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Indigenous case of disseminated histoplasmosis: A possible underdiagnosed disease in Taiwan

KEYWORDS
Galactomannan;
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Dear Editor,

Histoplasmosis diagnoses are difficult in Taiwan due to a lack of clinical suspicion and quick diagnostic tools. Herein, we report a case of disseminated histoplasmosis without known immunocompromised status.

A 74-year-old man from southern Taiwan presented with generalized weakness and intermittent cough lasting two months. He developed a fever one day earlier. His medical history included type 2 diabetes mellitus (HbA1C, 5.7%) and chronic kidney disease, stage 3. He owned a steel factory across from a poultry farm but had retired decades ago. He had traveled to southeast Asia and China decades ago for few days. During hospitalization, he had persistent fever despite broad-spectrum antibiotic treatment. A hemogram showed leukopenia and anemia. Blood tests for human immunodeficiency virus infection were negative. Positron emission tomography revealed increased ^{18}F-fluorodeoxyglucose uptake in the left upper lung field, several lymph nodes, and liver (Fig. 1A). Bronchoscopy was performed later, and the obtained bronchoalveolar-lavage (BAL) fluid was cloudy. The optical density index was 0.67 for BAL fluid galactomannan (Platelia Aspergillus EIA; Bio-Rad) and 6.7 for serum galactomannan. Bone marrow examination and paracentesis were performed. Gram, Gomori methenamine–silver, periodic-acid Schiff, and acid-fast staining of the bone marrow specimens were all negative. The patient received intravenous voriconazole for suspected invasive aspergillosis; however, he subsequently experienced clinical deterioration and died of respiratory failure and septic shock. A blood culture, sampled one day before his death, initially revealed a yeast-like organism but grew *Histoplasma capsulatum* (confirmed by the sequence of internal transcribed spacers of ribosomal DNA) after one week of incubation (Fig. 1B). Ascites and bone marrow cultures, incubated for one and three weeks, respectively, also grew *H. capsulatum*. Thus, disseminated histoplasmosis was diagnosed.

Histoplasma capsulatum is a thermally dimorphic fungus mostly found in the United States and Central and South America. Sporadic cases have been reported in some southeast Asian countries, but rarely in Taiwan. The estimated prevalence rate of histoplasmosis was 0.24/100,000 in 2013 (57 cases) according to national insurance data of Taiwan.[1] There were 12 case reports of histoplasmosis in PubMed within the past 30 years, of which no travel history to foreign countries was reported in three cases.[2,3] In one case, the patient may have developed histoplasmosis while renovating a chicken farm.[2] However, data on environmental *Histoplasma* in Taiwan are lacking.

For patients without known immunocompromised conditions, evaluation of anti-interferon-γ autoantibodies is recommended. Interferon-γ plays a critical regulatory role in macrophage-mediated killing and granuloma formation in response to important intracellular pathogens including *Mycobacterium*, *Salmonella*, and *Histoplasma*. Furthermore, anti-interferon-γ autoantibodies have been strongly associated with disseminated histoplasmosis in previously healthy adults.[4] However, the test could not be performed in this case because of the patient's death.

Galactomannan is a component of *Aspergillus* spp. Cell wells. Other fungi, including *H. capsulatum*, have similar cell wall structures and exhibit cross-reactivity.[5] Here, microscopic examination of blood culture revealed a yeast-like organism initially but with serum galactomannan positivity; *Histoplasma* should be considered.

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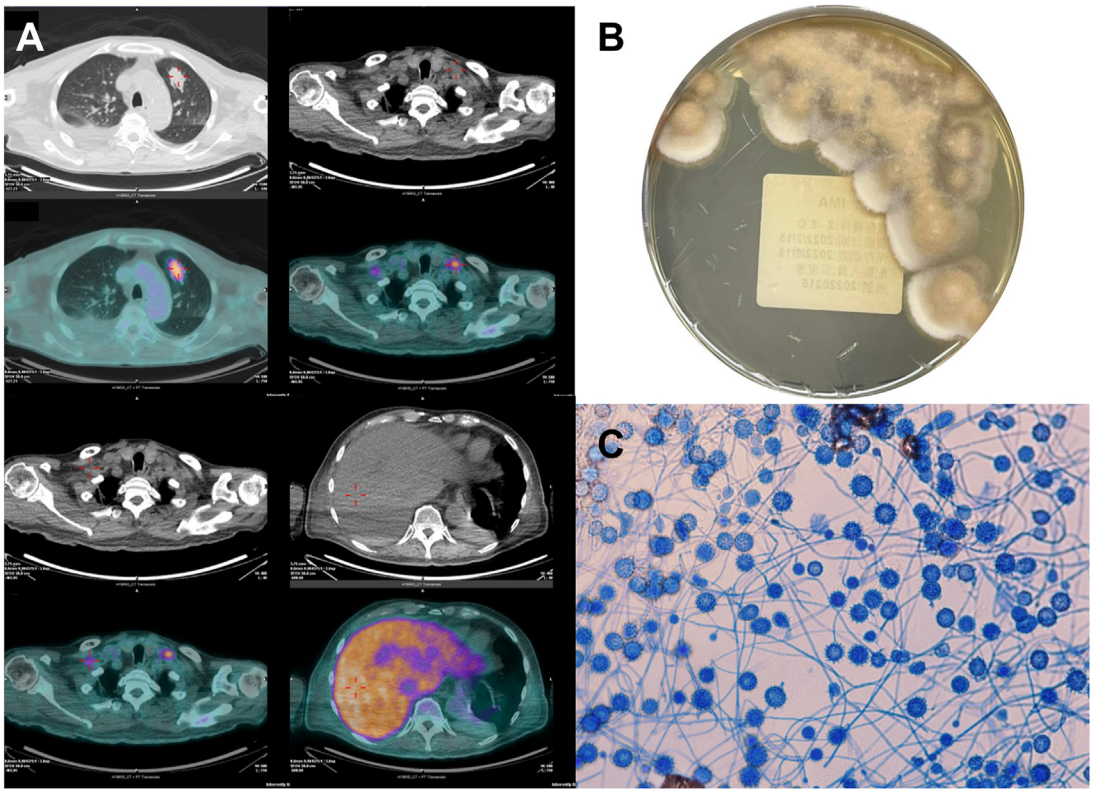

Figure 1. Disseminated histoplasmosis and culture from blood. (A) Positron emission tomography scan showing ^{18}F-fluorodeoxyglucose uptake in the left upper lung field, multiple lymph nodes, and liver. (B) Colony of *Histoplasma capsulatum* on inhibitory mold agar: white, suede-like to cottony with a pale yellow-brown reverse. (C) Lactophenol blue stain of *Histoplasma capsulatum* from blood culture showing the presence of rounded, single-celled, and tuberculate macroconidia.

Histoplasmosis may be underdiagnosed in Taiwan due to a lack of a quick diagnostic tools and because it is considered a non-endemic disease. Further investigations on environmental surveillance are necessary.

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Declaration of competing interest

The authors have no conflicts of interest to declare.

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Chien-Hsiang Tai
Division of Infectious Diseases, Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan

Pei-Lun Sun
Department of Dermatology and Research Laboratory of Medical Mycology, Chang Gung Memorial Hospital, Linkou Branch, Taoyuan, Taiwan
College of Medicine, Chang Gung University, Taoyuan, Taiwan

Chun-Chih Chien
Department of Laboratory Medicine, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan

Chien-Hua Chiu
College of Medicine, Chang Gung University, Taoyuan, Taiwan
Division of Nephrology, Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan

Yi-Chun Chen*
Division of Infectious Diseases, Department of Internal Medicine, Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan

*Corresponding author. No.123, Dapi Rd., Niaosong Dist., Kaohsiung city, 833, Taiwan. Fax: +886 7 7322402.
E-mail address: sonice83@cgmh.org.tw (Y.-C. Chen)

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