

Immunodeficiency, Autoimmune Disease & Allergies: Work-up of the complex CRS Patient

Elisabeth Ferenc, MD MPH

USC

Case 1

- 25 yo F
- > 1 year of nasal obstruction, post nasal drainage, loss of smell
- Treated with maximum medical management
- CT scan with pan-sinusitis
- Performed full ESS
- Post-operatively received oral and topical antibiotics

Keck Medicine
of USC

Preschool Zoom



Keck Medicine
of USC

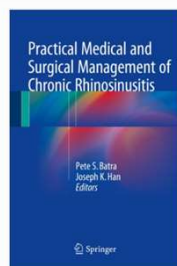
4 months post-operatively



Keck Medicine
of USC

Outline

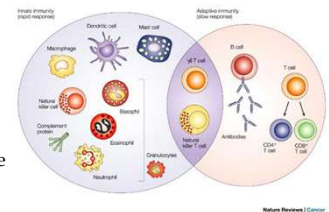
- 3 cases



Keck Medicine
of USC

Immunodeficiency

- Can be categorized as
 - B cells (humoral immunity)
 - T cells (cellular immunity)
 - Phagocytes (innate immunity)
 - Complement system (innate immunity)
- Most commonly antibody deficiency (humoral)

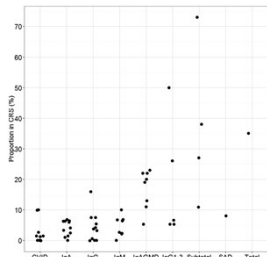


Keck Medicine
of USC

Nature Reviews Cancer, 4, 11-22, 2004.

Immunodeficiency Prevalence

- Recurrent CRS: not controlled by conservative management for 4 months
 - IgG, IgA, or IgM deficiencies in 13% of patients with recurrent
- Difficult to treat CRS: surgery or conservative management for 1 year
 - 23% of patient with difficult to treat



Schwitzguebel AJ, Jandus P, Lacroix JS, et al. Immunoglobulin deficiency in patients with chronic rhinosinusitis: systematic review of the literature and meta-analysis. *J Allergy Clin Immunol.* 2015;136:1523-1531

Immunodeficiency Treatment

- Vaccination: low levels of specific antibodies against pneumococcal serotypes
 - Not respond normally to polysaccharide vaccine → conjugated Pneumococcal antigen vaccine (T-cell dependent)
- Early treatment with antibiotics
- Prophylactic antibiotics
- Immunoglobulin replacement (CVID, SAD, not IgA deficiency)
- ESS

Immunodeficiency Workup

- Personal and Family History
- Lab tests
 - CBC with differential
 - IgG, IgM, IgA
 - Response to *S. Pneumoniae* vaccine (T cell independent)
 - HIV testing
- Other
 - IgG subclasses
 - Flow cytometry to quantify B and T cell subsets
 - Response to tetanus (T cell dependent)

Case 2

- 40 yo M presenting with nasal obstruction and smell loss
- Also with blisters in his mouth, hoarseness, weight loss, dysphagia



Findings in Primary and Secondary Antibody Deficiencies

| Diagnosis | IgG | IgA | IgM | Vaccine | |
|-------------------------------|--------|--------------|---------------|---------------|---------------|
| | | | | response | B cells |
| Normal | Normal | Normal | Normal | Normal | Normal |
| SAD | Normal | Normal | Normal | Low | Normal |
| SIGAD | Normal | Undetectable | Normal | Normal | Normal or low |
| CVID ^a | Low | Low | Normal or low | Low | Normal or low |
| Secondary immune deficiencies | Low | Normal | Normal | Normal or low | Normal or low |

Chiarella SE, Grammer LC. "Immune deficiency in chronic rhinosinusitis: screening and treatment." *Expert Rev Clin Immunol.* 2017; 13(2): 117-123.

Case 2 Video



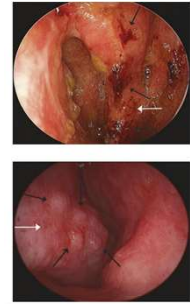
Work-up

- Sedimentation rate (ESR)
- C-reactive protein (CRP)
- Antineutrophil cytoplasmic antibodies (ANCA)
- Rheumatoid factor
- Biopsy of sinus and nasal structures
 - Absence of granulomas does not rule out the disease

Keck Medicine
of USC

Non-ANCA-Associated Granulomatous Disease

- Sarcoidosis:
 - lupus pernio
 - noncaseating granulomas
 - atrophic rhinitis
- Diagnosis: mucosal biopsy, ACE levels, chest xray for hilar lymphadenopathy
- TX: steroids, immunosuppressants

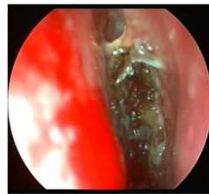


Keck Medicine
of USC

Reed J, deShazo RD, Houle TT, Stringer S, Wright L, Moak 3rd JS. Clinical features of sarcoid rhinosinusitis. Am J Med. 2010;123(9):856-62.

ANCA-Associated Granulomatous Disease

- Granulomatosis with Polyangiitis (GPA)
 - ANCA positivity 80-90%,
 - PR3 (c-ANCA) > MPO (p-ANCA)
 - 89% with sinonasal complaints
 - Nasal crusting, obstruction, bloody discharge/epistaxis
 - Septal perforation, saddlenose deformity
- TX: steroids, cyclophosphamide, anti-CD20 antibody rituximab, etc



Keck Medicine
of USC

Sachse, Florian and Wolfgang Stoll. "Nasal surgery in patients with systemic disorders." *GMS current topics in otorhinolaryngology, head and neck surgery*.vol. 9 (2011): Doc02.

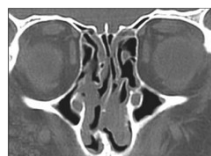
Other Auto-immune Disease

- Sjogren's Syndrome: nasal dryness
 - Anti-SSA, Anti-SSB
- Mucous membrane pemphigoid: blisters, scarring
 - direct immunofluorescence
- Relapsing polychondritis: anterior nasal inflammation, septal perforation
- Systemic Lupus Erythematosus: edema, nasal crusting, septal perforation
 - ANA

Keck Medicine
of USC

ANCA-Associated Granulomatous Disease

- Eosinophilic granulomatosis with polyangiitis (EGPA)
 - ANCA positivity 50%, MPO (p-ANCA) > PR3 (c-ANCA)
 - Asthma 100%, Rhinosinusitis 70%
 - Nasal polyposis 25-75%
- TX: steroids, methotrexate, cyclosporin A, Azathioprine



Keck Medicine
of USC

Swietlik E, Doboszynska A. "Treatment of Churg-Strauss Syndrome with an inhaled corticosteroid after oral steroids discontinuation due to side effects." *Journal of Physiology and Pharmacology*. 2008; 689-965.

Case 3

- 36 yo F presenting with nasal obstruction
- Symptoms worse in Spring and near cats
- "Should I get allergy shots?"

Keck Medicine
of USC

Case 3 Video



Keck Medicine
of USC

Immunotherapy

- CRS: Weak evidence to support as adjunctive treatment¹
- AERD: clear seasonal or perennial allergy symptoms
 - 62% of patients reported no benefit²
- Allergic Fungal Sinusitis: number of treated patients small
 - Decrease reliance on systemic and topical steroids³

1. DeYoung, K et al. "Systematic review of immunotherapy for chronic rhinosinusitis." *Am Journal of Rhinol & Allergy*. 2014; 28(2): 145-50.
2. IAVI, White AA. Survey-defined patient experiences with aspirin-exacerbated respiratory disease. *J Allergy Clin Immunol Pract*. 2015; 3(5):711-8.
3. Greenhaw B, deStazo KD, Arnold J, Wright L. "Fungal immunotherapy in patients with allergic fungal sinusitis." *Ann Allergy Asthma Immunol*. 2011 Nov; 107(3):432-6.

Keck Medicine
of USC

Allergy and CRS

ORIGINAL ARTICLE

International Consensus Statement on Allergy and Rhinology: Allergic Rhinitis

- No controlled studies examining the role of allergic rhinitis in development of CRSsNP
 - No evidence treatment of AR alters progression of CRSsNP
- No clear association between AR and CRSwNP
 - Both associated with T helper 2-mediated inflammation
 - Nasal polyps with high levels of tissue eosinophils, mast cells and basophils

Keck Medicine
of USC

Wise SL et al. "International consensus statement on allergy and rhinology: Allergic rhinitis." *Int Forum Allergy Rhinol*. 2018; 8(2):108-357

Summary

- Evaluation considerations in the patient with difficult to treat disease
 - Immunologic
 - CBC, Immunoglobulins, Response to vaccines, HIV
 - Auto-immune and granulomatous disease
 - CBC, ESR, CRP, RF, ANCA, ACE
 - Allergy
 - Allergy testing

Keck Medicine
of USC

Allergy Testing

- Seasonal symptoms
- Environmental triggers
- Itching of nose and eyes
- Conjunctivitis, nasal congestion, sneezing

→ Skin testing or mRAST



Keck Medicine
of USC



Thank You
Eerence@USC.edu

USC