To the Editor:

The main criticism arising from Kastelik et al. [1] on the study of allergic bronchopulmonary aspergillosis (ABPA) based on the data of the European Registry of Cystic Fibrosis (ERCF) [2] regards the criteria adopted for the ABPA diagnosis: positive markers of hypersensitivity to Aspergillus fumigatus plus a physician’s suspicion that the patient has ABPA. We agree that the clinical suspicion is subject to some diagnostic inaccuracy. However, the ERCF required that the clinical suspicion was based to some extent on “reversible bronchoconstriction, pulmonary infiltrations, elevated serum immunoglobulin (Ig)-E and/or IgG specific for A. fumigatus, peripheral eosinophilia (>1000 mL⁻¹), recovery of A. fumigatus from sputum or hyphae present on smear, and response to steroids”.

The true problem for the ABPA diagnosis in cystic fibrosis (CF) is that ABPA shares many clinical characteristics with poorly controlled CF lung disease, which makes the recognition of this entity very difficult [3, 4].

Airway obstruction/wheezing, fleeting pulmonary infiltrates and central bronchiectasis, which are still the three classical clinical findings required for the ABPA diagnosis in non-CF patients [5], are really very common in CF patients. Conversely, this difficulty was met in any publication concerning this issue in CF, also in the most recent ones, in which ABPA patients are characterized only on the basis of immunological markers [6–8].

We believe that a clear hypersensitivity to A. fumigatus, combined with a significant rise in the total serum IgE level and the presence of some clinical markers of disease, particularly if they are refractory to antibiotics and regress after corticosteroid therapy, is at the moment the most acceptable compromise for an epidemiological study to be carried out on a large CF population, in which the large number of patients tends to compensate for both overestimation and underestimation of diagnosis. Even a recent study by Nepomuceno et al. [9], using similar criteria to our study, showed a comparable ABPA prevalence in CF of 9%.

The future of ABPA diagnosis in CF relies perhaps on some serological markers which are still under study [10, 11]. Both Ig subclasses specific for A. fumigatus [7, 8] and serum or skin IgE which bind to some A. fumigatus allergens, rAsp2, rAsp4 and rAsp6 [10, 11], are promising specific markers for ABPA disease. However, these markers once again have to be faced with the difficulty of characterizing exactly the patients with ABPA before being accurately validated as disease-specific.

In our study, it was not possible to present separately the immunological data, with and without clinical suspicion of ABPA, as they were not collated separately.

As regards the role of ABPA in disease progression, our study has shown that the decline in lung function of CF patients with ABPA is not more rapid than that observed in patients without ABPA, even if the ABPA patients presented on average at the enrollment a lower forced expiratory volume in one second value compared to the non-ABPA subjects. There is a strong suspicion that ABPA affects, as a rule, patients already clinically compromised: worse lung function and nutritional status, more bacterial colonization and more antibiotic treatment. However, a real understanding of the true role of ABPA on the disease progression should be based on prospective longitudinal studies of large cohorts of CF patients. This is not possible, even with the best intentions, through a wide CF registry supported by more than 200 CF centres.

However, we believe that the allergic bronchopulmonary aspergillosis information, derived from the European Registry of Cystic Fibrosis database, has given, yet with some approximation, a panoramic view of allergic bronchopulmonary aspergillosis in European cystic fibrosis patients, which could stimulate both an improved attention to detect this complication by cystic fibrosis physicians and further clinical and biological studies aimed to better define the true nature of this complication and its true influence on the course of cystic fibrosis lung disease.


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References