LITERATURE REVIEW

Discussions on fungal taxonomy and nomenclature of allergic fungal rhinosinusitis

Florin-Dan Popescu
Department of Allergology, “Nicolae Malaxa” Clinical Hospital, “Carol Davila” University of Medicine and Pharmacy, Bucharest, Romania

ABSTRACT

There is a significant debate regarding the role of fungi in chronic rhinosinusitis and whether allergic fungal rhinosinusitis truly represents an allergic subtype. The diverse nomenclature and heterogeneous taxonomy of fungi involved in the etiopathogenesis of this entity is important to be discussed in order to clarify the organisms detected and involved in this complex disease.

KEYWORDS: fungi, allergic fungal rhinosinusitis

INTRODUCTION

Fungal diseases of the nose and sinuses include a diverse spectrum of disease. Although confusion exists regarding fungal rhinosinusitis (FRS) classification, a commonly accepted system divides FRS into invasive and noninvasive diseases based on histopathological evidence of tissue invasion by fungi. The noninvasive diseases include saprophytic fungal infestation, fungal ball and fungus-related eosinophilic FRS (EFRS) that includes allergic fungal rhinosinusitis (AFRS).

ALLERGIC FUNGAL RHINOSINUSITIS AND FUNGAL TAXONOMY

AFRS is a type of chronic rhinosinusitis (CRS) in which patients classically exhibit nasal polyps, IgE-mediated hypersensitivity, characteristic findings on computed tomography scans, eosinophilic mucin and positive fungal stain. Initiation of the inflammatory cascade in AFRS is a multifunctional event, requiring the simultaneous occurrence of IgE-mediated sensitivity, specific T-cell HLA receptor expression and exposure to specific fungi. Early recognition of AFRS may be facilitated by screening patients with polypoid chronic rhinosinusitis or CRS with nasal polyps (CRSwNP) patients for serum specific IgE to molds. Such specific IgE antibodies are also detectable in nasal lavage fluid and eosinophilic mucin. Sinus mucosa homogenates may be assessed for IgE localization by immunohistochemistry and for antigen-specific IgE to fungal antigens by fluorescent enzyme immunoassay. More fungal specific IgE is expressed in inferior turbinate and sinus tissues of AFRS patients, compared with patients with CRS without nasal polyps. Compared with patients with only nasal polyps, AFRS patients have significantly elevated serum levels of fungus-specific IgG. Elevated levels of fungal-specific IgG seem to be a consistent finding. In the etiopathogenesis of AFRS additional data have involved also non-IgE and cell-mediated pathways, including fungal antigens stimu-
lated T-cell activation with induction of a predominantly T helper 2 (Th2) immune response. AFRS and CRSwNP have increased numbers of local dendritic cells (DC) displaying costimulatory molecules, DC chemoattractants, and their corresponding receptors in the sinus mucosa versus controls. These differences may explain the mechanism for the increased numbers of DC with a Th2-skewed profile.

There is a significant debate regarding the role of fungi in CRSwNP and whether the diagnostic group of AFRS truly represents a unique disease. There is a subset of patients defined by the classic Bent-Kuhn criteria for AFRS who demonstrate some phenotypic differences when compared to other CRSwNP patients. These criteria consist of the following: nasal polyposis, fungi on staining, eosinophilic mucin without fungal invasion into sinus tissue, type I hypersensitivity to fungi and characteristic radiological findings with soft tissue differential densities on CT scanning. Many issues remain unclear related to the existence of significant underlying immunologic differences between AFRS and other forms of CRSwNP, the relevance and immunologic role of fungi or fungal specific IgE in the pathophysiology of AFRS.

Although there are several potential deficits revealed in the innate and probably also in the acquired immunity of CRS patients that might reduce or modify their ability to react to fungi, there are not many data to suggest a clear causative role for fungi in CRS with or without nasal polyps. However, fungi might have a disease-modifying role.

Allergic fungal rhinosinusitis, as a phenotype of CRSwNP, characterized by IgE-mediated hypersensitivity to fungi, eosinophilic mucin with fungal hyphae in sinus secretions, and propensity for mucocoele formation and bone erosion, is a noninvasive form of FRS with a prevalence of 6-9% among all rhinosinusitis cases requiring surgery. The fungi causing AFRS have a great diversity and regional variation in the incidence of AFS has been reported worldwide.

Diagnosis of AFRS is complicated because of the presence of fungi on mucosal surfaces of sinonasal passages. Fungal load colonization may modify the classic eosinophilic inflammation in AFRS. With novel laboratory techniques, in patients with CRS the amount of positive fungal cultures increased significantly. In patients with AFRS a modern approach may include the detection of fungi in sinus aspirate by fungal cultures, the detection of fungal DNA by polymerase chain reaction (PCR) assay and the measuring of fungal-specific IgE levels in sinus aspirate (not always accompanied with fungal growth).

The history of the fungal nomenclature is an important source of confusion. Discussion on the taxonomy of fungi is useful to provide information regarding the causative organisms involved in AFRS; usually fungi from the subkingdom Dikarya, belonging to the phylum Ascomycota, and sometimes to the phylum Basidiomycota. Ascomycetes are characterized by the ascus, a microscopic sexual structure in which ascospores are formed. Phylum Basidiomycota is characterized by reproductive spores called basidiospores, produced by specialized fungal cells called basidia.

The most common fungi associated with AFRS are species belonging to the phylum Ascomycota, the classes:

- **Dothideomycetes**, family Pleosporaceae.
  - Bipolaris species (spp.).
  - Cochliobolus lunatus (Curvularia lunata)
  - Alternaria alternata,
  - Cladosporium spp.,
  - Setosphaeria rostrata,
- **Sordariomycetes**, order Hypocreales:
  - Sarocladium kiliense,
  - Fusarium spp.
- **Eurotiomycetes**, family Trichocomaceae:
  - Aspergillus spp.,
  - Penicillium spp.

From the phylum Basidiomycota, class Agaricomycetes, Schizophyllum commune (synonyms: Daedalea commune, Merulius communis, Scaphoporum agaricoides, Agaricus alneus) may cause AFRS and may be misdiagnosed as Aspergillus, because the fungus is difficult to be identified in culture and the histopathological findings are similar for these fungi.

**Bipolaris spicifera**, a fungal plant pathogen, is often named as one of its synonyms, **Drechslera spicifera**, **Helminthosporium spiciferum**, **Cochliobolus spicifer**, **Pseudocochliobolus specifer** which can lead to confusion.

**Bipolaris hawaiiensis** has also similar synonyms, such as **Drechslera hawaiiensis**, **Helminthosporium hawaiense**.

**Cochliobolus lunatus**, another fungal plant pathogen, was previously named **Curvularia lunata**. Other synonyms are **Acrethecium lunatum** and **Pseudocochliobolus lunatus**.

**Alternaria alternata** has several synonyms, such as **Alternaria tenuis**, **Alternaria rugosa** and **Torula alternata**.

**Setosphaeria rostrata** has many synonyms: **Drechslera halodes**, **Exserohilum halodes**, **Helminthosporium halodes var. tritici**, **Setomelanomma rostrata** and others.

**Sarocladium kiliense** is also named **Acremonium kiliense**, **Acremonium incoloratum** or **Cephalosporium acremonium**.

**Penicillium expansum**, **Aspergillus flavus** and **Aspergillus niger** are also involved etiologically in AFRS.

Species of **Bipolaris**, **Curvularia** and **Aspergillus** seem to be the prevalent isolated species in AFRS.

Detection of fungi in sinus aspirate by fungal cultures is important, because the presence of fungi in
the allergic mucin is a significant finding. Dematiaceous fungi are naturally pigmented molds whose hyphae and conidial cells contain melanin. Fontana-Mason silver stain is useful to demonstrate pigments in dematiaceous organisms, such as Bipolaris and Curvularia. These dematiaceous fungi are associated with eosinophilia and allergic rhinosinusitis or allergic bronchopulmonary mycosis. Septate hyaline hyphae of filamentous fungi can represent species of Aspergillus, Fusarium or Acremonium. Squash cytology of the paranasal sinus contents is useful for proving the presence of fungi. Histopathologic sections from tissue samples containing mucin from the paranasal sinuses obtained by endoscopic sinus surgery may reveal hyphal elements within the allergic mucin but no tissue invasion. Detection of fungal surface antigens by enzyme linked immunosorbent assays (ELISA) with monoclonal antibodies and immunofluorescence microscopy (IMF) are useful to distinguish between the fungi. The detection of fungal DNA by polymerase chain reaction (PCR) assay is a superior method of detecting fungal growth versus fungal cultures.

CONCLUSIONS

All the biological and clinical data presented above reveal the fact that the diverse nomenclature and heterogeneous taxonomy of fungi involved in the etiopathogenesis of AFRS is important to be discussed in order to clarify the organisms detected and involved in this complex disease.

REFERENCES


31. www.speciesfungorum.org