improved, and control scanograms revealed a gradual disappearance of the lesions in the right kidney, liver, spleen, diaphragm, and thyroid at the end of consolidation treatment. Residual lesions in the left kidney and lung were treated surgically. Direct examination and culture of surgical necrotic specimens were negative. Therapy with liposomal amphotericin B was continued for 3 months, until the end of the next phase of chemotherapy intensification. Granulocyte colony-stimulating factor was administered several times to keep the duration of neutropenia at <10 days.

Therapy with liposomal amphotericin B (cumulative dose, 27 g) was well tolerated; fever, chills, nausea, or chronic renal dysfunction was not observed at any time during the 9 months of treatment. Low-dose oral potassium supplementation was used to preserve a normal serum level. Twenty months after the diagnosis of the malignancy, the child was still in complete remission from leukemia and disseminated mucormycosis.

Disseminated mucormycosis is rarely diagnosed while patients are alive (only 17 of 185 cases in adults were diagnosed during life in one review [1]) and is still associated with a high mortality rate despite therapy with amphotericin B. Our patient was first treated in Portugal with AmBisome, which has been reported to be effective for rhinocerebral [3–5] and pulmonary [6] mucormycosis in immunocompromised adults. The diffusion rate of AmBisome in the kidneys is lower than that in other organs. However, in a case of posttraumatic cutaneous and secondary renal infection in a previously healthy man, use of the liposomal preparation combined with direct renal instillation of amphotericin B through a nephrostomy tube was successful, as it was in our case [7]. AmBisome was also reported to be effective and well tolerated in a number of immunocompromised children with invasive fungal infections [8].

As no differences in the lipid formulations of amphotericin B have been demonstrated for antifungal treatment, we switched to ABLC because of its better availability in our institution. However, progression of the patient’s infection while he was receiving ABLC forced us to reintroduce AmBisome, suggesting that this lipid formulation might be more effective for the treatment of mucormycosis.

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References

Invasive Infection Caused by *Penicillium marneffei*: An Emerging Pathogen in Taiwan

Penicilliosis due to *Penicillium marneffei* has been increasingly recognized as an important opportunistic fungal infection in patients who live in or travel to areas of endemicity, including Southeast Asia, Thailand [1, 2], Hong Kong [3], and the southern part of China [4]. Despite its geographic location near the areas of endemicity and increasing international travel to and from these areas, indigenous infection due to *P. marneffei* has not been reported in Taiwan.

Six patients with *P. marneffei* infection who did not have a history of travel to areas of endemicity were identified at National Taiwan University Hospital (Taipei) between January 1987 and December 1996 (table 1). Three were AIDS patients with a mean CD4+ lymphocyte count of 10/mm³, and three were non-HIV-infected patients who received immunosuppressive therapy at the onset of infection. *P. marneffei* infection was the first presenting opportunistic infection in one patient with AIDS. *P. marneffei* was isolated from multiple sites (table 1).

*P. marneffei* that was isolated from sputum was interpreted as a contaminant in case 3. In case 5, the patient was treated as if he had pulmonary tuberculosis, since the diagnosis was initially based on the patient’s chronic productive cough and the findings on a chest radiograph. Three patients died before diagnosis of *P. marneffei* infection was made, and appropriate antifungal therapy was not administered. Itraconazole (200 mg b.i.d.) was given to two AIDS patients as secondary prophylaxis after they completed amphotericin B therapy. In case 1, the patient did not relapse even though she did not receive antifungal maintenance therapy.
Table 1. Characteristics of six indigenous cases of invasive infection due to Penicillium marneffei in Taiwan.

<table>
<thead>
<tr>
<th>Case no.</th>
<th>Age (y)/sex</th>
<th>Underlying condition/medications</th>
<th>Type(s) of infection</th>
<th>Site(s) of isolation</th>
<th>Concomitant infection</th>
<th>Treatment (duration)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16/F</td>
<td>CD4⁺ lymphocytopenia</td>
<td>Arthritis, osteomyelitis</td>
<td>Bone, synovial fluid</td>
<td>Disseminated tuberculosis</td>
<td>Amphotericin B (10 wk)*</td>
<td>Cured</td>
</tr>
<tr>
<td>2</td>
<td>35/F</td>
<td>ITP/steroids</td>
<td>Fungemia</td>
<td>Blood</td>
<td>None</td>
<td>None</td>
<td>Died</td>
</tr>
<tr>
<td>3</td>
<td>28/M</td>
<td>AIDS</td>
<td>Fungemia</td>
<td>Blood, sputum</td>
<td>Cryptosporidium diarrhea</td>
<td>Fluconazole (2 d)</td>
<td>Died</td>
</tr>
<tr>
<td>4</td>
<td>43/M</td>
<td>Renal transplant recipient/stereoids, azathioprine</td>
<td>Peritonitis (disseminated)</td>
<td>Ascites, blood</td>
<td>Salmonella bacteremia</td>
<td>Amphotericin B (2 d)</td>
<td>Died</td>
</tr>
<tr>
<td>5</td>
<td>28/M</td>
<td>AIDS</td>
<td>Bronchopneumonia</td>
<td>Bone marrow, sputum</td>
<td>None</td>
<td>Amphotericin B (4 w)*</td>
<td>Cured</td>
</tr>
<tr>
<td>6</td>
<td>33/M</td>
<td>AIDS</td>
<td>Cavitary pneumonia</td>
<td>Lung aspirate, sputum</td>
<td>None</td>
<td>Amphotericin B (4 w)*</td>
<td>Cured</td>
</tr>
</tbody>
</table>

NOTE. ITP = idiopathic thrombocytopenic purpura.

* Patients 5 and 6 received itraconazole (200 mg b.i.d.) as maintenance therapy and did not have a recurrence of infection while patient 1 did not receive this therapy.

during a 4-year follow-up period after receiving 10 weeks of amphotericin B therapy at a dose of 0.3 mg/(kg·d).

The six cases of P. marneffei infection reported herein provide evidence that P. marneffei can be acquired indigenously by immunocompromised patients in Taiwan. Two other populations are at risk of infection (i.e., renal transplant recipients and patients with idiopathic CD4⁺ lymphocytopenia) in addition to other non-HIV-infected patients with penicilliosis (the latter patients include those with Hodgkin’s lymphoma, chronic alcoholism, systemic lupus erythematosus, and autoimmune hemolytic anemia treated with steroids) [3, 6, 7]. P. marneffei was isolated in sputum obtained from three patients with respiratory symptoms, supporting the hypothesis that P. marneffei infection may be acquired by inhalation of fungal spores [5]. It also can be acquired by direct inoculation [8]. Although osteoarticular P. marneffei infection is one of the manifestations of systemic penicilliosis [7], isolated osteomyelitis and arthritis without dissemination after sustaining an abrasion, as occurred in case 1, was rare.

Clinical presentations of penicilliosis may be misinterpreted as tuberculosis, and P. marneffei isolated from respiratory specimens may be considered a contaminant, especially in areas in which tuberculosis is endemic [3, 7]. The mortality rate is high [2] if there is a delay in the administration of antifungal therapy or if it is not administered [3, 7]. Therefore, timely diagnosis of P. marneffei infection by culture and histopathological examination of appropriate clinical specimens is important. Bone marrow, skin, and blood are the three clinical specimens with the highest diagnostic yields [2].

In summary, Taiwan should be regarded as an area of endemicity for P. marneffei infection, and P. marneffei should be considered in the differential diagnosis of infections occurring in any patients who reside in or travel to Asia, since the distribution of this organism may be wider than we anticipated.


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References