Evidence of fungal co-colonization in cystic fibrosis children chronically colonized with *Aspergillus fumigatus*

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Purpose

Background: Cystic fibrosis (CF) is an inherited multisystem disorder characterized mainly by chronic obstructive lung disease. Although bacteria are considered the primary pathogens, fungi, such as *A. fumigatus*, have recently gained the attention for their possible negative effect on lung function. Evidence suggests that mixed colonization indicate a poorer prognosis. The aim of our study was to investigate the microbiota of patients chronically colonized with *A. fumigatus* in our CF center.

Results

- ❖Twenty AC patients matched with 60 controls.
- ❖AC patients:10 different types of microorganisms were detected, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Candida albicans*, *Aspergillus terreus*, *Stenotrophomonas maltophilia*, *Candida parapsilosis*, *Scedosporium apiospermum*, *Achromobacter xylosoxidans*, *Aspergillus flavus* and *Pseudomonas fluorescens*.
- ❖Control patients: 6 different types of microorganisms were detected, *S. aureus*, *P. aeruginosa*, *C. albicans*, *Haemophilus influenza*, *Achromobacter xylosoxidans* and *Stenotrophomonas maltophilia*.
- ❖The presence of *C. albicans* in sputum samples was significantly higher among AC than control patients (65.0% vs 23.3%; $P=0.001$), but an independent association was not confirmed from the logistic regression analysis after adjustment for confounders.
- ❖No significant differences were detected regarding *S. aureus* and *P. aeruginosa* (70.0% vs 66.7%; $P=0.783$ and 70.0% vs 50.0%; $P=0.119$, respectively).

Methods

A retrospective case-control study of CF patients born from 1989 to 2002 was performed. Chronic colonization was defined as two or more positive sputum cultures in a given year. Each patient chronically colonized with *A. fumigatus* (AC) was matched with three control CF patients never colonized with *A. fumigatus* for age, sex and year of birth (± 3 years). All sputum cultures from regular visits at the CF center by the time of enrollment were collected.

Table. Patients’ characteristics by the time of enrollment in the study

	Control patients (n=60)	AC patients (n=20)	P
Age (years)	14 [12, 15,75]	14 [12, 15,75]	1,000
FEV ₁ (% predicted)	103,37 $\pm$ 16,87	78,65 $\pm$ 26,74	0,001
BMI (kg/m ²)	20,51 $\pm$ 3,28	19,25 $\pm$ 2,64	0,125
CFRD	2 (3,3)	0 (0,0)	1,000
ABPA	2 (3,3)	2 (10,0)	0,259
IgE total (IU/mL)	88,00 [24,15 201,50]	74,15 [34,68 280,75]	0,567
<i>Aspergillus fumigatus</i> specific IgE (IU/mL)	0,00 [0,00 1,55]	0,05 [0,00 0,49]	0,824
Hospitalizations	20 (33,3)	17 (85,0)	<0,001
Patients’ microbiota			
<i>Pseudomonas aeruginosa</i>	30 (50,0)	14 (70,0)	0,119
<i>Staphylococcus aureus</i>	40 (66,7)	14 (70,0)	0,783
<i>Candida albicans</i>	14 (23,3)	13 (65,0)	0,001
Antibiotic treatment			
Inhaled	38 (63,3)	19 (95,0)	0,007
Oral	52 (86,7)	18 (90,0)	0,696
Corticosteroid treatment			
Inhaled	9 (15,0)	6 (30,0)	0,137
Oral	2 (3,3)	2 (10,0)	0,259
Azithromycin treatment	4 (6,7)	6 (30,0)	0,006
Antifungal treatment	2 (3,3)	3 (15,0)	0,097

Categorical data are presented as number (%). Normally distributed data are presented as mean $\pm$ SD and not normally distributed data as median [interquartile range]. FEV₁, Forced expiratory volume in one second; BMI, Body mass index; CFRD, Cystic fibrosis-related diabetes; ABPA, Allergic bronchopulmonary aspergillosis.

Conclusion

- In our CF center, AC children seem to be co-colonized with *C. albicans* in high frequency even if this observation, which is in line with our clinical experience, was not confirmed from the statistical analysis.
- The lung microbiota of AC patients merits further study as mixed colonization may alter the levels or spectrum of virulence factors produced by bacteria or fungi.

Figure. Microorganisms detected among CF patients by the time of enrollment in the study

[1] Noni M et.al. *Aspergillus fumigatus* chronic colonization and lung function decline in cystic fibrosis may have a two-way relationship. Eur J Clin Microbiol Infect Dis. 2015 Nov;34(11):2235-41.