

Fungus in the Sinuses: A Case-Based Review



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Disclosures

- Patent Pending
 - 61/624, 105; Sinus diagnostics and therapeutics

UCSF Otolaryngology-
HNS
2001-2002



UCSF Otolaryngology-
HNS
2001-2002



Goals

- Review clinical presentations of the common variants of fungal disease of the paranasal sinuses
- Identify imaging characteristics associated with fungal sinus disease
- Discuss treatment approaches for fungal sinus disease



Case #1

Case #1

- Called to ED to evaluate 52 y/o Diabetic with right visual loss, orbital swelling, and pain
- Orbital symptoms evolved over the past 12 hours
- Blood sugar in ED in the 400s

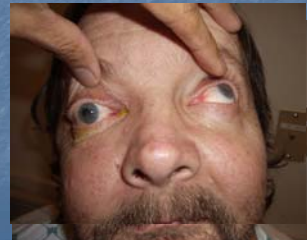


Case #1



Case #1

- "Look up sir"
- "Look down sir"



Invasive Fungal Sinusitis

- Immunosuppression
- Involvement of surrounding tissues
 - Orbit
 - Cavernous Sinus
 - Palate
 - Facial soft tissues
- Imaging

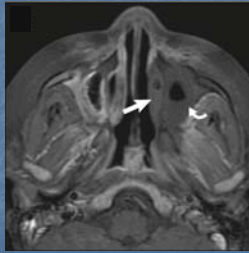


Imaging Findings – Invasive Fungal Sinusitis

- CT
 - Unilateral edema
 - +/- bone erosion
 - +/- extension into surrounding soft tissues
- MRI
 - Loss of contrast enhancement
 - Extra-sinus soft tissue involvement



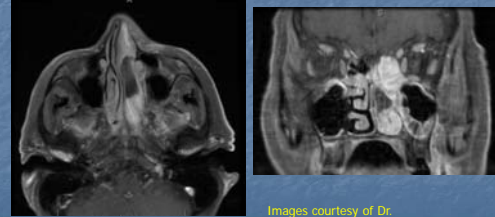
Loss of Contrast Enhancement



Groppo et al. Arch Otolaryngol Head Neck Surg. 2011 Oct;137(10)



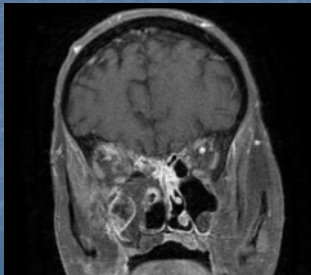
Loss of Contrast Enhancement



Images courtesy of Dr. Matthew Russell



Case #1



Diagnosis

- Tissue evidence of fungal invasion
 - Frozen section evaluation closely approximates permanent pathology results
- Morphology and Culture help guide treatment

Silveira et al. BMC Infectious Diseases 2019 19:310



Invasive Fungal Sinusitis


- Treatment
 - Debridement of involved tissue
 - Antifungal therapy
 - Reversal of underlying immune dysfunction
- Goals of Care?



Case #1

- Invasive Fungal Sinusitis
 - Acute (Fulminant)
 - Diabetes, Bone Marrow Transplant, Hematologic Malignancy
 - Mucorales and/or Aspergillus
 - Chronic Invasive
 - Slower Onset & Progression
 - Solid organ transplant, chronic steroids
 - Aspergillus

D'Anza et al. Int Forum Allergy Rhinol. 2016 Jul 27.
Tzelnick et al Am J Rhinol Allergy. 2019 Jan; 33(1):56-61



What's New?


RESEARCH ARTICLE Open Access

Impact of early detection of acute invasive fungal rhinosinusitis in immunocompromised patients

Mariana L. C. Silveira¹, Wilma T. Anastro-Lima², Francisca M. Faria², Danielle L. C. Queiroz², Rodrigo L. Nogueira², Marcelo G. J. Leite³, Ricardo M. Lessa⁴, Belinda P. Simões⁵, Edwin Tamashiro⁶ and Fabiana C. P. Valera⁷

- Retrospective study of 43 patients evaluated patient outcomes and accuracy of frozen section biopsy for diagnosis
- Mortality 30%
 - Improved survival with higher neutrophil count and disease limited to turbinates

Silveira et al. *BMC Infectious Diseases* (2019) 19:310




RESEARCH ARTICLE Open Access

Impact of early detection of acute invasive fungal rhinosinusitis in immunocompromised patients

Mariana L. C. Silveira¹, Wilma T. Anastro-Lima², Francisca M. Faria², Danielle L. C. Queiroz², Rodrigo L. Nogueira², Marcelo G. J. Leite³, Ricardo M. Lessa⁴, Belinda P. Simões⁵, Edwin Tamashiro⁶ and Fabiana C. P. Valera⁷

- Retrospective study of 43 patients evaluated patient outcomes and accuracy of frozen section biopsy for diagnosis
- Sensitivity of frozen section analysis > 90%

Silveira et al. *BMC Infectious Diseases* (2019) 19:310



Original Research—Sinusitis

Frozen Section as a Rapid and Accurate Method for Diagnosing Acute Invasive Fungal Rhinosinusitis

Max Hennessy¹, Jonathan McGee Bartholomew White, MD¹, Sakar Joshua L. Warwick, MD¹, and Hani

Original Research—Sinusitis Disorders

The Use of Frozen Section in the Early Diagnosis of Acute Invasive Fungal Sinusitis

Otolaryngology—Head and Neck Surgery
2017, Vol. 157(2) 314-319
C. Claire Melancon, MD¹ and John D. Clinger, MD¹

Utility of intraoperative frozen sections in surgical decision making for acute invasive fungal rhinosinusitis

Peter Papagiamopoulos, MD¹, Diana Mirza-Gra, MD¹, Sameer Al-Khatib, MD¹, Kumar Rajan, PhD¹, Sagar Bhatia, MD¹, Paul J. Fontana, MD¹, Robert Trachten, MD¹, and Paul C. Sauer, MD¹

ORIGINAL RESEARCH

Frozen-section biopsy analysis for acute invasive fungal rhinosinusitis

Murtaza T. Ghadiali, MD, Nathan A. Deckard, BS, Uzma Farooq, MD, Frank Astor, MD, Phillip Robinson, MD, and Roy R. Casiano, MD, Miami, FL.

Otolaryngology—Head and Neck Surgery (2007) 136, 714-719




Article

Inpatient Mortality After Endoscopic Sinus Surgery for Invasive Fungal Rhinosinusitis

Annals of Otolaryngology, Rhinology & Laryngology
2018, Vol. 127(10) 208-209
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DOI: 10.1177/0004713218782821
journals.sagepub.com/home/oto
SAGE

Brittany N. Burton, MHS, MAS¹, Aria Jafari, MD², Betal Asmerom, BA¹, Matthew W. Swisher, MD, MS¹, Rodney A. Gabriel, MD, MAS^{1,4}, and Adam DeConde, MD²

- Identified 979 adult patients with mucormycosis or aspergillosis and sinus surgery in the national inpatient database between 2000 & 2014
- Inpatient mortality rate 16%




Article
Inpatient Mortality After Endoscopic Sinus Surgery for Invasive Fungal Rhinosinusitis
 Brittany N. Burton, MHS, MAS¹, Aria Jafari, MD¹,
 Betal Asmerom, BA¹, Matthew W. Swisher, MD, MS²,
 Rodney A. Gabriel, MD, MAS^{1,4}, and Adam DeConde, MD²

Annals of Otolaryngology, Rhinology & Laryngology
 2019, Vol. 128(1) 200-208
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 DOI: 10.1177/0003489418822867
 annot.sagepub.com/home/ann


SAGE

- Mucormycosis associated with 3-fold increase in mortality compared to Aspergillosis
- Diabetes associated with a 50% reduction in mortality



ORIGINAL ARTICLE
Fungal infections of the central nervous system and paranasal sinuses in onco-haematologic patients. Epidemiological study reporting the diagnostic-therapeutic approach and outcome in 89 cases
 A. Candoni¹ | N. Klimko² | A. Busca³ | R. Di Biasi⁴ | O. Shadrivova⁵ | S. Cesaro⁵ |


Review of 89 cases from oncology centers throughout Europe
 Use of multiple antifungal drugs common
 1 year disease-specific survival 66%



Clinical Infectious Diseases
MAJOR ARTICLE
Revision and Update of the Consensus Definitions of Invasive Fungal Disease From the European Organization for Research and Treatment of Cancer and the Mycoses Study Group Education and Research Consortium
 J. Peter Donnelly,¹ Sharon C. Chen,² Carol A. Kauffman,³ William J. Steinbach,⁴ John W. Baddley,⁵ Paul E. Verwey,⁶ Cornelius J. Clancy,⁷ John R. Wingard,⁸ Steven R. Lockhart,⁹ Andrew N. Greig,¹⁰ Tania C. Sorrell,¹¹ Matteo Bassetti,¹² Harold Alan,¹³ Barbara D. Alexander,¹⁴ David Asch,¹⁵ Eric Amundson,¹⁶ Rafi Busch,¹⁷ Robert W. Brachler,¹⁸ Stephanie Brumson,¹⁹ Thomas Chakrabarti,²⁰ August W. Chakrabarti,²¹ Eric Castagnola,²² Maria Casanova,²³ Manuel Casanova Estrada,²⁴ Catherine F. Donlan,²⁵ Edgar B. Dvorak,²⁶ Brian Fisher,²⁷ Thomas Hartman,²⁸ Chao Peter Heussel,²⁹ Ronald E. Jensen,³⁰ Christopher C. Kibbler,³¹ Benjamin P. Kostyranov,³² Paul-Jean Kubacki,³³ Karsten Lagersted,³⁴ Frederick Lammel,³⁵ Thomas Lieberknecht,³⁶ Jürgen Liesche,³⁷ Oliver Lortholary,³⁸ Jukka Maasilta,³⁹ Dieter Muehlebach,⁴⁰ Karen A. Muir,⁴¹ Henry Munn,⁴² Jacques F. Meunier,⁴³ C. Srin Murthy,⁴⁴ Martin Nuzzi,⁴⁵ Lisa Ostrowsky-Zechner,⁴⁶ Lina Pagano,⁴⁷ Thomas P. Patterson,⁴⁸ John R. Perfect,⁴⁹ Ghazal Rishi,⁵⁰ Francesco Salmassi,⁵¹ Marina Savelkoul,⁵² Cornelia Scheele-Probst,⁵³ Sherali Shaban,⁵⁴ Monica A. Sloan,⁵⁵ David A. Stevens,⁵⁶ George B. Thompson III,⁵⁷ Joon A. Whang,⁵⁸ Claudio Vitarello,⁵⁹ Thomas J. Walsh,⁶⁰ Adria Warris,⁶¹ Joseph White,⁶² Li-Li Wang,⁶³ Donald E. Zancan,⁶⁴ and Peter B. Pappas⁶⁵


Definitions of Invasive Fungal Disease • CID 2019

- Defines Proven, Probable, and Possible Invasive Fungal Disease




Culture-Independent Detection of Fungi

- Antigen Testing
 - Galactomannan
 - Beta-D Glucan
- Fungal PCR testing



The role of galactomannan *Aspergillus* antigen in diagnosing acute invasive fungal sinusitis
 C. Claire Melancon, MD¹, Jennifer Lindsey, BA¹, Gregory B. Russell, MS² and John D. Clinger, MD¹
 International Forum of Allergy & Rhinology, Vol. 9, No. 1, January 2019


- Evaluation comparing galactomannan to pathology results in patients with acute invasive fungal (Aspergillus) sinusitis
- Serum galactomannan test is specific (100%), but not sensitive (44%)



PCR-based Fungal Diagnostic Assays

- Not widely available
- Turnaround time about 48 hours (104 hours for culture)
- Sensitivity and Specificity not well defined

Lieberman et al American Journal of Clinical Pathology, Volume 149, Issue Suppl_1, January 2018



Diagnosis and Treatment of Acute Invasive Fungal Sinusitis in Cancer and Transplant Patients

Monica Fung¹ · Jennifer Babik¹ · Ian M. Humphreys² · Greg E. Davis²

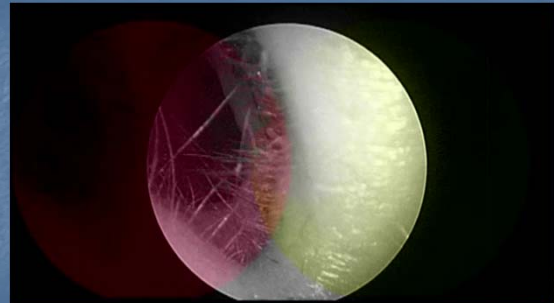
Published online: 26 November 2019 Curr Infect Dis Rep (2019) 21: 53



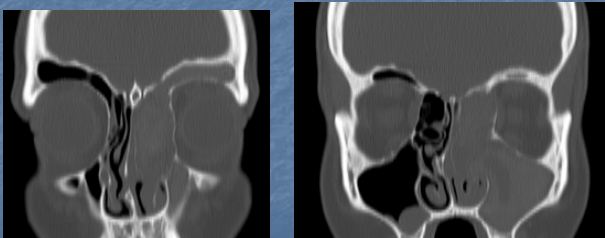
Case #2

Case #2

- 21 y/o woman with left-sided diplopia, proptosis, nasal congestion and headache
- Diplopia, proptosis & congestion began 3 months ago
- Severe headache for past week
- Polyps in the left nasal cavity on anterior rhinoscopy



Case #2



Most Likely Diagnosis

- Sinonasal Tumor
- Odontogenic Sinusitis
- Allergic Fungal Rhinosinusitis
- Aspirin-Exacerbated Respiratory Disease



Allergic Fungal Sinusitis

Table 1. Bent and Kuhn Diagnostic Criteria

Major	Minor
Type I hypersensitivity	Asthma
Nasal polyposis	Unilateral disease
Characteristic CT findings	Bone erosion
Eosinophilic mucin without invasion	Fungal cultures
Positive fungal stain	Charcot-Leyden crystals
	Serum eosinophilia

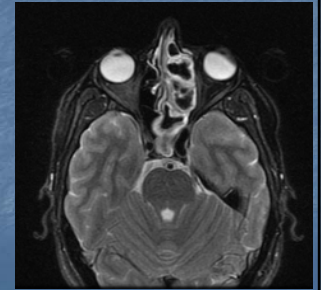
CT, computed tomography

Bent JP 3rd, Kuhn FA. Diagnosis of allergic fungal sinusitis. *Otolaryngol Head Neck Surg.* 1994;111(5):580-588.



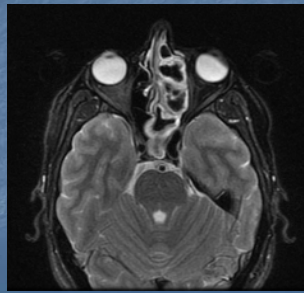
Case #2

- Headache improved following treatment with antibiotics and systemic steroids
- MRI scan performed

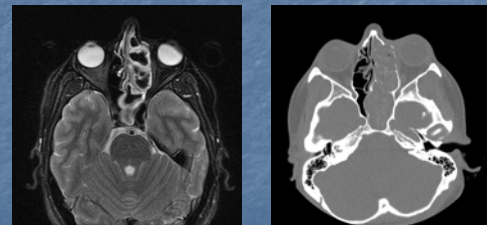


Interpretation of Imaging

- Sinonasal tumor
- Persistent mucosal inflammation with aeration of most ethmoid cells following treatment
- Ongoing poorly controlled fungal disease
- Don't know, lemme call the radiologist



MRI for AFRS Diagnosis



Meng et al *J Thorac Dis.* 2019 Aug;11(8):3569-3577

Allergic Fungal Rhinosinusitis

- Geographic Variance – Southeastern U.S.
- Steroid Sensitive
- Young age, Low socioeconomic status, African American

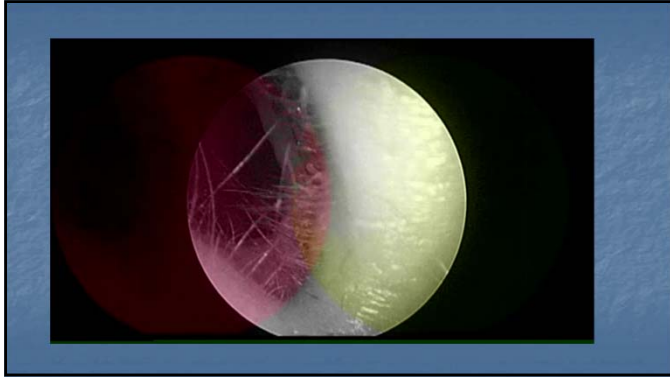
Rowan et al. *Am J Rhinol Allergy.* 2019 May;33(3):310-316.



Allergic Fungal Rhinosinusitis

- Treatment
 - Removal of fungal burden
 - Oral corticosteroids
 - Topical steroid maintenance
 - Immunotherapy?
 - Biologics?

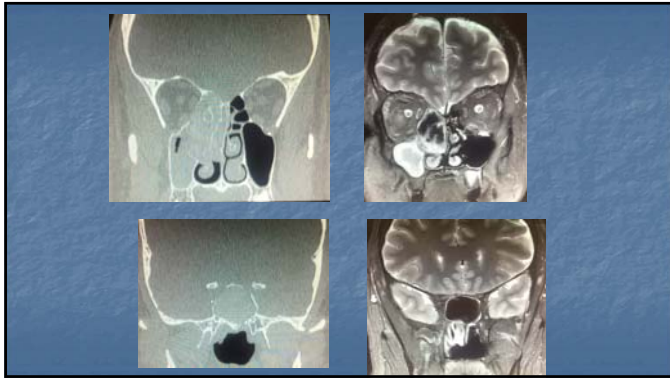
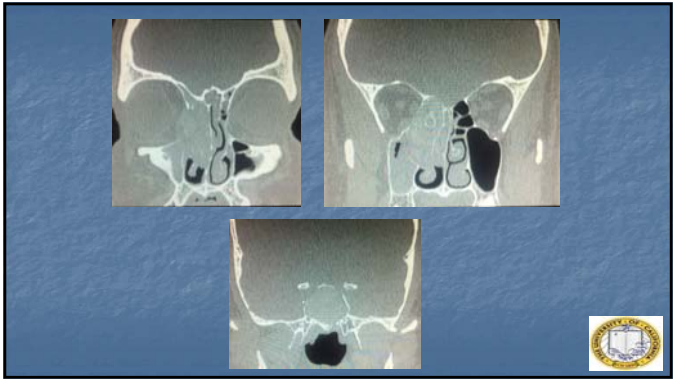





Case #3

Case #3

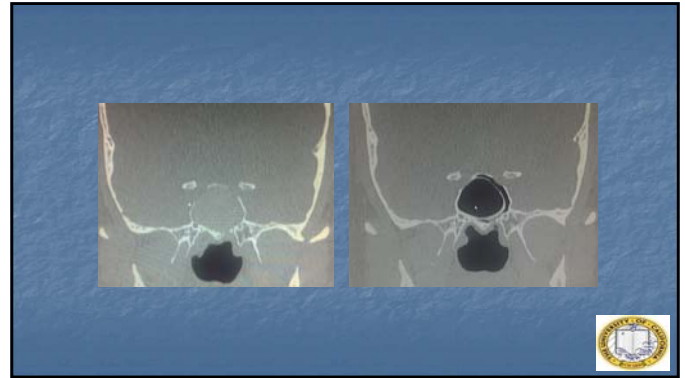
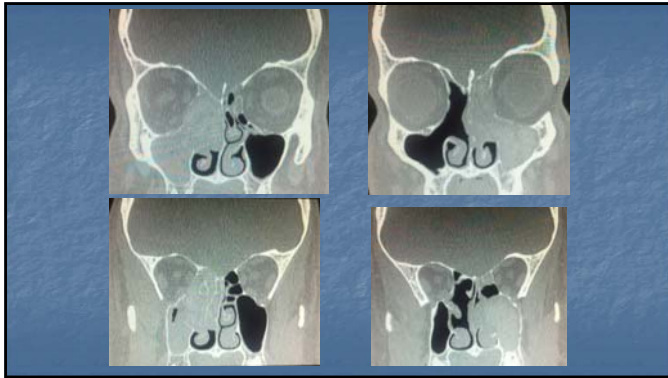
- 28 y/o man with right-sided proptosis and nasal obstruction



6 Months Later

- Proptosis resolved
- Right facial pressure and nasal congestion resolved
- Left (Contralateral) nasal congestion





What's New?

Biologics?

Rhinology | Published: 24 September 2019

Omalizumab versus intranasal steroids in the post-operative management of patients with allergic fungal rhinosinusitis

Badr Eldin Mostafa, Michael Fadel, Mohammed Amir Mohammed, Tarek Abdel Hamid Hamdi & Anas Mohammed Askoura

European Archives of Oto-Rhino-Laryngology 277, 121–128(2020)

Immunotherapy

- Limited evidence demonstrating benefit
- Listed as "option" in recent evidence-based review

Gan et al International Forum of Allergy & Rhinology, Vol. 4, No. 9, September 2014



Revision surgery rates in chronic rhinosinusitis with nasal polyps: meta-analysis of risk factors

Catherine A. Lofus, MS, Zachary M. Soler, MD, MSc, Sina Koochakzadeh, BS, Vincent M. Desiato, DO, Frederick Yoo, MD, Shaun A. Nguyen, MD and Rodney J. Schlosser, MD

International Forum of Allergy & Rhinology, Vol. 10, No. 2, February 2020

- Meta-analysis of 45 studies with 34,220 patients
- Highest revision rate was seen in the AFRS group (29% vs. 16%)

Conversion to Chronic Invasive Fungal Sinusitis From Allergic Fungal Sinusitis in Immunocompetence

Luke Edelmayr, MD ; Christopher Ito, MD ; Wuu Suk Lee, MD, MPH; James Kimbrough, MD; Stilianos E. Konstantis, MD, PhD; J. Kenneth Byrd, MD
Laryngoscope, 129:2447-2450, 2019

- Progression from Allergic to Invasive fungal sinusitis
- Authors suspect repeated high-dose prednisone treatment resulted in immune deficiency and progression to invasive disease



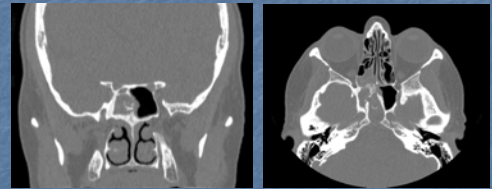
Case #4

Case #4

- 68 y/o woman referred for "sinus evaluation" for incidental finding on head CT
- No nasal congestion, facial pressure, nasal drainage, or change in smell



Case #4



Fungus Ball (Mycetoma)

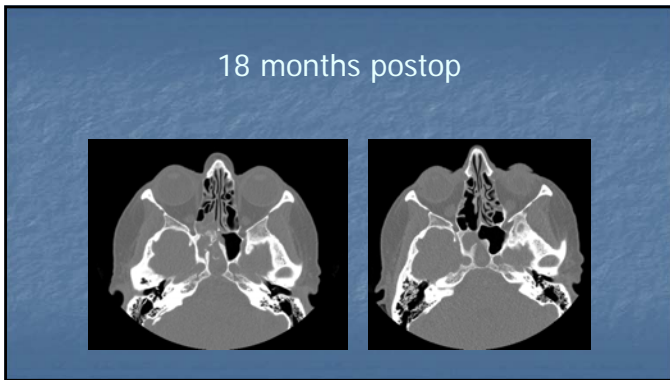
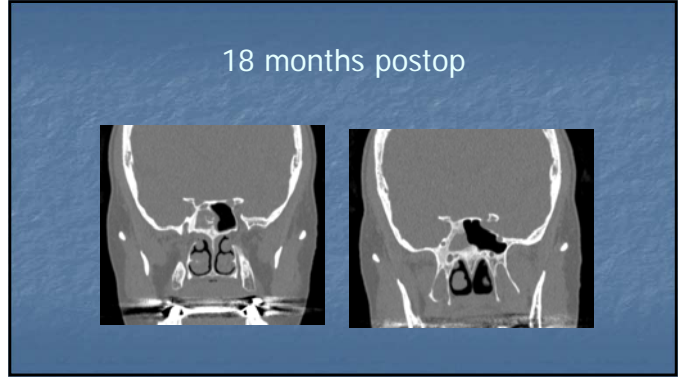
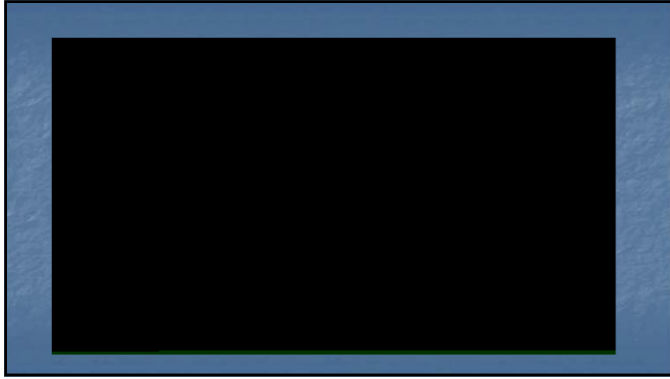
- Hyperdensity within unilateral sinus disease
 - Predominately Maxillary & Sphenoid
- Often incidental finding – Treat or Observe?
 - Symptomatic
 - Bone erosion
 - Patient considerations & preference



Operative Findings

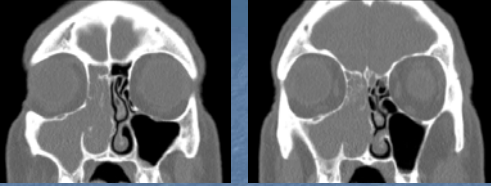

- Green debris filling right sphenoid sinus with surrounding mucopurulence
- Pathology "Tangles of fungal hyphae"
- Fungal Cultures "No Growth"






Case #5

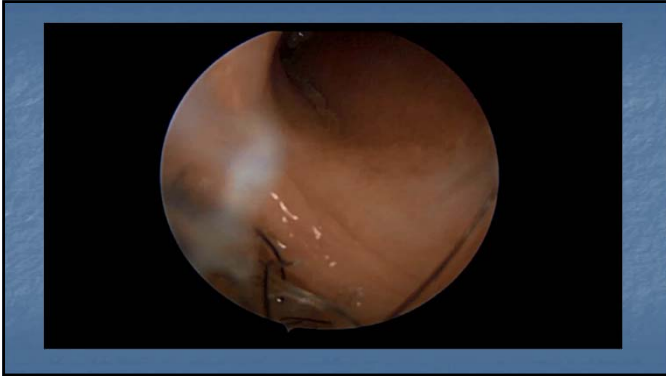
- 76 y/o psychiatrist with 4 weeks of unilateral nasal congestion and purulent nasal drainage
- Minimal response to antibiotics
- Moderate facial pressure
- Urgent referral following CT imaging



There is destruction of the medial wall of the right maxillary sinus with soft tissue extension into the nasal cavity filling the nasal cavity and displacing the nasal septum and leftward direction.

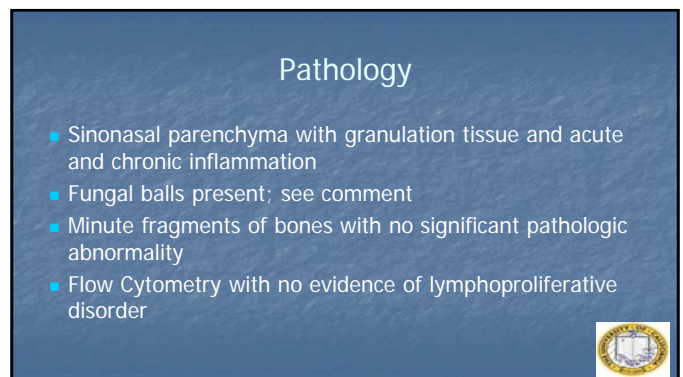
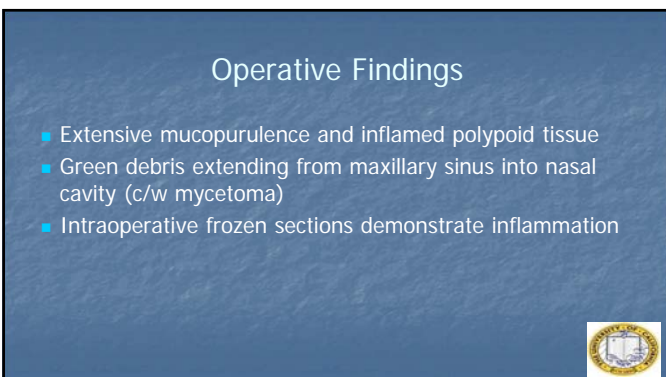
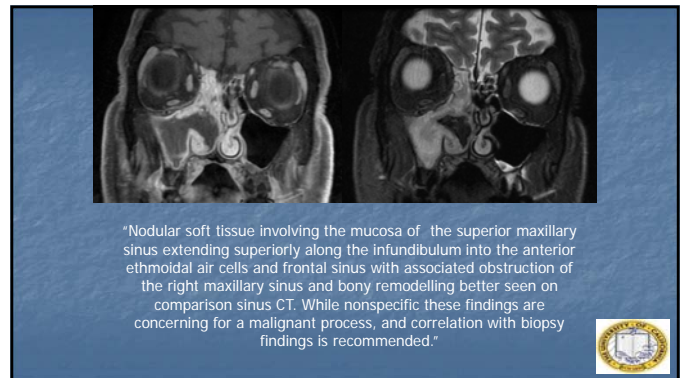
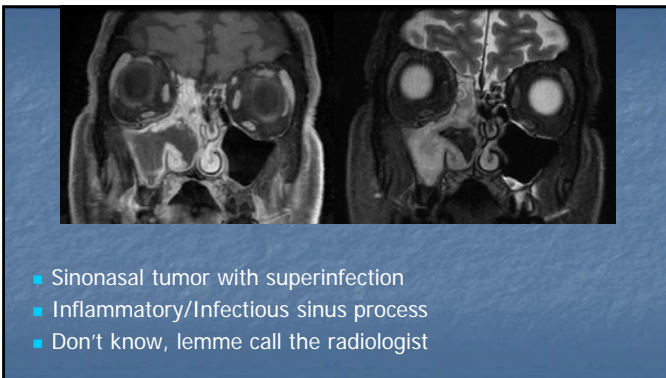
IMPRESSION:
1. Extensive opacification involving the right frontal ethmoid and maxillary sinuses with associated bony destruction. Although this could be secondary to chronic inflammatory disease underlying neoplasm should also be a consideration.

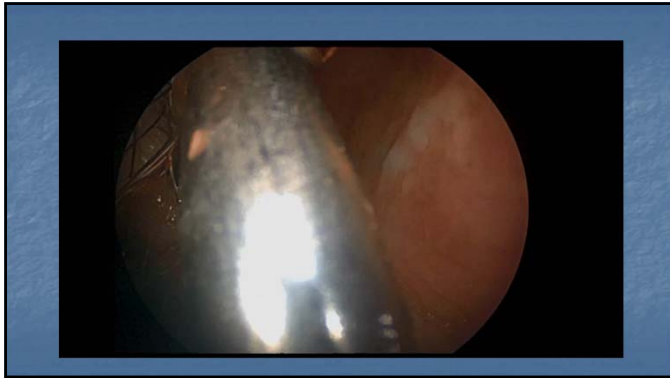




Biopsy

Inflamed Granulation Tissue

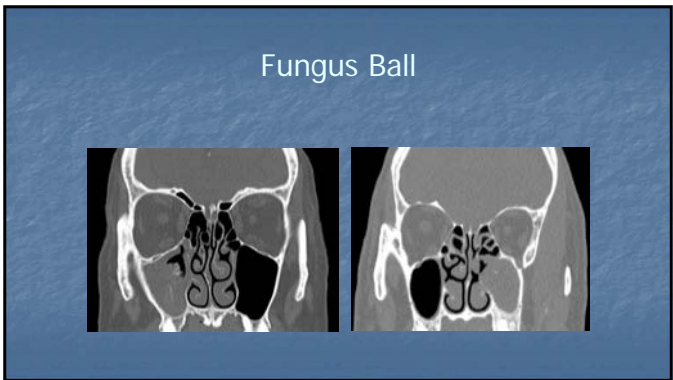




Diagnosis of a Maxillary Sinus Fungus Ball Without Intralesional Hyperdensity on Computed Tomography

Che-Fang Ho, MD, Ta-Jen Lee, MD, Pei-Wen Wu, MD, Chi-Che Huang, MD, Po-Hung Chang, MD, Yen-Lin Huang, MD, PhD, Yueh-Lin Lee, MD, Chien-Chia Huang, MD
 Laryngoscope 129: May 2019

- Identify intralesional hyperdensity, irregular border, osteoneogenesis and bone erosion as distinguishing imaging findings



Diverse phenotypes and endotypes of fungus balls caused by mixed bacterial colonization in chronic rhinosinusitis

Dong-Kyu Kim, MD, PhD, Young Chan Wi, MD, Su-Jin Shin, MD, PhD, Kyung Rae Kim, MD, PhD, Dae Woo Kim, MD, PhD and Seok Hyun Cho, MD, PhD
 International Forum of Allergy & Rhinology, Vol. 9, No. 11, November 2019

- Some clinically diagnosed fungal balls are mixes of bacterial and fungal debris

	Nasal	Maxillary	CT	Gross
Fungus ball				
Bacterial ball				
Mixed ball				
Double ball				

FIGURE 1. Clinical and radiologic findings of fungus ball, bacterial ball, mixed ball, and double ball during endoscopic sinus surgery. Various phenotypes of colonized microorganism materials (bacterial balls), which are similar and thus difficult to distinguish. CT = computed tomography.

A Retrospective Analysis of 1,717 Paranasal Sinus Fungus Ball Cases From 2008 to 2017

Xin Liu, MM, Chengyao Liu, MD, Hongzheng Wei, MM, Shuai He, MM, Shouxiang Dong, MM, Bing Zhou, MD, Luo Zhang, MD, Yunchuan Li, MD
 Laryngoscope 130: January 2020

- Increase in incidence over the past decade
- Direct smear positive for fungus in 69%
- Cultures positive in 23%

Association with Dental Implants

Dental implant and fungus ball in the ethmoid sinus

Int J Oral Maxillofac Surg. 2019 Dec;48(12):1594-1598.
D.H. Lee, T.M. Yoon, J.K. Lee, S.C. Lim, P. B.

A fungal ball within a maxillary sinus with dental root canal filler and rare fungal propagules

Masutomo Kitaura¹ | Akifumi Enomoto² | Osamu Maenishi¹ | Takashi Chikugo^{3,4} | Takashi Sugita⁵
Pathology International. 2019;69:360-365.



Clinical Presentations of Fungal Sinusitis

- Invasive Fungal Sinusitis
 - Acute Fulminant
 - Chronic
- Allergic Fungal Sinusitis
- Fungus Ball (Mycetoma)



THANK YOU

