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Letter to the Editor

Pneumonia and brain abscess likely due to *Cladophialophora bantiana* in a patient with systemic lupus erythematosus in Taiwan

Dear Editor,

Cladophialophora bantiana is a melanized mycelial fungus that inhabits living and dead plant materials and soils.[1] Here, we report the first human *C. bantiana* infection in Taiwan.

A 42-year-old woman who resided in an urban area of Taiwan had systemic lupus erythematosus (SLE) since her teenage years and a medical history of diabetes mellitus with insulin control, coronary artery disease, and chronic kidney disease. Her SLE was controlled with prednisolone 0.4 mg/kg/day and hydroxychloroquine. She was admitted (Day 1, D1) due to lupus myocarditis that presented as progressive dyspnea. Methylprednisolone pulse therapy was given along with inotropic agents and hemodialysis. Septic shock developed at the 5th week, and she underwent tracheal intubation and mechanical ventilation. Her disease course was then complicated with bacteremia and ventilator-associated bacterial pneumonia. Her condition continued to deteriorate and was accompanied by progressive altered consciousness and seizures. Chest computed tomography (CT) on D66 revealed left upper lung cavitary mass lesions (Fig. 1A), and fungal hyphae were found on cytospin smears of bronchoalveolar lavage fluid (BALF) obtained on D67. Therefore, deoxycolate amphotericin B (dAMB) 0.7 mg/kg/day was given starting on D67 for presumed fungal pneumonia. Meanwhile, cerebrospinal fluid (CSF) analysis on D67 (before dAMB) showed neutrophilic pleocytosis (WBC 150/μl; neutrophils 67 %) and was finally reported to be culture-negative. Brain CT on D71 revealed multiple new hypodense nodules (Fig. 1B), which were absent one month earlier. Growth of dematiaceous molds in BALF (2000 CFU/ml) was reported 10 days after culturing. Despite broad-spectrum antibacterials and dAMB treatment, she succumbed to multiorgan failure on D84.

The mold isolate was identified as *C. bantiana* by morphology and internal transcribed spacer region (ITS) sequencing using ITS1 and ITS4 primers postmortemly.[2] It developed velvety dematiaceous colonies and long coherent chains of dark-walled, single-celled conidia (Fig. 1C and D) and had an ITS sequence (GenBank ID: LC789285) with 100 % identity compared with the *C. bantiana* strain PWQ2235 (GenBank ID: KP131825.1).

C. bantiana is recognized as a highly neurotropic dematiaceous fungus, with cerebral abscess being the predominant clinical presentation.[3] Extracerebral infections such as sinusitis and pneumonia have occasionally been reported.[3] *C. bantiana* infections occur worldwide, with the majority of cases reported from India.[1,3] In a review of 120 cases of *C. bantiana* cerebral infections, the disease was distributed more in immunocompetent than immune-debilitated hosts (58.3 % vs. 41.7 %), and corticosteroid use was the most common underlying condition.[3] The hypothesized route of infection is inhalation of airborne conidia followed by hematogenous spread to the brain.[3] Diagnosis mainly relies on microscopic examination and culture.[3] Given its neurotropic nature and absence of malignant cells in CSF and BALF, pneumonia and brain abscesses caused by *C. bantiana* were highly considered in this case. While therapy has not yet been standardized, *in vitro* data suggested that itraconazole, voriconazole, posaconazole, and AMB were active against *C. bantiana*.[3] Overall, *C. bantiana* cerebral infections carried a high mortality (65 %).[3] Complete excision of brain lesions has been shown to be associated with favorable outcomes, but as observed in our case, early diagnosis remains challenging owing to nonspecific radiological findings, the long turn-

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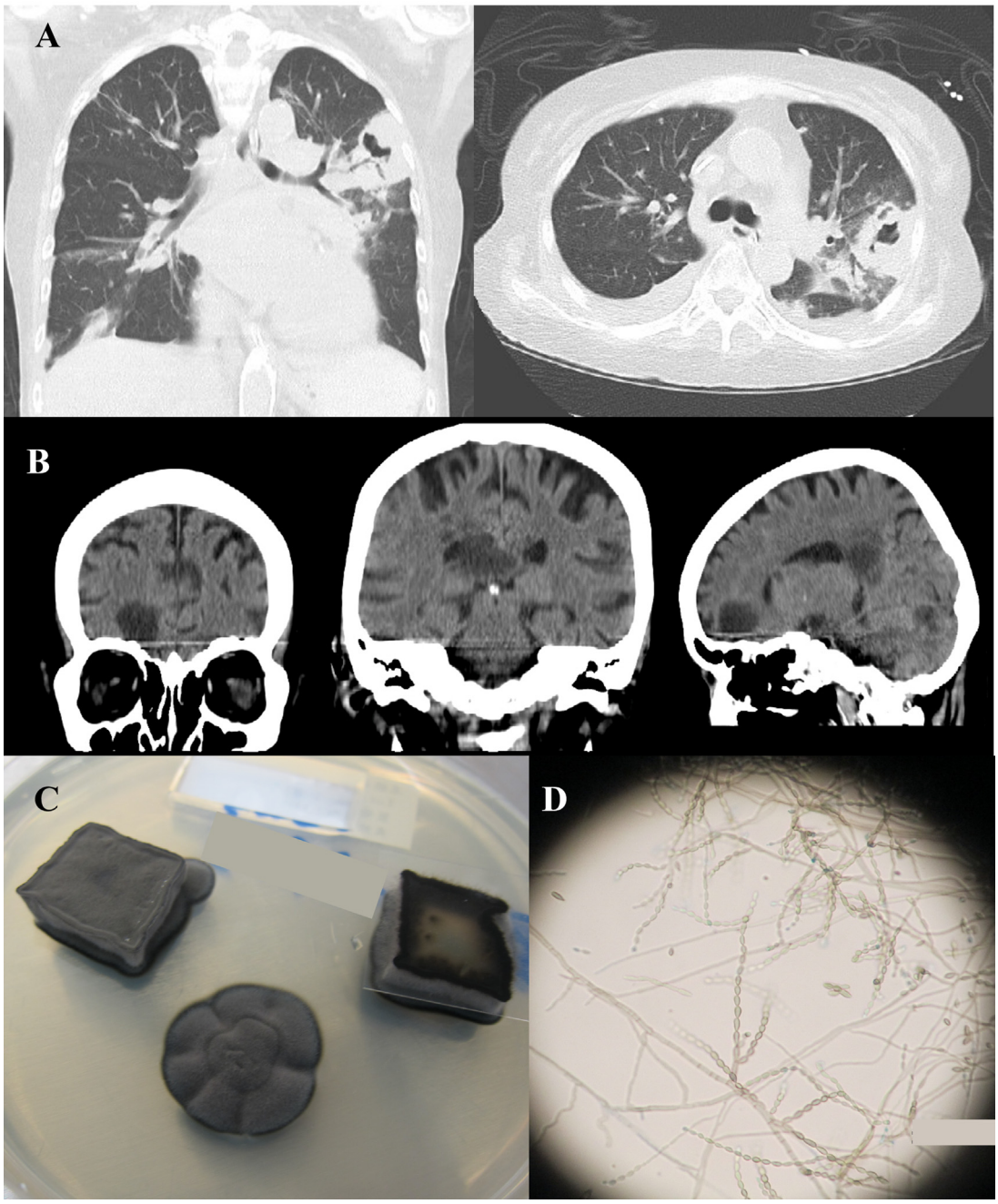

Figure 1. Radiological findings and colonial and microscopic appearance of *Cladophialophora bantiana* from the present patient. (A) Chest computed tomography (CT) revealed a cavitary mass lesion over the left upper lung. (B) Brain CT revealed multiple hypodense nodules in cerebral hemispheres and the right cerebellum. (C) Velty, powdery dematiaceous fungal colonies on Sabouraud dextrose agar after incubation at 25 °C for 25 days. (D) Dark-walled, septate hyphae and ellipsoidal to fusiform, single-celled conidia had formed in long, coherent chains. (Note: The appearance of nonfragile conidia chains helps distinguish *C. bantiana* from nonpathogenic *Cladosporium* species; the latter develops fragile conidia chains.)

around time of culture, and the high probability of culture-negative results in CSF.[1,3] Notably, owing to its neurotropism and potential to cause cerebral infections in healthy hosts through inhalation, *C. bantiana* is classified as a Risk Group 3 pathogen, and biosafety level 3 laboratories are recommended for handling sporulating cultures.[3,4]

In conjunction with a report of *C. bantiana* eumycetoma in a Maltese dog,[5] the occurrence of canine and human cases underscores the need for clinical and laboratory vigilance regarding *C. bantiana* infections in Taiwan, particularly when dematiaceous molds are recovered from patients with brain abscesses.

Institutional review board statement

The study was approved by the Institutional Review Board of National Cheng Kung University Hospital (IRB numbers B-ER-101-342 and A-EC-112-031).

Declaration of competing interest

All authors report no conflicts of interest.

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