Allergic Fungal Sinusitis

**TERMINOLOGY**
- Eosinophilic fungal rhinosinusitis (EFRS)
- Allergic response within sinonasal tract mucosa to aerosolized fungal allergens, amplified and perpetuated by eosinophils

**ETIOLOGY/PATHOGENESIS**
- Allergic reaction to inhaled fungal elements
- *Aspergillus* species most common

**CLINICAL ISSUES**
- Atopy is common (allergy)
- Polyps with putty-like material
- Peripheral eosinophilia
- Elevated fungal-specific IgE
- Extensive debridement and complete evacuation of impacted mucin is mainstay of therapy
- Postoperative anti-inflammatory therapy, including oral corticosteroids

**MACROSCOPIC**
- Foul odor
- Putty or crunchy peanut butter-like consistency
- Muddy or greasy consistency

**MICROSCOPIC**
- “Tide lines,” “tree rings,” waves, or ripples of mucin material alternating with inflammatory debris
- Charcot-Leyden crystals (degenerated eosinophils)

**ANCILLARY TESTS**
- PAS-D easier to interpret
- Gomori methenamine silver (GMS)

**TOP DIFFERENTIAL DIAGNOSES**
- Invasive fungal sinusitis
- Mycetoma

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(Left) Hematoxylin & eosin shows “tide lines,” “tree rings,” or alternating bands of nuclear and cytoplasmic debris, findings characteristic for allergic fungal sinusitis. (Right) Hematoxylin & eosin shows degenerated inflammatory cells and eosinophils with Charcot-Leyden crystals (breakdown products of eosinophils).

(Left) Radiologic image shows opacification but no destruction of the left nasal cavity and sinuses by allergic fungal sinusitis. Polyps are noted in the contralateral maxillary sinus, a frequent concurrent finding. (Right) Gross photograph shows a polypoid fragment of tissue with multiple projections. The tissue was greasy with a putty-like consistency on cut section.
Allergic Fungal Sinusitis

TERMINOLOGY

Abbreviations
• Allergic fungal sinusitis (AFS)

Synonyms
• Allergic mucin
• Eosinophilic fungal rhinosinusitis (EFRS)
• Eosinophilic mucin rhinosinusitis (EMRS)
• Allergic fungal rhinosinusitis
• Hypertrophic sinus disease (HSD)
• Atopical fungal sinusitis

Definitions
• Allergic response in sinonasal tract mucosa to aerosolized fungal allergens, amplified and perpetuated by eosinophils

ETIOLOGY/PATHOGENESIS

Environmental Exposure
• Allergic reaction to inhaled fungal elements
  ○ Class II genes in major histocompatibility complex are involved in antigen presentation and immune response/modulation
  ○ Allergic reaction develops in immunocompetent people
  ○ Aspergillus species most common
    - Dematiaceous (brown-pigmented) fungi
      - Widespread in soil, wood, and decomposing plant material
      - Alternaria
      - Bipolaris
      - Curvularia
      - Exserohilum
      - Phialophora species
    - Mucor is uncommon agent

Pathogenesis
• Atopic host is exposed to finely dispersed fungi
• Inflammatory response is mediated by immunoglobulin E (IgE)
  ○ Type 1 hypersensitivity reaction
• Tissue edema with sinus obstruction and stasis
• Proliferation of fungus results in increased antigenic exposure
• Self-perpetuating cycle producing allergic mucin and possibly polyps

CLINICAL ISSUES

Epidemiology
• Incidence
  ○ Common
    - Approximately 10% of patients with chronic rhinosinusitis or nasal polyposis have AFS concurrently
    - Increased frequency in patients with asthma, allergies (atopy), and allergic bronchopulmonary aspergillosis (ABPA)
  ○ Increased in warmer climates
• Age
  ○ Usually in 3rd to 7th decades
  ○ Not a disease seen in children
• Sex
  ○ Equal gender distribution
    - Males more likely to present with bone erosion than females

Site
• Nasal cavity
• Paranasal sinuses
  ○ Maxillary and ethmoid sinuses most common

Presentation
• Atopy is common (allergy)
• Chronic, unrelenting rhinosinusitis
• Mass
  ○ May result in facial dysmorphia and proptosis
    - If proptosis is present, visual disturbances are reported
• Discharge
• Rhinorrhea
• Headache

Laboratory Tests
• Peripheral eosinophilia
• Elevated fungal-specific IgE
  ○ May also have elevated levels of fungal-specific IgG3
• Cultures performed to identify etiologic fungal agent
• Results used to conduct desensitization treatments
• Cultures are not used to provide antibiotic sensitivities since there is no invasive fungal infection

Treatment
• Options, risks, complications
  ○ Usually requires combination of surgery and medical therapy to yield best long-term outcome
• Surgical approaches
  ○ Extensive debridement and complete evacuation of impacted mucin is mainstay of therapy
  ○ Polypectomy and marsupialization of involved sinuses at minimum
  ○ Procedures may be endoscopic
    - Functional endoscopic sinus surgery (FESS)
• Drugs
  ○ Allergic desensitization (immunotherapy)
  ○ Postoperative anti-inflammatory therapy
    - Oral corticosteroids usually yield best outcome
  ○ Postoperative azoles (specifically, itraconazole) may reduce recurrences
  ○ Medical management of allergic inflammatory disease

Prognosis
• Good with integrated medical and surgical approach
• Recurrences develop with fair frequency
  ○ Can be problematic to functional status of patient

IMAGING

CT Findings
• Expansile, sometimes destructive mass within nasal cavity and paranasal sinuses
• Bone remodeling or destruction
  ○ Orbital expansion and bony erosion are prominent features
  ○ Bone erosion can be seen in advanced cases
Nasal Cavity and Paranasal Sinuses

Invasive Fungal Sinusitis

Histochemistry
- Charcot-Leyden crystals (degenerated eosinophils)
- Degenerated material composed of neutrophils, eosinophils, and mucinous debris
- Gomori methenamine silver (GMS)
- PAS-D
- Greasy to palpation
- Muddy consistency
- Putty or crunchy peanut butter-like consistency
- Mean overall aggregate: Up to 8 cm
- Range: 0.1-0.4 cm fragments of tissue
- Yields overall “blue and pink” alternating appearance
- Fruiting heads are common in this fungal disease
- Lacks alternating pattern
- Degenerated material composed of neutrophils, eosinophils, and mucinous debris
- Fungal hyphae identified
- Significant host response within stroma
- “Tide lines,” “tree rings,” waves, or ripples
- Nuclear debris tends to aggregate
- Polypoid structures with intact surface epithelium
- Fruiting heads are common in this fungal disease
- Usually no host response
- “Mucinous” material is free floating, unattached to surrounding respiratory tissues
- Eosinophils and their breakdown products
- May be difficult to interpret due to debris
- Polyps may show inflammation but not abscesses or necrotic material
- Fungal hyphae are visible
- Respiratory epithelial adenomatoid hamartoma
- Dematiaceous fungi most common

Differential Diagnosis

Pathologic Interpretation Pearls
- Alternating “tide lines” or “tree rings”
- Eosinophils and their breakdown products
- Do not need to prove fungal elements are present (i.e., no need to do fungal stains)

SELECTED REFERENCES