# CHRONIC DISSEMINATED HISTOPLASMOSIS

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## ABSTRACT

Histoplasmosis is a disease of varied clinical and roentgenographic manifestations caused by the dimorphic fungi Histoplasma capsulatum and its variant H. duboisii. The former is much the more important organism of the two and exists in its mycelial form as a saprophyte in soil, and as an oval, 2-to 5-um yeast form in infected animals and humans (1).

A simple classification of histoplasmosis[1] is shown in the table 1.

A case of chronic disseminated histoplasmosis was presented and was considered rare in Thailand.

## CASE REPORT

A 60-year-old male patient had chronic ulcer at the tongue for 2 months prior to the admission. PA chest film showed diffuse reticulonodular lesions in both lungs at the upper and middle zones and less at both lower zones (Fig.1). The patient was treated as a tuberculosis case without improvement. Sputum AFB was negative. Biopsy from the ulcer of the tongue showed positive Histoplasma capsulatum.The patient was responded to the Itraconazole which is an antifungal agent. Follow-up chest film 6 months (Fig.2) and three years later (Fig.3) showed slow clearing of the infiltration of both lungs.

## DISCUSSION

Disseminated histoplasmosis is the less common form of histoplasmosis. It develops primarily in persons with defective host immunity, including infants with immature systems, compromised hosts, such as corticosteroid treated organ recipients and HIV infected persons, and individuals with either measurable defect or a highly selective defect, such as the failure of host lymphocytes to undergo in vitro blast transformation upon exposure to H. capsulatum antigen (2). The severity of the symptoms and signs of disseminated disease and the attendant histopathologic findings in a given patient mirror the level of immunocompetence of the individual. In patients with the mildest and most chronic forms of disseminated disease, well developed tuberculoid granulomas, typical of the response in normal hosts, can be found in reticuloendothelial tissues. In contrast, in patients with overwhelming multiorgan histoplasmosis superimposed on a severely immunocompromising condition, such as AIDS, the host response is suboptimal, with the pathologic findings consisting of large numbers of diffusely scattered macrophages filled with yeast forms and minimal or no granuloma formation.

Fever, chills, and other nonspecific constitutional symptoms predominate. Enlargement of the liver and spleen is common; less frequently, peripheral lymphadenopathy is present. Mucous membrane ulceration, especially of the oropharynx, occurs in about 25 to 75 per cent of patients with subacute disease. Laboratory clues may include anemia, leukopenia and thrombocytopenia as evidence of impaired bone marrow function or replacement of the marrow, elevated alkaline phosphatase levels, elevated erythrocyte sedimentation rate, and electrolyte abnormalities suggestive of adrenal insufficiency. Chest x-ray films may be normal or show findings suggestive of earlier primary infection or an intersititial pneumoitis consistent with hematogenous spread of infection. Unusual syndrome, including cardiac involvement

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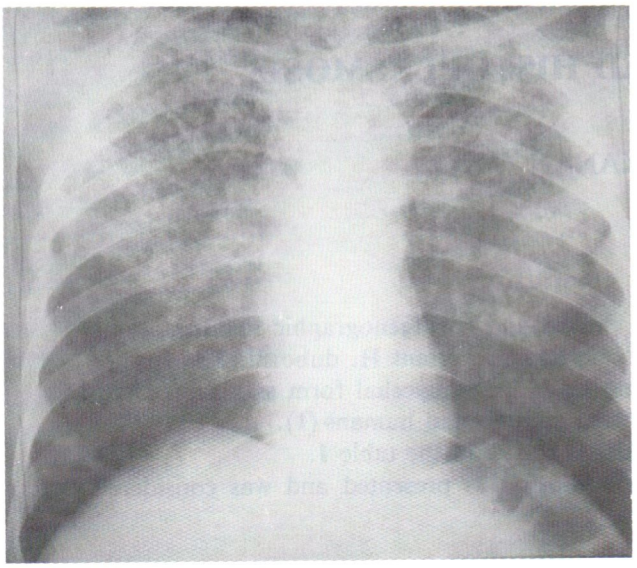

Fig.1 PA chest film on the admission day showed diffuse reticulonodular lesions in both lungs at upper and middle zones and less at both lower zones.

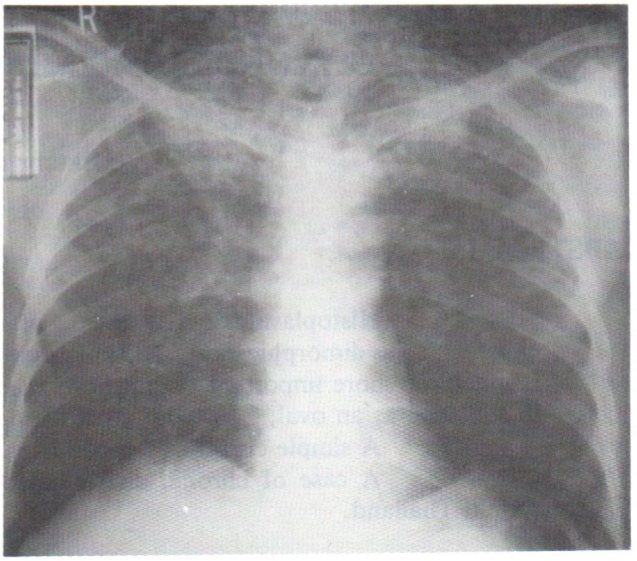

Fig.2 Partial clearing of pulmonary infiltration, 6 months post treatment for Histoplasmosis.

with culture-negative endocarditis associated with large emboli, gastrointestinal involvement with bleeding secondary to mucosal ulceration, or central nervous system involvement with chronic lymphocytic meningitis (3-6).

Chronic pulmonary histoplasmosis often occurs in men with underlying chronic obstructive pulmonary disease and resembles pulmonary tuberculosis in symptomatology and radiographic manifestations although this type of histoplasmosis tends to be milder and more indolent than that of tuberculosis. The pathogenesis and course of chronic pulmonary histoplasmosis are highly complex; pathologic studies indicate two basic lesions. An interstitial pneumonitis featuring mononuclear infiltration, periarteriolar inflammation, areas of infarctlike necrosism and few organisms is characteristic of the early lesion. The inflammatory process often surrounds apical emphysematous blebs and bullae. In contrast, the chronic lesion is manifested by organization of diseased tissue, with prominence of giant cells and progressive cavitation. Organisms are typically found in the necrotic lining or in surface exudate. In the thicker walled cavities, infection is persistent, with continuing necrosis, leading to progressive cavity enlargement. In 80 per cent of cases, the pneumonitis stage tends to resolve spontaneously over 2 to 3 months, with a small fibrotic residuum, whereas the cavitation stage, especially that associated with thick-walled cavities, tend to be relentlessly progressive, leading to destruction and diminution of lung parenchyma, fibrosis and respiratory insufficiency (1, 7-9).

The presented patient had ulcer of the tongue and interstitial process in the lungs. The patient had no prior pulmonary emphysema nor evidenced of defective immunity. The healing of the tongue ulcer was complete while the pulmonary infiltration resolved satisfactorily but slowly. The complete disappearance of the infiltration was not seen in this patient; he did not come for follow-up after the last film shown in fig.3

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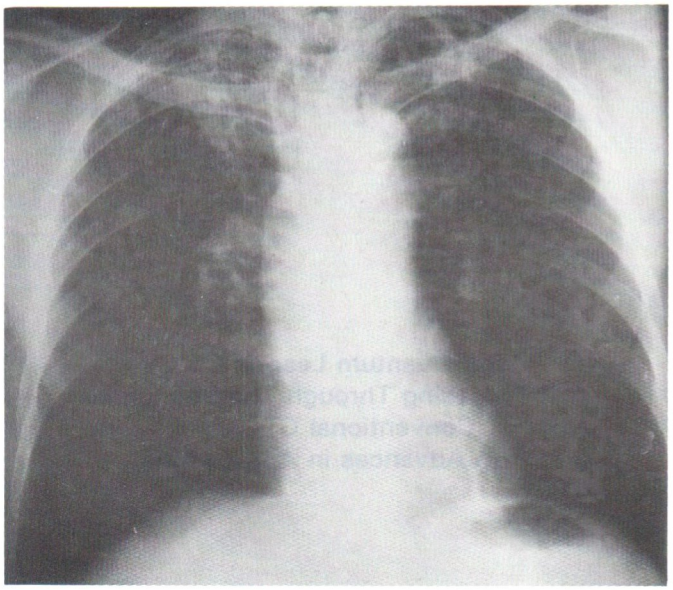

Fig.3 Incomplete clearing of the lesions after three years indicates slow process of clearing.


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**TABLE 1. CLASSIFICATION OF HISTOPLASMOSIS**

- Asymptomatic
- Symptomatic
  - Acute Histoplasmosis
    - Acute "flu-like" syndrome
    - Acute pulmonary histoplasmosis
    - Acute diffuse nodular disease (epidemic)
    - Histoplasmoma
    - Lymph node involvement
  - Chronic Histoplasmosis
    - Chronic pulmonary histoplasmosis
    - Mediastinal histoplasmosis
      - Pericarditis
      - Esophageal encroachment
      - Superior vena cava obstruction
      - Pulmonary arterial and venous obstruction
      - Tracheal and major airway encroachment
  - Disseminated Histoplasmosis
    - Acute
    - Subacute
    - Chronic