

Dear Editor

Impact of *Bjerkandera adusta* Colonization on Chronic Cough

The significance of isolation of basidiomycetous (BM) fungi from the respiratory tract has been gradually recognized.¹ Fungus-associated chronic cough (FACC)² was introduced as a new chronic cough condition together with “obstructive sleep apnea” and “chronic tonsillar enlargement”.³ FACC is defined as chronic cough associated with colonization by BM fungi found in induced sputum, and therefore recognition of FACC has provided the possibility of using antifungal drugs as new treatment strategies. Among various cough-related laryngeal sensations, our recent studies indicated that a sensation of mucus in the throat (SMIT)⁴ is correlated with positive results for fungal colonization in the sputum of chronic cough patients, which has facilitated identification of FACC patients in ordinary cough clinics.

Bjerkandera adusta is a wood decay BM fungus with high prevalence rates in both indoor and outdoor samples,⁵ which has attracted attention because of its potential role in enhancing the severity of allergic fungal cough by sensitization to this fungus.⁶ It is generally considered that sensitization to *B. adusta* occurs due to repeated colonization by this fungus under conditions of continuous exposure. Although the clinical significance of sensitization to this fungus on FACC has been reported,⁷ the influence of *B. adusta* colonization itself on chronic cough patients has not been investigated in detail. Therefore, it re-

mains unclear whether determining if the BM involved in FACC is or is not *B. adusta* would be important for treatment.

Here, we report the results of a preliminary study to investigate whether FACC colonized with *B. adusta* demonstrates peculiar clinical findings. The following data on the first visit for 31 FACC patients, in whose sputum samples the fungi were identified by molecular biological methods, such as polymerase chain reaction (PCR),⁸ were collected and reviewed retrospectively from the medical records: name, date of birth, gender, and the results of examinations including blood tests, chest radiography, pulmonary function tests, and capsaicin cough inhalation test. The capsaicin cough threshold was defined as the lowest concentration of inhaled capsaicin solution eliciting five or more coughs (C₅). C₅ was expressed as the geometric mean value with geometric standard error of the mean (GSEM). Bronchial reversibility was assessed as an increase in FEV₁ after inhalation of 300 µg of salbutamol sulfate.

The results of laboratory tests and physiological examinations were compared between the *B. adusta* colonization group (BJ-colonizer) and the BM other than *B. adusta* colonization group (non-BJ-colonizer). The patients had a median age of 58 (range: 23-73) years and 51.6% were female. The results of examinations in each group are shown in Table 1. C₅ was significantly ($P < 0.01$) lower in the BJ-colonizer (2.69 µM, GSEM 1.49) compared to the non-BJ-colonizer (24.8 µM, GSEM 1.65). Other variables were not significantly different between the two groups. The results of this study suggested that there is a correlation between heightened cough reflex sensitivity and

Table 1 Differences in clinical manifestations between the *B. adusta* colonization group and the BM other than *B. adusta* colonization group of FACC patients

	BJ-colonizer	non-BJ-colonizer	P-value
Number of patients	14	17	
Gender	F 6, M 8	F 10, M 7	N.S.
Mean (SD)			
Age	53.8 (15.2)	54.5 (14.4)	N.S.
WBC (/µL)	5754 (1249)	5842 (1595)	N.S.
Eo (%)	3.2 (3.1)	2.0 (1.4)	N.S.
IgE (IU/mL)	570.8 (818.7)	66.3 (67.5)	N.S.
%FVC	108.5 (17.5)	116.7 (15.4)	N.S.
%FEV ₁	106.3 (18.9)	107.5 (34.7)	N.S.
FEV ₁ %	81.7 (7.2)	82.8 (6.7)	N.S.
Bronchial reversibility (%)	2.2 (4.5)	0.8 (4.0)	N.S.
Geometric mean (GSEM)			
Cough threshold; C ₅ (µmol/L)	2.69 (1.49)	24.8 (1.65)	$P < 0.01$

BJ-colonizer, the *B. adusta* colonization group; BM, basidiomycetous; FACC, fungus-associated chronic cough; non-BJ-colonizer, the BM other than *Bjerkandera adusta* colonization group; SD, standard deviation; GSEM, geometric standard error of the mean; F, female; M, male; FVC, forced vital capacity; FEV₁, forced expiratory volume in 1 sec; FEV₁%, FEV₁/FVC.

positive results of *B. adusta* colonization in FACC patients.

Although Ichinose *et al.*⁹ reported that the bronchial lavage fluid of mice stimulated with *B. adusta* showed marked eosinophil accumulation, the mechanisms by which the cough reflex sensitivity of cough patients was heightened by *B. adusta* have not been investigated. When some particular BM fungi that can induce eosinophil infiltration in the bronchial walls have colonized the airways of patients, treatment strategies for FACC should focus not only on eradicating fungal colonization but also on suppressing eosinophilic airway inflammation.

Therefore, we hypothesized that the heightened cough sensitivity was due to eosinophilic airway inflammation caused by *B. adusta* colonization. To validate this hypothesis, it is necessary to investigate the sputum cell differentiation, fractional exhaled nitric oxide (FeNO), and capsaicin cough threshold before and after antifungal therapies.

If *B. adusta* colonization is related to specific pathophysiological findings as hypothesized above, the use of a rapid quantitative real-time PCR assay for *B. adusta* that can be applied directly to sputum samples on the first visit would be advantageous in dealing with chronic cough patients with SMIT.

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