, coughing, and shortness of breath [10, 11]. Based on the current case, the patient only complained of significant weight loss within two months, without fever or shortness of breath. Colonoscopy examination revealed internal hemorrhoids, rectal polyposis, and colitis in the transverse and ascending colon. In DH, the majority of complaints involve the gastrointestinal tract [12-14]. Endoscopic examination performed in an area with a lesion will show segmental inflammation, ulcerative lesions, and polypoid masses, which are often mistaken for a malignancy or inflammation of the gastrointestinal tract [15]. Nonetheless, most patients with gastrointestinal manifestations of DH show usually sub-clinical symptoms.

The spectrum of clinical manifestations of DH in HIV-infected patients are non-specific; therefore, it is difficult to distinguish it from other infectious diseases, such as disseminated TB [16]. Laboratory findings in patients with DH often show pancytopenia, elevated liver enzymes, increased C-reactive protein (CRP), lactate dehydrogenase (LDH), and ferritin serum. Such non-specific results cause difficulties in making the right diagnosis, especially in patients with reduced immune system [2]. The proven gold standard diagnostic criteria for histoplasmosis are outlined by the European Organization for Research and Treatment of Cancer and the Mycoses Study Group Education and Research Consortium (EORTC/MSGERC), and include a positive culture, histopathology, or finding of *Histoplasma capsulatum* var. *capsulatum* (HCC) on direct microscopy assessment from clinical specimens. If all proven criteria are unavailable or show negative results, the patient is immunocompromised with a typical clinical picture, environmentally exposed to fungi, and histoplasma antigen found in body fluids, then the patient is classified as a probable case of DH [17].

In the current case, the presence of rectal polyposis and colitis in the transverse and ascending colon indicated that the infection has spread from the initial fungal respiratory infection; moreover, the patient was diagnosed with HIV infection. Hence, the diagnosis of DH was established.

Another method supporting the diagnosis of DH is detecting histoplasma antigen circulating in the urine, using enzyme-linked immunosorbent assay (ELISA) method, which was proven very efficient (95%). However, this method is hampered by the limited availability of diagnostic tools [7]. Serological tests that detect antibodies can provide a rapid diagnosis. Recently formed antibodies can be found in the peripheral blood approximately 4 to 8 weeks after exposure to HCC and persist for years, making serological tests suitable for diagnosing sub-acute and chronic infection of histoplasmosis. However, this method has significant limitations, especially in immunocompromised patients, who cannot enhance the humoral immune response, giving false negative results.

Anti-fungal therapy in histoplasmosis is indicated in cases with severe or moderate acute lung infections, DH, and histoplasmosis of the central nervous system. Anti-

fungal agents, which have been proven effective, are amphotericin B and itraconazole [18]. The main azole group for the treatment of histoplasmosis is itraconazole, which can be administered for 6-9 months. Fluconazole can be used as a second-line agent, but is not as effective as itraconazole. Other azole anti-fungal agents, such as voriconazole and posaconazole, may be effective in treating histoplasmosis [2, 19]. In HIV-positive patients, it is essential to ensure that CD4+ cell count is > 150 cells/ μ l, HIV viral load is < 50 copies/ml, and the patient is on antiretroviral therapy before discontinuing treatment for histoplasmosis. If positive evidence of histoplasma infection is still found, the treatment should be continued.

The initiation of ARV therapy in histoplasmosis treatment is still a controversy. Some study advise to delay ART until the acute phase of fungal infection is under control. The decision is made based on clinical case, considering the severity of fungal infection, patient overall condition, and the risk of immune re-constitution of inflammatory syndrome (IRIS) [19].

Conclusions

Most DH patients present with gastrointestinal problems. In this case report, an HIV-positive patient (WHO clinical stage IV HIV infection) with descending transverse colon colitis due to histoplasmosis is presented. The spectrum of clinical manifestations of DH in HIV-infected patients are non-specific. Colonoscopy and biopsy of specimens support the diagnosis of histoplasmosis. Anti-fungal therapy in histoplasmosis shows a good clinical response.

Disclosures

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2. Assistance with the article: None.
3. Financial support and sponsorship: None.
4. Conflicts of interest: None.

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