Penicillium marneffei infection: An AIDS-defining illness

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ABSTRACT

A 29-year-old HIV seropositive male patient from Manipur presented with fever, cough, weight loss and asymptomatic papules and nodules all over the body. Differential diagnoses of secondary syphilis, histoplasmosis, cryptococcosis and penicilliosis were considered. Histopathological and mycological study of the skin biopsy tissue, and blood culture confirmed the diagnosis of penicilliosis. Although penicilliosis, an AIDS-defining illness, is restricted to Southeast Asia, more and more cases are being recognized in non-endemic countries.

Key Words: Penicillium marneffei, Dimorphic fungus, AIDS-defining illness, Amphotericin-B

INTRODUCTION

Penicillium marneffei is the only penicillium species that is a dimorphic fungus and can cause systemic mycosis in human beings. It is endemic in Southeast Asia and China.[1] The prevalence of *Penicillium marneffei* infection has increased substantially during the past few years. This increase has occurred exclusively among patients infected with HIV in endemic regions as well as in eastern India where the disease was not known before and where bamboo groves abound.[2] These groves are the habitat of bamboo rats which are putative carriers of *Penicillium marneffei*. Still, no reservoir for the fungus has been defined even though the soil is believed to be the natural source. The disease has now been reported among HIV-infected persons in Thailand, Myanmar (Burma), Vietnam, Cambodia, Malaysia, northeastern India, Hong Kong, Taiwan and Southern China.[3] The first report of four autochthonous cases of indigenous disseminated *Penicillium marneffei* infection in HIV-infected patients came from the State of Manipur, India in 1999.[4]

CASE REPORT

A 29-year-old married male from Manipur who had never visited Southeast Asia presented with generalized asymptomatic skin lesions for six months, fever and cough with expectoration for two months, and significant weight loss. There were no oro-genital lesions. Multiple erythematous, discrete papules and nodules with umbilication, varying in size (5-20 mm) were situated over the face, chest, back and proximal parts of the extremities [Figure 1]. Oral candidiasis was present. Systemic examination was normal. Differential diagnosis of histoplasmosis, secondary syphilis, cryptococcosis and penicilliosis was considered.

Investigations revealed Hb 8.1 g/dl, WBC 2800 / cmm, and ESR 120 mm at the end of one hour. ELISA test for

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HIV was reactive. Absolute CD4 count was 48/ cmm. Mantoux test was negative. Skin biopsy revealed granulomatous infiltrates rich in foamy macrophages in the mid-dermis. PAS and GMS stains showed spherical yeast cells with central septa within histiocytes[5] [Figures 2, 3]. Skin biopsy tissue and blood culture on Sabouraud's agar grew glabrous moist and red colonies with radial folds and the underside of the colonies showed intense red diffusible pigment diagnostic of *Penicillium marneffei* infection [Figure 4]. Hyaline yeast cells were seen on KOH mount. Ellipsoidal conidia were

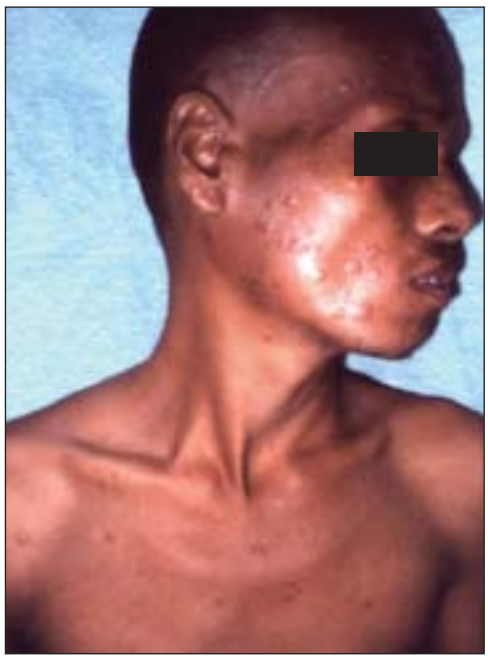

Figure 1: Erythematous papules and nodules with umbilication

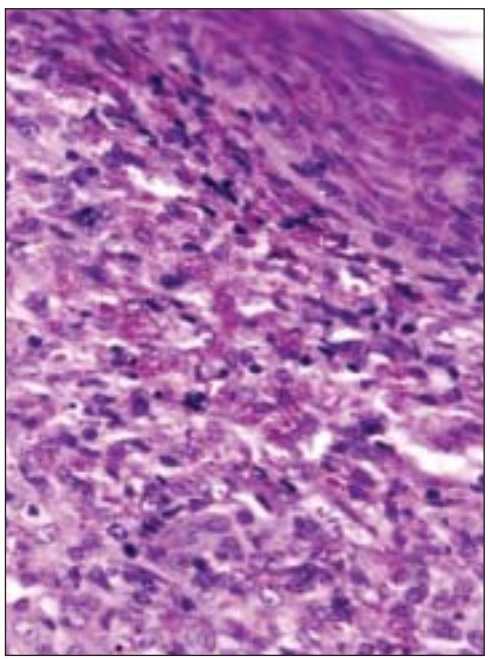

Figure 2: PAS stain: Yeast cells within histiocytes

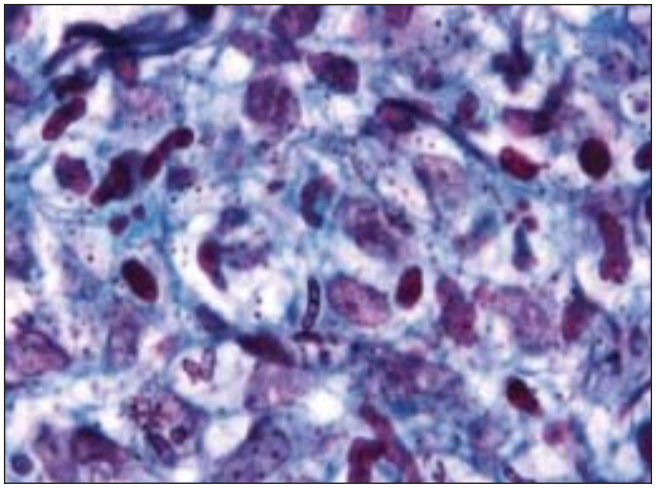

Figure 3: GMS stain: Ellipsoidal yeast cells with central septa

Figure 4: Culture on Sabouraud's agar: Wooly colony with radial folds and diffusible red pigmentation on the reverse

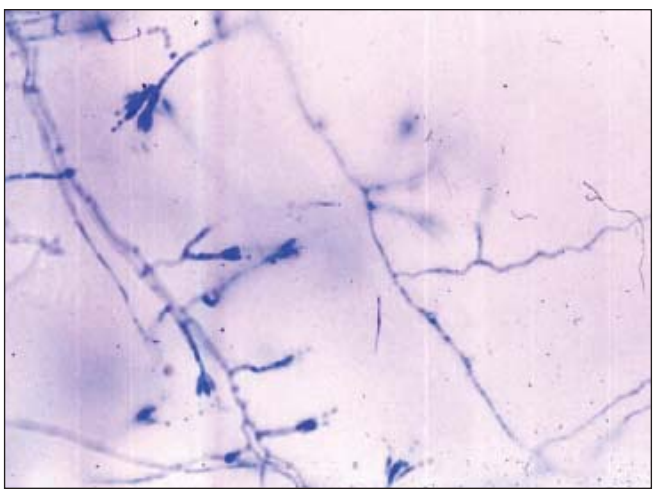

Figure 5: KOH mount shows elliptical conidia

detected on light microscopy of the mycelial phase of colony[6] [Figure 5]. The patient was treated with Inj. Amphotericin-B 0.6 mg/kg intravenously daily for 21 days, followed by oral itraconazole 200 mg 12 hourly for three months. The improvement was evident by the disappearance of skin lesions, fever, and weight gain. The option of antiretroviral therapy was discussed with the patient but was deferred due to financial constraints.

DISCUSSION

Penicillium marneffei infection is an important disease among HIV-infected in Southeast Asia. Discovered in 1956 from the bamboo rat *Rhizomys sinensis* in Vietnam,[7] *Penicillium marneffei* was first identified in an HIV-infected patient in 1988.[8] This infection has been predominantly reported from Southeast Asia where it has been reported to be the third most common illness that defines AIDS.[9] To date 46 cases of *Penicillium marneffei* infection were reported from Manipur—a northeastern State of India which was not known to be endemic for this infection before[2] and which shares borders with Myanmar, a country that has a high rate of HIV infection. *Penicillium marneffei* can cause focal or disseminated infection. Our patient suffered from disseminated infection. The incubation period of varies from a few weeks to many years. The common presenting symptoms and signs of infection are: fever of unknown origin (PUO), anemia, weight loss, and skin eruptions. These skin eruptions are classically generalized papules/nodules with central umbilication which may be confused with molluscum contagiosum, histoplasmosis and cryptococcosis. Generalized lymphadenopathy and hepatomegaly are common.[10] Most of the patients show absolute CD4 count less than 100 / c.mm. As *Penicillium marneffei* is an emerging pathogen, a high index of suspicion is required in areas which have geographical proximity to Southeast Asia, northeastern India and Bangladesh. History of travel to endemic areas was a major clue to diagnosis in a recent case from Vellore, India.[11]

The fungus is sensitive to amphotericin B, itraconazole, and ketoconazole. The current recommended treatment regimen is to give amphotericin B 0.6 mg/ kg/ day for 2 weeks followed by itraconazole 400 mg/ day orally in two divided doses for the next 10 weeks as corroborated in our case.[12] After initial treatment the patient should be given itraconazole 200 mg/day, as secondary prophylaxis for life, if highly active antiretroviral therapy (HAART) cannot be offered.[13] Penicilliosis requires further in-depth study with respect to its global distribution, natural history, pathogenesis and the impact of antiretroviral therapy.

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