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A Young Man with High-grade Fever and HIV infection

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Abstract:

A 23-year-old man, a hilltribe in northern Thailand with HIV infection but poor compliance to antiviral treatment presented with acute onset of fever, fatigue with palpitation. He also experienced easily fatigue and tiredness for 1 month. He went to local hospital and was treated symptomatically without any improvement. Then he went to another hospital for management. Initial investigation showed anemia and thrombocytopenia. The bone marrow examination revealed yeast-like microorganism with binary fission. Final diagnosis of disseminated talaromycosis (penicillosis) was made. So, in case of fever of unknown origin in HIV-infected patients, bone marrow examination should be performed which can be helpful for definite diagnosis.

Keywords: HIV infection, Disseminated talaromycosis, High-grade fever

Introduction

Untreated HIV-infected patients usually have fever which some of them are initially unable to identify the causes. Most of them are from opportunistic infection (OI) due to bacteria, viruses, fungi, and protozoa. In Thailand, there are high incidence of some OI such as mycobacterial infection (tuberculosis and atypical mycobacterium), cryptococcal meningitis, disseminated histoplasmosis and talaromycosis (penicillosis). Although other infections such as Pneumocystis carinii, toxoplasmosis, parvovirus B19 and CMV infection can be encountered. Besides infection, HIV-infected patients are also having higher incidence of lymphoma which can cause fever. The problem of physicians taking care of these patients is unable to diagnose the causative infection. Some physicians use therapeutic diagnosis with antituberculosis drugs. This method can cause delayed diagnosis and increased morbidity and mortality. Prompt investigation with rapid result is needed especially in resource-restricted rural hospital.

Case Presentation

A 23-year-old man, a hilltribe in northern Thailand with HIV infection but poor compliance to antiviral treatment presented with acute onset of fever, fatigue with palpitation and non-productive cough for 1 month. He had no diarrhea, nausea

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or vomiting. He went to the local hospital and received symptomatic treatment without improvement. So, he came to another hospital for management. He had previous admission to the hospital 3 months prior to this admission because of anorexia, weight loss, non-productive cough, low grade fever and was diagnosed AIDS with pneumocystis carinii infection. On admission to this hospital, vital signs showed body temperature of 37.8°C (after taking paracetamol), heart rate 120/minute, blood pressure 113/74 mmHg, respiration 20/min, height 159 cm, weight 44 kgs with BMI of 17.4 kg/m^2. He was moderately anemic without jaundice. He had no palpable lymphadenopathy but palpable liver and spleen 4 cm. and 6 cm. respectively below costal margins. No any skin lesion was detected. Investigation revealed Hct 26%, Hb 8.0 g/dL, WBC 5.39 x 10^9/L, PMN 76%, L 9%, M 3%, E 11%, platelet 100.0 x 10^9/L, MCV 70 fL, MCH 23 pg, BUN 14 mg/dL, Cr 0.77 mg/dL, GFR 128 mL/min, Na 126 mmol/L, K 3.9 mmol/L, Cl 94 mmol/L, CO2 25 mmol/L, total protein 6.6 g/dL, albumin 3.2 g/dL, globulin 3.4 g/dL, total bilirubin 0.3 mg/dL, direct bilirubin 0.1 mg/dL, AST 36 U/L, ALT 23 U/L, ALP 59 U/L, CD4 36/μL. Chest x-ray: no pulmonary infiltration. Ultrasound of whole abdomen: hepatomegaly with diffuse increased parenchymal echogenicity and splenomegaly with wedge shaped patchy hypoechogenicity, possible infarction and several enlarged lymph nodes along periportal regions. Review of blood smear found mild hypochromic red blood cells with frequent polychromasia. Bone marrow aspiration and biopsy was performed. The finding revealed hypercellular bone marrow with intracellular yeast-like organisms, some had binary fission compatible with talaromycosis (penicillosis) as shown in Figure 1. So, the patient was started with Amphotericin B 1 mg/kg on the admission day. On the following day, he was doing better with fever down. He subsequently received oral fluconazole. A week later, blood culture for fungus was reporting *Penicillium marneffei*. The bone marrow biopsy came back 1 week later and revealed talaromyces as in Figure 2, 3 and 4.

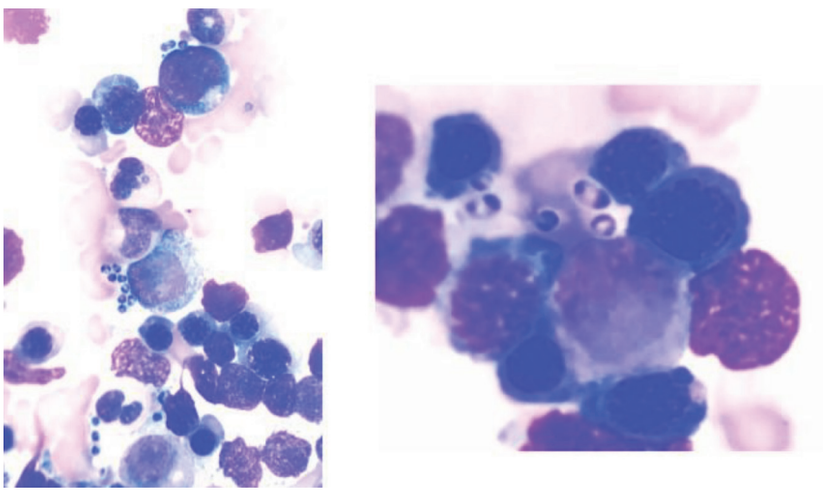

Figure 1 Bone marrow smear shows intracellular yeast-like organisms with binary fission consistent with talaromycosis (penicillosis). (left x 40, right x100)

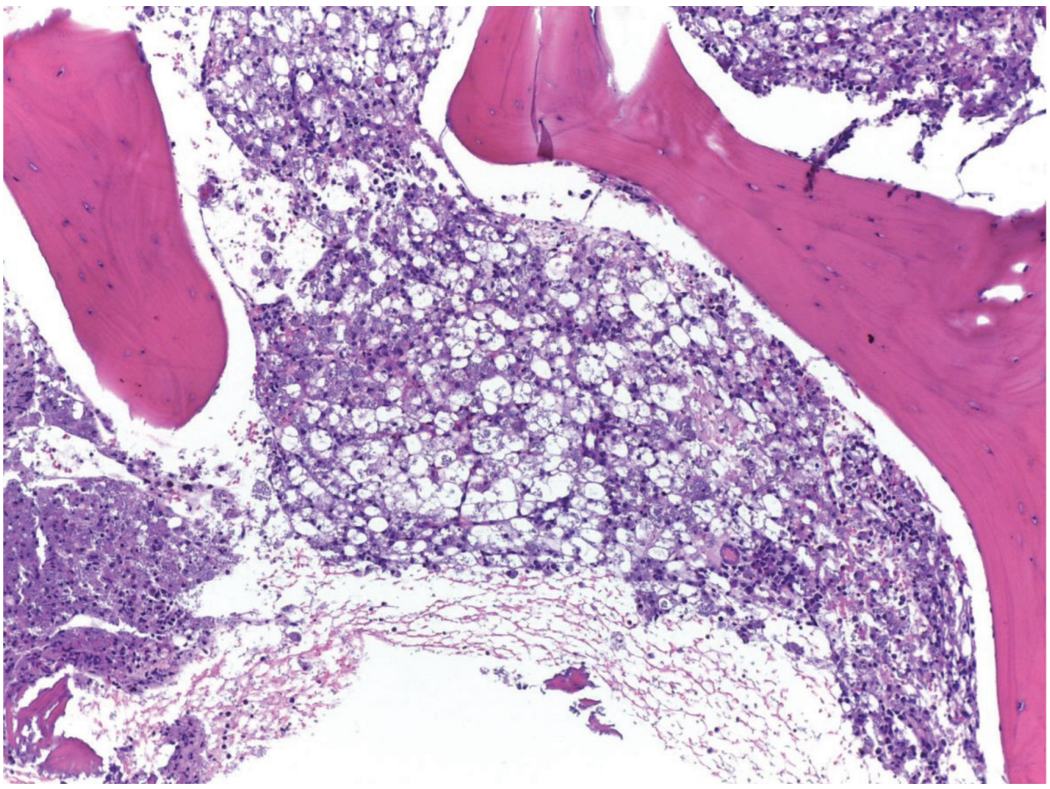

Figure 2 The bone marrow biopsy x40 shows marked hypercellularity.

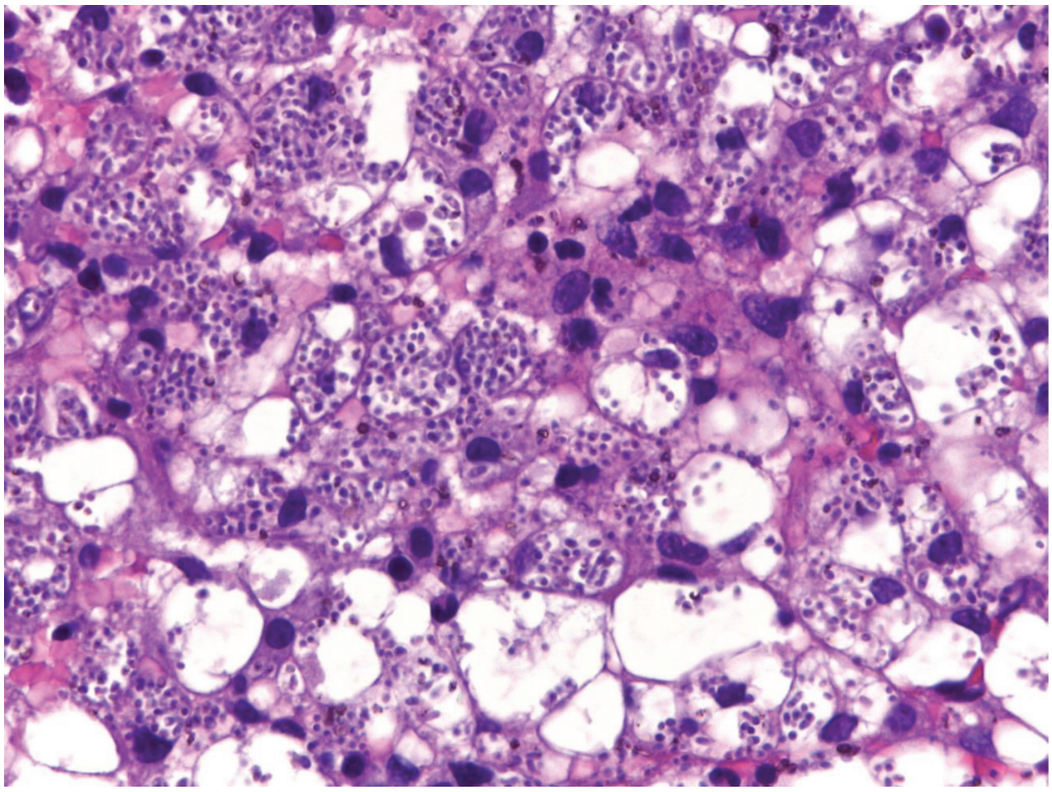

Figure 3 The bone marrow biopsy x 100 shows many aggregates containing many yeast-like particles.

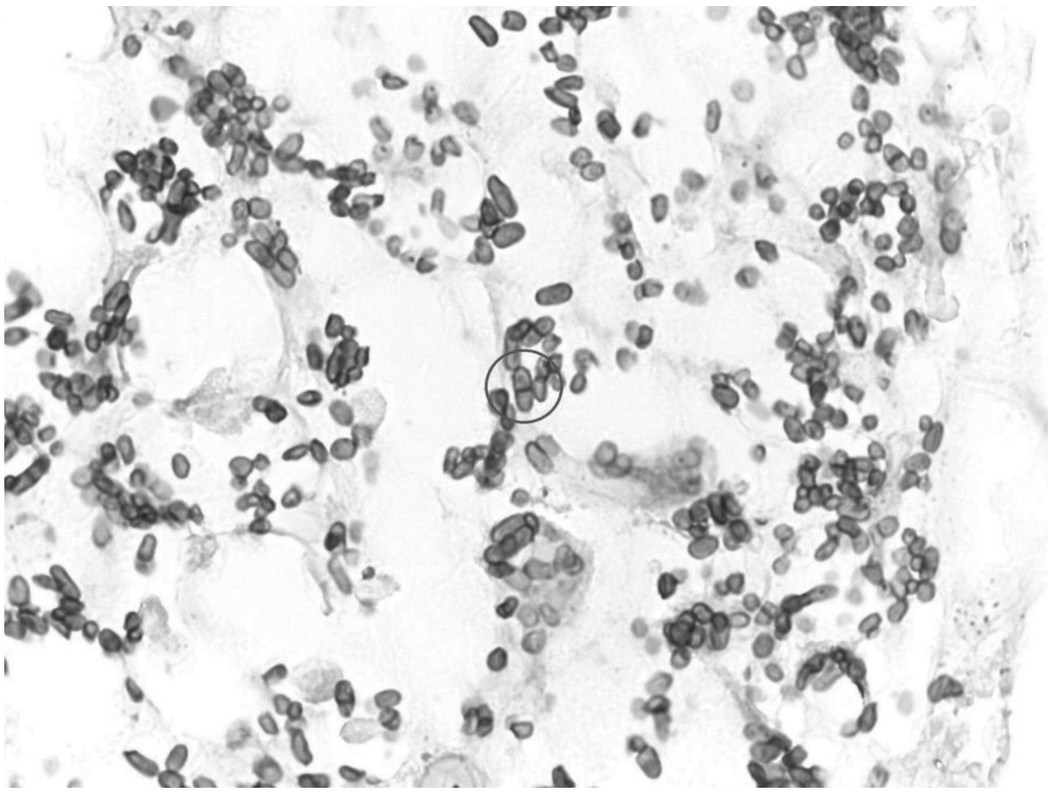

Figure 4 GMS stain in the bone marrow highlights many oval-shaped yeasts without budding but occasional binary fission (in circle).

Discussion

This patient was a 23-year-old hilltribe man with acute onset of fever, fatigue with palpitation. He was also diagnosed HIV infection with possible pneumocystis carinii pneumonia 3 months ago with poor compliance to antiretroviral treatment. By physical examination, he had anemia, hepatosplenomegaly without any obvious skin lesions. So, differential diagnosis should be opportunistic infections such as mycobacterial infection both TB (tuberculosis) and MAC (mycobacterium avium complex), cryptococcal infection although having no significant headache of stiff neck, other disseminated fungal infection and because he had intraabdominal lymphadenopathy, lymphoma should be in the differential diagnosis. Initial CBC showed anemia and thrombocytopenia, although blood smear did not show myelophthisis, this could not totally exclude infection or malignancy in the bone marrow. If we were waiting for culture result or therapeutic trial with antituberculosis drugs, this could be more harmful because of delayed diagnosis and adverse drug reaction. Bone marrow examination in this patient was justified and could make rapid diagnosis.

Talaromycosis[1] (formerly Penicilliosis[2]) is an infection caused by the fungus *Talaromyces marneffei*. Talaromycosis commonly affects people who live in Southeast Asia[3], southern China[4], or eastern India. Most people who get talaromycosis have defective immune function, especially HIV/AIDS[5]. In Thailand, this infection usually found in northern part[6] such as Chiang Rai or Chiang Mai. Patients with this infection mostly experience high-grade fever, anorexia, weight loss, painless skin lesion. Some patients have cough,

difficulty breathing, diarrhea, abdominal pain, lymphadenopathy and palpable hepatosplenomegaly[7].

In people with HIV-infected patients, talaromycosis is more likely to spread through the blood and affect the whole body. Skin lesions due to talaromycosis usually have a small dent in the center. In non-HIV infected patients, talaromycosis commonly affects the lungs, liver, and mouth. Sometimes it spreads through the blood and affects the whole body. Patients with other immune dysfunction such as cancer, organ transplant, adult-onset immunodeficiency syndrome and other autoimmune diseases can be infected with talaromycosis[8].

Bone marrow examination can identify this organism in macrophages or neutrophils. Histoplasma and talaromyces are yeast like organism. Both look similar, but talaromyces has typical binary fission. However, definite diagnosis requires fungal culture.

Talaromycosis is usually treated with amphotericin B for two weeks, followed by itraconazole or voriconazole given by mouth for 10 weeks. Patients with HIV infection should receive antiretroviral one week after starting amphotericin B[9].

Conclusion

The authors reported case of disseminated *Talaromyces (Penicillium) marneffei* infection in HIV-infected patient. We suggest bone marrow examination and culture for diagnosis fever of unknown origin in this setting.

Conflict of interest

The author has declared no conflict of interest.

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