Allergic Fungal Sinusitis

William Reisacher, MD FACS FAAOA
Assistant Professor
Weill Cornell Medical College
NewYork-Presbyterian Hospital
Background

- Chronic rhinosinusitis (CRS) is reported by approximately 35 million Americans\(^1\)
- Direct cost of CRS in the USA is $4.3 billion annually\(^2\)
- 25-30% of CRS patients have nasal polyps (NP)\(^3\)
- NP are found in 1-4% of the general population\(^4\)
- Incidence slightly higher in males and elderly\(^5\)
Classification of NP^6

- CRS w/ NP
- CRS w/o NP
- AFS
Background of AFS

- Similarities with allergic bronchopulmonary aspergillosis (ABPA)
- Combination of Gell and Coombs types 1 and 3 hypersensitivities
- Bent and Kuhn diagnostic criteria (1994) – Type I hypersensitivity
  - Nasal polyps
  - Characteristic radiologic findings
  - Eosinophilic mucus without fungal invasion into sinus tissue
  - Positive fungal stain of sinus contents removed at surgery
Demographic Features of AFS

- Young, atopic and immunocompetent
- Mean age of presentation is 28.9
- Lower socioeconomic status
- More common in southeastern United States
- 5-10% of all patient undergoing surgery for CRS
- Present in 51% of patients in Northern India with CRS
- Wise et al. – African Americans with AFS presented with mean age 11.7 years younger than Caucasians
- Ghegan et al. – African American males were 15x more likely to have bone erosion than Caucasians and African American females combined
Clinical Presentation of AFS

- Headache
- Unilateral nasal congestion
- Diminished sense of smell and taste
- Postnasal drip
- Refractory sinusitis
- Proptosis, telecanthus
- History of sinus surgery
Differential Diagnosis of AFS

- CRS with nasal polyposis
- EMCRS
- Invasive fungal sinusitis
- Mycetoma ("Fungus ball")
- Antrochoanal polyp
- Neoplasm
  - Inverting papilloma
  - Carcinoma
  - Nasolacrimal duct cyst
  - Glioma, dermoid lesions, encephaloceles
- Inflammatory / Autoimmune
  - Wegener’s granulomatosis
  - Sarcoidosis
- Polypoid mucosal changes
Radiologic Findings of AFS

CT scan

T1 - MRI
Gross and Histologic Appearance of AFS

- Thick, dark, tenacious mucus
- Sheets of necrotic and degranulating eosinophils
- Charcot-Leyden crystals
- Scant fungal hyphae
Management of AFS

- Medical management
  - Anti-inflammatory medication
  - Anti-fungal therapy

- Surgery

- Immunotherapy
Medical Management

- **Anti-inflammatory**
  - Systemic corticosteroids (pre-op/post-op)
  - Topical corticosteroids
  - Leukotriene receptor antagonists
  - Macrolide antibiotics

- **Anti-fungal**
  - Systemic
  - Topical (Jen, Kacker, Huang et al. 2004)\(^{13}\)
Surgical Management

- Prior radical procedures replaced by complete, but conservative endoscopic surgery.
- Follow the polyps to the mucin
- Image-guidance if available
- Don’t forget to send the mucin for fungal staining
- Post-operative debridement and irrigation
- Kupferberg staging system
  - Stage 0: NED
  - Stage 1: Edematous mucosa/allergic mucin
  - Stage 2: Polypoid mucosa/allergic mucin
  - Stage 3: Polyps and fungal debris
- Need for revision surgery is about 30%
Immunotherapy for AFS

- Mabry, et al. 1995 - 9 AFS patients with no controls. Less crust formation and post operative mucin and no adverse effects.¹⁵

- Bassichis, et al. 2006¹⁴
  - 60 patient with AFS
  - 24 patients, no IT. 36 patients, IT
  - Average follow-up was 48.5 months
  - Significant reduction of office visits
  - Decrease in need for re-operation from 33% to 11%
Dematiaceous Fungi

- “Darkly pigmented”
- Present in 87% of culture positive-cases of AFS\(^{16}\)
  - Alternaria
  - Bipolaris
  - Curvularia
  - Helminthosporium
  - Fusarium
- 13% were aspergillus
Ponikau et al. from Mayo Clinic suggested that NP may arise from immune hyper responsiveness to fungi that commonly colonize the nose of patients with CRS\(^{17}\).

Gosepath et al. demonstrated Alternaria DNA in 100% of surgical polyp specimens from CRS patients\(^{18}\).

Sabirov et al. studied the role of local IgE specific for Alternaria\(^{19}\):
- CRS w NP (N=21) vs. CRS w/o NP (N=13) and healthy controls (N=8).
- Serum levels of Alternaria-specific IgE were no different between groups.
- Alternaria-specific IgE in polyps was significantly higher than in the nasal tissues of the other two groups.

An association was present between alternaria-specific IgE and increased ECP and eosinophil levels in patients with nasal polyps\(^{19}\).
Is AFS really “Allergic”?

- **Stewart and Hunsaker, 2002**
  - 13 AFS, 11 AFS-like, 27 non-AFS polypoid CRS
  - 9 mold RAST panel
  - Elevated IgG in all groups
  - Elevated IgE in AFS group to average of 5 molds vs. 0.1 in the AFS-like group

- **Wise, et al., 2008**
  - Sinus mucosa homogenates from AFS (11), CRSsNP (8) and non-CRS patients (9)
  - ImmunoCAP for 14 common antigens
  - AFS group had significantly higher levels of IgE for Cladosporium, Aspergillus, Timothy grass, red maple, cockroach, ragweed and cocklebur
Can non-allergic patients develop Allergic Fungal Sinusitis?

- Non-AFRS EMCRS\textsuperscript{22}
  - Fungus not identified histologically
  - Higher incidence of asthma, ASA sensitivity
  - Lower incidence of allergies
  - Always bilateral

- Collins, et al., 2004\textsuperscript{23}
  - Comparison of AFRS with non-AFRS EMCRS (negative for allergy and no fungus identified in the mucin)
  - 17/24 AFRS had fungal specific IgE in mucin compared to 20% in non-AFRS EMCRS
  - Possibly a local IgE-mediated immune response
References


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