

Two sporadic cases of *Penicillium marneffe* infection associated with human immunodeficiency virus infection from West Bengal: A word of caution

Penicilliosis, caused by the dimorphic fungus *Penicillium marneffe*, is endemic in South-east Asian countries such as Thailand, Malaysia, South China, and Indonesia. In India, this infection has been documented in acquired immune deficiency syndrome (AIDS) patients from northeastern states such as Manipur, Nagaland, Mizoram and some parts of Assam. We herein report two such cases from Kolkata: one person traveled from Manipur and the other traveled from southern part of Assam. West Bengal, though a nonendemic state, but is in close proximity to other endemic states such as Assam, and Manipur. This implies sporadic cases of *P. marneffe* infection can occasionally seen outside the endemic area, may be connected to the same. Thus, a high index of suspicion of *P.marneffe* should be made in patients with typical clinical manifestations, especially if they originate or migrate from areas endemic for the disease.

Our first patient was a 40 year-old male from Assam, presented with continuous highgrade fever, diarrhea, cough, severe weight loss, and multiple umbilicated papules all over his body for the last 6 months [Figure 1]. On examination, we found lymphadenopathy and oral thrush in addition to dome-shaped umbilicated painless papules distributed over the face, neck, trunk, and limbs. Differential diagnosis of molluscum contagiosum, histoplasmosis, cryptococcosis, and penicilliosis was considered on the basis of the skin lesions. The patient was tested for human immunodeficiency virus (HIV) at the Voluntary Counselling and Testing Centre of our hospital and was found reactive. His hemoglobin was found to be 8.1 g/dl, leukocyte count 2600/ μ l, and erythrocyte sedimentation rate was 139 mm, at the end of the 1st hour. His absolute CD4 T-cell count was 40 cells/ μ l of blood.

Our second patient was a 43-year-old HIV seropositive male with pulmonary tuberculosis already on highly active antiretroviral therapy (HAART) and antitubercular drug (ATD) for the last months. He clinically presented with crusted and umbilicated papules all over his face, upper limbs, and trunk [Figure 2]. On examination, we found multiple umbilicated papules of various sizes covered with crust which developed over the last 2 months. His hemoglobin was found to be 6.4 g/dl, leukocyte count 3200/ μ l, and erythrocyte sedimentation rate was 121 mm, at the end of the 1st hour. His absolute CD4 T-cell count was 67 cells/ μ l of blood.

Skin tissue section specimens from both the patients were stained with Gomori methenamine silver stain. Microscopy revealed the presence of 2–4 μ m intracellular and extracellular fission arthroconidia or unicellular round oval yeast cells. This yeast cell divides by cross wall division formation in the histiocytes, allowing differentiation from another intracellular fungus, *Histoplasma capsulatum* [Figure 3]. Aspirated papule fluid from both the patients was cultured in Sabouraud's dextrose agar (SDA). In SDA flat, glabrous, moist, radially folded colonies, with diffusible red pigment was isolated after 5 days of incubation at 25°C [Figure 4]. Fungal culture was diagnostic of *penicillium marneffe* infection.

Our first patient was started on amphotericin B at a dose of 0.6 mg/kg/day along with HAART therapy. However, he took discharge against medical advice and failed to follow-up. The second one did not turn up again even to collect investigation reports.



Figure 1: Clinical photograph from patient 1 showing multiple crusted umbilicated papules over the face



Figure 2: Clinical photograph from patient 2 showing multiple umbilicated papules over the trunk

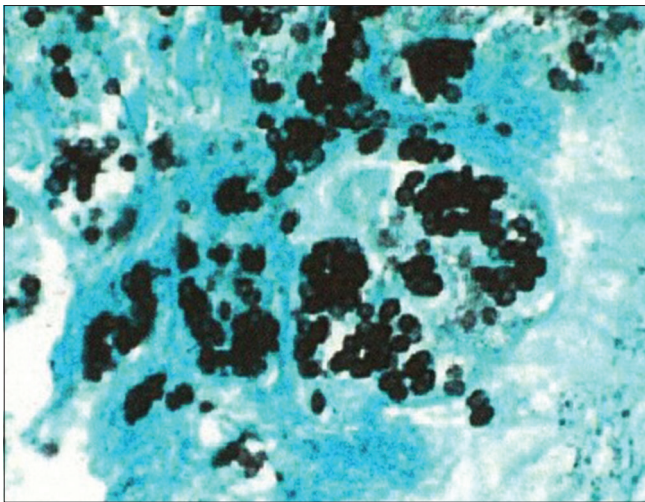


Figure 3: Skin tissue section stained with Gomori methenamine silver ($\times 400$) revealed the presence of 2 to 4 μm intracellular and extracellular fission arthroconidia

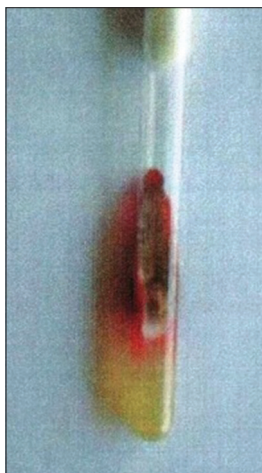


Figure 4: In Sabouraud's dextrose agar, flat, glabrous, moist, radially folded colonies, with diffusible red pigment was isolated after five days of incubation at 25 μm

P. marneffei appears in tissue as unicellular yeast-like organism that reproduces by planate division. The fungus is a mold at room temperature and it converts to the yeast form when incubated at 37°C. This dimorphism is not found in other known members of the genus *Penicillium*. In 1956, the fungus was discovered from bamboo rat in Vietnam.^[1] Disease endemicity corresponds to the distribution of bamboo rats. Infection seems to be more frequent in the rainy season. Recent history of occupational or other exposure to a potential environmental reservoir of organisms in the soil has been shown to be the predominant risk factor for infection in susceptible persons. Proper knowledge about natural reservoir and mode of transmission is an important issue to understand changing trend of epidemiology, if any which in turn prevents spread of this fatal infection. However, there are still gray areas on this note. Most probably, a spore either inhaled or from direct contact with carrier bamboo rats trapped by alveolar macrophages is the initial step of a disseminated infection. Except respiratory route, no other mode of transmission is known till date and an infected patient does not act as a source.

If we look into the history, four cases of penicilliosis were first reported way back in 1999 from Manipur.^[2] After that, the next groundbreaking publication came into light in 2002 where 46 more cases were detected from Manipur within a period of only 19 months.^[3] This finding brought about the concern that India's environmental factors are also suitable for bamboo rats or more particularly *P. marneffei*, persayse. According to this article^[4] and other available scientific literature, apart from characteristic skin lesions, other clinical features are very nonspecific and masquerading with many other important differentials. Clinical features such as fever, weakness, weight loss, productive cough, anemia, hepatosplenomegaly, and lymphadenopathy may bring bacterial pneumonia, tuberculosis, leishmaniasis, histoplasmosis, and cryptococcosis into consideration. Lack of proper awareness of the existence of this rare entity in India leads to delay in diagnosis and poor clinical outcome. Another recent article rightly denoted Penicilliosis as an indicator disease of AIDS.^[5] Fortunately, almost all articles found amphotericin B and itraconazole as highly effective drug. We came across only one literature where patients relapsed within 6 months of stopping treatment with previously mentioned drugs.^[4]

West Bengal is a nonendemic area and till date, no cases of penicilliosis had been reported from this state to the best of our knowledge. However, it is possible that many undiagnosed cases of

P. marneffe from northeastern part of India may migrate in the metropolitan cities like Kolkata in a quiescent stage and manifest only when the CD4 count falls below 100/mm.^[3] Till date, most of the cases have been reported from endemic areas; this could be one of the few rare articles reported from nonendemic areas. Loss of cases into the society may further increase the chance of infection spread if we consider active cases as source, though need to be established.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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