Dear Editor,

Invasive molds are the main cause of fungal diseases in immunocompromised patients; these diseases are diagnosed according to the guidelines of the European Organization for Research and Treatment of Cancer/Mycosis Study Group [1]. The mold species specified in these criteria are not clearly defined, but they usually include species with known pathogenic potential, such as Aspergillus, Fusarium, Mucorales, and Scedosporium spp. However, nonsporulating molds, especially basidiomycetes (BM), have been reported as emerging pathogens responsible for allergic and invasive diseases, most frequently involving the lungs [2]. As filamentous BM are white nonsporulating molds in culture, conventional identification is problematic. However, with recent advances in sequencing technologies, they have been reported as emerging pathogens [3]. Of the 218 global cases of human pathogenic BM, Schizopyllum commune is the most common (52%), followed by Coprinopsis cinerea (5.9%), Emnia lacerata (5%), and a few cases of Irpex lacteus [2].

Although BM are increasingly identified in clinical specimens, little is known about their clinical significance, and Korean cases are rarely reported. We describe five Korean cases of respiratory infections caused by BM among patients admitted to the Seoul St. Mary’s Hospital, Seoul, Korea, between June 2016 and July 2017. They were three cases of respiratory tract infection caused by C. cinerea, E. lacerate (formerly Ceriporia lacerate), and I. lacteus and two cases of suspicious infection caused by S. commune and P. spadiceum. The Institutional Review Board of Seoul St. Mary’s Hospital approved the study (approval no. KC19RESI0532) and waived the requirement to obtain informed consent from the patients because this is a retrospective study of clinical cases involving minimal risk to the patients.

The characteristics of the five cases and the fungal morphologies are presented in Table 1 and Fig. 1, respectively. They were all grown on Sabouraud dextrose agar after two weeks of incubation at 28°C under light. In all cases, the fungus was identified by sequencing the internal transcribed spacer (ITS)1/ITS2 and the 28S rRNA gene D1/D2 domains [4] using the following primer pairs: pITS1-F (5’-TCCGATAGTAGGAACTGCGG-3’) and pITS1-R (5’-GCTGCCGTCTTCTCATCGATGC-3’); pITS2-F (5’-GCATCGATGAAGGACG-3’) and pITS2-R (5’-TCTCCGCTTTATATGC-3’); and D1/D2 regions-F (5’-GCATACATAGCCGAAAAGAGAAGG-3’) and D1/D2 regions-R (5’-GGTCCGTTTCAAGCGG-3’). Then, the sequences were analyzed using Basic Local Alignment Search Tool (www.ncbi.nlm.nih.gov/BLAST).

Antifungal susceptibility testing of the five isolates was retrospectively performed in triplicate according to the CLSI-M38 protocol.
| Characteristics                                                                 | Coprinopsis cinerea | Emmia lacerata | Irpex lacteus                                      | Schizophyllum commune | Porostereum spadiceum |
|---------------------------------------------------------------------------------|--------------------|----------------|---------------------------------------------------|-----------------------|-----------------------|
| **Age (yr)/Sex**                                                                | 22/Male            | 38/Female      | 64/Female                                        | 66/Female            | 89/Male               |
| **Underlying conditions**                                                       | Acute leukemia     | Acute leukemia | Pulmonary tuberculosis, rheumatoid arthritis     | Multiple myeloma     | Prostate cancer       |
| **WBC count/neutrophil/eosinophil (%)**                                         | 0.4 × 10^9/L/68%/0%| 8.4 × 10^9/L/95%/0%| 14.9 × 10^9/L/72.8%/1.3% | 9.0 × 10^9/L/88%/0% | 6.8 × 10^9/L/81.6%/2.0% |
| **Diagnosis**                                                                   | Pneumonia          | Pneumonia      | Pneumonia                                        | Multi-organ failure  | Pneumonia             |
| **Respiratory symptom**                                                         | Cough              | Occasional hemoptysis | Cough, sputum, dyspnea                            | Dyspnea              | Dyspnea               |
| **Chest CT finding**                                                            | Nodular consolidation with halo | Small ill-defined nodular opacities | Atelectasis with pneumonic infiltration | Micronodules and cavities | Left pleural effusion | Both pleural effusion |
| **Co-infection**                                                                | Not detected       | Escherichia coli in urine | Pseudomonas aeruginosa in sputum | Candida tropicalis in urine | Escherichia coli in urine |
| **Respiratory virus**                                                           | Rhinovirus detected| Rhinovirus detected | Not detected | Not detected | Not detected |
| **Specimen type**                                                               | Bronchial washing  | Sputum         | Bronchial washing                                | Sputum               | Bronchial washing     |
| **Treatment**                                                                   | Voriconazole → Posaconazole | Itraconazole | Voriconazole | Antibiotics | Antibiotics |
| **Outcome**                                                                     | Recovered          | Recovered      | Recovered                                        | Death                | Death                 |
| **GenBank accession no**                                                        | ITS2 region; MF987832 D1D2; MF987831 | ITS2 region; MF987826 D1D2; MF987825 | ITS2 region; MF987830 D1D2; MF987829 | ITS2 region; MF987828 D1D2; MF987827 | ITS2 region; MF987824 D1D2; MF987823 |
| **Antifungal susceptibility test**                                              | Flucytosine NA     | NA             | NA                                               | NA                   | NA                   |
|                                                                                 | Amphotericin B NA  | NA             | NA                                               | 0.125 (MIC, μg/mL)  | 0.25 (MIC, μg/mL)   |
|                                                                                 | Voriconazole NA    | NA             | 0.06–0.125 (MIC, μg/mL)                          | 0.125–0.25 (MIC, μg/mL) | 0.25–0.5 (MIC, μg/mL) |
|                                                                                 | Itraconazole NA    | NA             | 0.125–0.25 (MIC, μg/mL)                          | 0.25–0.5 (MIC, μg/mL) | 0.25–0.5 (MIC, μg/mL) |
|                                                                                 | Ketoconazole NA    | NA             | 0.06–0.125 (MIC, μg/mL)                          | 0.25–0.5 (MIC, μg/mL) | 0.25–0.5 (MIC, μg/mL) |
|                                                                                 | Micafungin NA      | NA             | >16 (MEC, μg/mL)                                 | >16 (MEC, μg/mL)    | >16 (MEC, μg/mL)     |
|                                                                                 | Caspofungin NA     | NA             | >16 (MEC, μg/mL)                                 | >16 (MEC, μg/mL)    | >16 (MEC, μg/mL)     |
|                                                                                 | Anidulafungin NA   | NA             | >16 (MEC, μg/mL)                                 | 8 (MEC, μg/mL)      |                       |

*The results of antifungal agents showing variable MICs in triplicate tests are presented as a range. Galactomannan was not tested in Porostereum spadiceum; galactomannan was not detected in the other four cases. Abbreviations: NA, not available; MIC, minimum inhibitory concentration; MEC, minimum effective concentration; WBC, white blood cell; CT, computed tomography.
guidelines with a few modifications [5]. The isolates were cultured on potato dextrose agar for five days at 28°C and then shifted to 37°C incubation for five days for sporulation. The final inoculum of the homogenized fungal hyphae was adjusted to a density of 2.5–5.0 × 10^4 hyphal fragments/mL by adjusting the optical density at 530 nm to 0.13–0.18 using a spectrophotometer (VERSAmax microplate reader, Molecular Devices LLC, CA, USA). The microtiter plate was incubated at 35°C for 72 hours. Results were obtained only for S. commune and P. spadiceum. They showed low minimum inhibitory concentrations (MICs) for flucytosine, amphotericin B (AMB), voriconazole (VRC), itraconazole, and ketoconazole and high minimum effective concentrations for micafungin, caspofungin, and anidulafungin. For the remaining three isolates, we could not determine the MICs.

C. cinerea is normally found in compost and sewage; however, it rarely causes pulmonary infections, endophthalmitis, endocarditis, and chronic sinusitis [2]. A previous study reported an isolate susceptible to voriconazole and posaconazole but resistant to AMB, caspofungin, and micafungin [6]. Our patient also recovered from fungal pneumonia after treatment with voriconazole and posaconazole.

E. lacerate, an agent of white rot on wood, has recently been reported as a human pathogen with low MICs for azoles but high MICs for echinocandins [7, 8]. To our knowledge, this is the first clinical report of E. lacerate in Korea, and the patient recovered from fungal pneumonia after itraconazole treatment.

Another wood-decaying fungus, I. lacteus, has been rarely reported. A patient from Austria presenting with a pulmonary abscess was cured following treatment with voriconazole and AMB [9]. Our patient also showed improved chest computed tomography (CT) findings after treatment with voriconazole.

S. commune mainly causes sinusitis, allergic bronchopulmonary disease, fungal ball, and asthma. One Korean patient, who had a sino-orbital infection, was successfully cured using voriconazole and AMB [10], which is in line with our susceptibility test results.

P. spadiceum has also been isolated from respiratory specimens; however, its pathogenicity is yet to be established [2]. A study on antifungal susceptibility test using two isolates of P. spadiceum showed low MICs for AMB, voriconazole, and itraconazole [3], similar to our results.

As BM have been reported as human pathogens only recently and most of these reports mainly detail isolate characteristics, there are few clues to aid in the diagnosis of infection caused by these emerging pathogens. Of our five patients, three showed supportive chest CT findings, such as consolidation, nodular
opacity, air-fluid level, and cavitation, while the other two patients showed only pleural effusions that were insufficient to support fungal pneumonia. However, we hypothesized that these two cases were fungal infections because the patients were immunocompromised, and the respiratory tract specimens were negative for acid-fast bacilli, aerobic pathogens, and respiratory viruses. In addition, *S. commune* is the most common BM that causes respiratory tract infections in immunocompromised patients. *P. spadiceum* was isolated from a bronchial wash specimen. Of note, the three patients treated with appropriate antifungal agents survived, while the other two patients who received only antibiotics died.

To our knowledge, this is the first report on respiratory infections caused by BMs in Korea. Although there was insufficient clinical evidence for *S. commune* and *P. spadiceum* infections, it is still important to identify these rare pathogens using molecular techniques to accumulate data. These efforts will help us better understand these infections and develop future diagnostic and therapeutic guidelines.

**Author Contributions**

All authors contributed equally to this study.

**Conflicts of Interest**

No potential conflicts of interest relevant to this article were reported.

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