

# Disseminated cutaneous histoplasmosis in CD4+ lymphocytopenia patient: case report.

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## ABSTRACT:

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Histoplasmosis classically presents as opportunistic mycosis caused by the intracellular dimorphic fungus *Histoplasma capsulatum* and is frequently associated with HIV infection and other immunocompromised states. Disseminated histoplasmosis presenting as cutaneous lesions in an immunocompetent host is very rare. We report a case of disseminated cutaneous histoplasmosis presenting with multiple ulcer in patient with suspected CD4+lymphocytopenia.

**Key words:** Disseminated histoplasmosis, CD4+ lymphocytopenia

## บทคัดย่อ:

พริมรตา ตียะจินดา, จักรพงษ์ ชุนหเสวี รายงานผู้ป่วยโรค DISSEMINATED CUTANEOUS HISTOPLASMOSIS IN CD4+ LYMPHOCYTOPENIA PATIENT วารสารโรคผิวหนัง 2559; 32: 274-278.

สถาบันโรคผิวหนัง กรมการแพทย์ กระทรวงสาธารณสุข

Histoplasmosis เป็นโรคติดเชื้อราในกลุ่ม opportunistic fungi ที่มีสาเหตุมาจาก intracellular dimorphic fungi ที่ชื่อว่า *Histoplasma capsulatum* ซึ่งพบบ่อยในกลุ่มผู้ติดเชื้อ HIV และผู้ที่มีภาวะภูมิคุ้มกันบกพร่อง การติดเชื้อ Histoplasmosis แบบแพร่กระจายหรือ Disseminated histoplasmosis ที่มาด้วยอาการแสดงทางผิวหนังในผู้ป่วยที่มีภูมิคุ้มกันปกติพบได้ค่อนข้างน้อย รายงานฉบับนี้เป็นการนำเสนอผู้ป่วย disseminated cutaneous histoplasmosis ที่มาด้วยแผลที่ผิวหนังในผู้ป่วยที่สงสัยว่าจะมีภาวะ CD4+lymphocytopenia ร่วมด้วย

**คำสำคัญ:** การติดเชื้อ Histoplasmosis แบบแพร่กระจาย, CD4+ lymphocytopenia

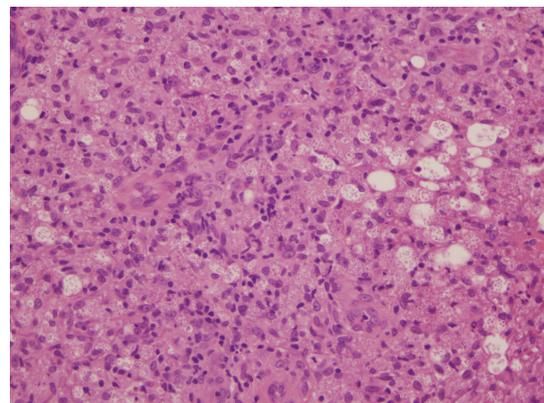
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A 66 year-old Thai man came to our patient clinic with multiple erythematous ulcers on trunk and extremities for 4 months. They gradually increased in size and number. He was treated with oral antibiotics but the lesions were not improved. He denied fever, malaise, night sweat, weight loss, or other constitutional symptoms. Dermatological examination revealed generalized, multiple discrete well-defined ulcerated indurated erythematous plaques with some hemorrhagic crust with yellowish debris with multiple indurated erythematous papules on trunk and extremities(Fig.1). A skin biopsy was performed from the arm and abdomen in which the hematoxylin and eosin-stained sections displayed slightly acanthotic epidermis with hyperkeratosis. The dermis showed multiple patchy infiltration of mixed inflammatory cells particularly of lymphocytes and histiocytes. Intracytoplasmic and extracytoplasmic organisms were noted(Fig.2). They were small rounded with capsules. GMS, PAS, methenamine silver stain showed organisms in the macrophages and freely within the tissue. Tissue culture grew *Histoplasma capsulatum*.



**Fig.1** Multiple discrete well-defined ulcerated indurated erythematous plaques with some hemorrhagic crust with yellowish debris with multiple indurated erythematous papules on trunk and extremities.



**Fig. 2** Histopathological image showing small rounded intracytoplasmic and extracytoplasmic organisms with capsules (hematoxylin and eosin, original magnification x40)



Routine investigations revealed haemoglobin level of 12 g/dL and white blood count 4400/cu.mm. HIV testing was done twice and HIV P24 antigen level was negative. Ultrasonography of the whole abdomen was unremarkable. Computed tomography scan of upper abdomen was normal. His CD4+ T-cell count was at 70 / $\mu$ l [700-1,100], CD8+ T-cell 760 / $\mu$ l. [500-900]. The patient was treated with intravenous amphotericin B 0.7 mg/kg daily for 4 weeks followed by oral itraconazole 200 mg twice daily. After 2 months of treatment, regression of skin lesion was observed.

#### Discussion

Histoplasmosis classically presents as opportunistic mycosis caused by the intracellular dimorphic fungus *Histoplasma capsulatum* and is frequently associated with HIV infection and other immunocompromised states.<sup>1</sup>

The clinical spectrum are vary including asymptomatic, acute pulmonary histoplasmosis, chronic pulmonary histoplasmosis, acute progressive disseminated histoplasmosis, chronic progressive disseminated histoplasmosis and primary cutaneous histoplasmosis.<sup>2</sup> Our patient presented with multiple ulcerated erythematous plaques on trunk and extremities. Skin biopsy and clinical manifestation were compatible with histoplasmosis. The patient underwent a series of investigations to look for other organ involvements. All of them were

normal. This patient falls into the category of chronic disseminated cutaneous histoplasmosis.<sup>3</sup> Therapeutic options for cutaneous histoplasmosis depend on the extent and severity of the disease. For widespread areas, oral and intravenous therapy has been beneficial. The major choices for therapy are amphotericin B or an azole drug, particularly itraconazole for at least 12 months.<sup>4,5,6</sup>

Chronic disseminated histoplasmosis usually occurs against a background of immune suppression, such as human immunodeficiency virus (HIV), malignancy, or diabetes. Approximately 20% have no identifiable risk factor.<sup>3</sup> Considering the possibility of disseminated histoplasmosis, the patient underwent a series of investigations to look for any immune dysfunction. All of the investigations including immunoglobulin, complement and antibody levels were normal. HIV testing was done twice and HIV P24 antigen level was negative. However CD4 count were consistent low at 70/ $\mu$ l with normal CD8+ counts. In our case, a differential diagnosis for lymphocytopenia includes transient immunosuppression from infection or idiopathic CD4+ lymphocytopenia. For transient immunosuppression from infection, several reports showed that CD4 T lymphocyte value was however back to the normal in the period varying from three weeks up to nine months.<sup>7-10</sup>

For idiopathic CD4<sup>+</sup> lymphocytopenia, diagnostic criterias include

(1) CD4<sup>+</sup> T-lymphocyte depletion

- absolute CD4<sup>+</sup> T-lymphocyte level <300  $\mu\text{L}^{-1}$  or <20% of total lymphocytes

- two times, at least 6 weeks apart

(2) no evidence of HIV infection

(3) the absence of any defined immunodeficiency or therapy associated with depressed levels of CD4 T-cells<sup>12</sup>

The definite diagnosis should be confirmed by flow cytometry at the end of treatment. If the CD4 cell count persistent low, the diagnosis is idiopathic immunosuppression. However if CD4 level is normal, transient immunosuppression from infection should be preferred. In this patient, the diagnosis and follow-up examination of CD4 is still on process. Our patient has been treated with intravenous amphotericin B for 4 weeks followed by oral itraconazole 200 mg twice daily. The patient response well to itraconazole. All the cutaneous lesions have disappeared at 2 months, except for hypertrophic scars at the sites of previous lesions. There has been no adverse drug reaction to itraconazole and his relevant laboratory values remain unchanged. In the third month,

CD4 was improved but was not yet normal at 300 cells per microliter. We plan to repeat CD4 level after a full 12-months of treatment.

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