GRANULOMATOUS DISEASES OF THE HEAD AND NECK

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OUTLINE

• Granuloma?
• Bacterial
• Fungal
• Autoimmune/vasculitis
• Neoplastic
GRANULOMA

- **Pathophysiology**
  - Is a type of chronic inflammation
  - Neutrophils usually remove agents that initiate an acute inflammatory response by phagocytosis and digestion. If an agent is indigestible it provokes a vicious cycle of acute inflammatory responses that can cause local tissue damage. The body deals with these reactions by forming granulomas.
GRANULOMAS

- The principle cells involved in granulomatous inflammation are macrophages and lymphocytes.
  - Macrophages live longer than neutrophils and can phagocytose an indigestible agent. This causes macrophages to lose their motility and thus accumulate at the site of injury.
  - Macrophages undergo structural changes and become epithelioid cells (larger with more cytoplasm, resemble epithelial cells). These cells (50+) can fuse together and form multinucleated giant cells.
  - Lymphocytes surround these cells.
  - When the nuclei of these giant cells form a horse show pattern, the cell is named a “Langhans Giant Cells”.

Pathogenesis of granuloma formation

Expert Reviews in Molecular Medicine 2005. Published by Cambridge University Press.
Caseous refers to a form of necrosis that can be seen without a microscope, “cheese-like” appearance.
BACTERIAL INFECTIONS
CAT SCRATCH DISEASE

- **Bartonella Henselae**
  - Gram negative rod
- **Hx of cat exposure in 90% of patients**
- **Mainly affects children and adolescents**
- **Clinical Manifestations**
  - Primary lesion small erythematous papule or pustule at sight of inoculation followed by tender lymphadenopathy (pre-auricular/submandibular), fevers, malaise
  - Parinaud oculoglandular syndrome:
    - granulomatous non-suppurative conjunctivitis
    - adjacent ipsilateral preauricular lymphadenopathy
CAT SCRATCH DISEASE

• **Diagnosis:**
  • Serology IgG, IgM
  • Biopsy/FNA
    • Warthin-starry silver stain - bacilli
    • Pyogenic granulomas (early)
    • Necrotizing granulomas (late)

• **Treatment**
  • Supportive/reassurance (average length of disease 14 weeks)
  • Azithromycin x 5 days has shown to speed resolution of lymphadenopathy
  • I&D; Needle aspiration
**BACILLARY ANGIOMATOSIS**

- **B. Henselae or B. quintana**
- **Vasculoproliferative cutaneous**
  - Papules, nodules
- **Immunocompromised (HIV)**
- **Diagnosis:**
  - Serology (IgG, IgM)
  - Biopsy/FNA
    - Warthin-starry stain
- **Treatment:**
  - Requires Antibiotic treatment
    - Erythromycin or doxycycline
    - Resolution is seen in 3-4 weeks
M. TUBERCULOSIS

- **Mycobacterium tuberculosis**
  - Immigrants, Healthcare workers, HIV
  - 1º-Asymptomatic, Lower lobe lesion
  - 2º-reinfection, weight loss, fevers, NS, non-productive cough, apical lung lesion

- **Head and Neck manifestations**
  - Constitutional symptoms
  - Cervical lymphadenopathy → Scrofula
    - Lymph nodes are bilateral, multiple, matted, non-tender
  - Oral
    - +/-pain, single/multiple lesions
    - Fissures, nodules, plaques, vesicles, ulcers
    - Tongue most commonly involved
    - Gingiva, buccal folds → Parotid gland
TUBERCULOSIS

- **Laryngeal TB**
  - Hematogenous /lymphatic spread
  - TVC>Epiglottis>False VC>
    Ventricular fold> Arytenoids> Post Commissure>Subglottis
  - Edematous, granulomatous, ulcerative lesions

- **Otologic TB**
  - Multiple small perforations-
    > complete loss of TM, seropurulent drainage
  - Pale granulation tissue within middle ear

  a) Ulcerative
  b) Granulomatous
  c) Polypoid
  d) Nonspecific
TUBERCULOSIS

• Diagnosis
  • Sputum culture
    • Ziehl-Neelsen stain- acid-fast bacilli
  • Biopsy
    • Necrotizing granuloma,
    • Acid fast bacilli
  • CXR
  • FNA>incisional biopsy
  • PPD (screening)

• Treatment:
  • Isoniazid, Rifampin, Pyrazinadine, Ethambutol x 2 month, then Isoniazid + Rifampin x 4 months
  • Lymph node excision may lead to draining fistula
TUBERCULOSIS

A. Necrotizing granuloma
B. Acid fast stain
C. Granuloma + multinucleated giant cell
D. Granulomatous Inflammation
ATYPICAL MYCOBACTERIUM

- M. avium, M. Kansaii, M. scrofulaceum, M. gordonii, M. fortuitum
- Common in children and immunocompromised

Clinical Manifestations

- Corneal ulcerations
- Cervical lymphadenopathy (scrofula)
  - Unilateral within the anterior cervical, pre-auricular, submandibular regions
  - Nodes are tender, discrete and separate → abscess
  - Corneal ulceration
ATYPICAL MYCOBACTERIUM

- **Diagnosis:**
  - Culture
  - Acid fast stain
  - PPD is often (-)

- **Treatment:**
  - Scrofula
    - Surgical excision (treatment of choice)
  - Erythromycin, Rifampin, streptomycin

2A: Chronic granulomatosus inflammation.
2B: Acid fast staining of organisms (arrow).
MYCOBACTERIUM LEPRAE

• Leprosy (Hansen’s Disease)
  • Acid fast bacillus
  • Humans (natural host), Armadillo (reservoir)
  • Common in tropical climates, but grows in cooler areas of the body → Nose, skin, superficial nerves
  • Transmission via nasal secretions, weeping ulcers/wounds, breast milk
MYCOBACTERIUM LEPRÆ

• **Tuberculoid**
  • Peripheral Nerves > cutaneous lesions
  • Muscle atrophy, neuropathy
    • Trauma, amputation
    • Cutaneous lesions are hypopigmented
  • Granulomas result from cell mediated Immunity
    • CMI response results in Nerve damage
MYCOBACTERIUM LEPRAE

- Lepromatous
  - Cutaneous lesions > Peripheral Nerves
    - Cutaneous: Brows, cheeks, nose, ear
      - Eyebrows/eyelashes are lost
      - Leonine facies
    - Nasal mucosa (95%)
      - Mucous membranes: nodules, plaques, pale-yellow and thickened
      - Anterior Inferior Turbinate/septum → septal perforation, saddle nose
    - Larynx, hard/soft palate
      - Ulcers/nodules
MYCOBACTERIUM LEPRAE

• **Diagnosis:**
  - Nasal/Skin scrapping
  - Tuberculoid
    - Few acid fast bacilli; Granulomas (+)
  - Lepromatous
    - Lipid-laden macrophages “Foam Cells” containing many acid fast bacilli; few/rare granulomas
  - Cultures are negative
  - No serology
  - Lepromin test (+)-tuberculoid

• **Treatment**
  - Tuberculoid
    - Dapsone+Rifampin
  - Lepromatous
    - Dapsone+rifampin+clorfazimine
SYPHILIS

- Treponema Pallidum
- Sexually transmitted; mother to child
- Clinical stages:
  - Primary (chancre), secondary (fever, malaise, rash, genital codyloma lata, mucous patches, ) Latent (asx), tertiary (CNS, Gummas, aortic)
- Head and Neck Manifestations:
  - Primary: oropharyngeal and nasal chancers, LAD
  - Secondary: localized alopecia, mucous-cutaneous involvement→ rhinitis, laryngitis, pharyngitis, tonsillitis
  - Tertiary: Gummatous lesions->septal perforation, saddle nose deformity, TM perforation
  - Argyll-Robertson pupil
SYphilis

- **Otologic**
  - SNHL, Meniere's symptoms, labyrinthitis, OM, ossicular fibrosis, temporal bone osteitis, Tullio's phenomenon, Hennebert's sign (false positive fistula test in absence of middle ear disease)

- **Hoarseness**
  - direct damage to VF mucosa, perichondritis, subglottic stenosis, RLN neuropathy, CNS

- **Congenital**
  - Hutchinson's Triad: abnormal central incisors, interstitial keratitis, SNHL
  - LAD, MR, saddle nose, frontal bossing, short maxilla

- **Diagnosis**
  - RPR or VDRL (both non specific), FTA-ABS (specific), dark field microscopy,

- **Treatment:**
  - benzathine PCN (tetracycline/erythromycin), +/-steroids
ACTINOMYCOsis

• Filamentous, branching, gram-positive bacillus
  • Normal flora of mouth/tonsillar crypts

• Clinical Manifestations
  • Hx or poor dental hygiene, dental abscess, trauma
  • Submandibular/anterior cervical, parotid swelling +/- Draining sinuses, bone involvement
    • Red, indurated, painless

• Diagnosis:
  • Culture: sulfur granules

• Treatment
  • Penicillin
  • Surgical debridement
RHINOSCLEROMA

- Caused by *Klebsiella rhinoscleromatis*
  - Gram negative, encapsulated bacillus
  - Air-borne transmission
- Endemic to Eastern/Central Europe, Central/South America, Africa, India
  - poor hygiene, crowded living conditions, poor nutrition
RHINOSCLEROMA

• Clinical Manifestations
  • Three stages of disease
    • Catarrhal (atrophic)
      • non specific rhinitis, honey-comb nasal crusting
      • Larynx-hoarseness, interarytenoid hyperemia, VF edema
    • Proliferative (granulomatous)-Mikulicz cells
      • Nose: Epistaxis, nasal obstruction; Nasal polyps adherent to Nasal septum
      • Larynx: glottic, subglottic granulomas
    • Cicatricial (sclerotic)-lesions heal with extensive scarring
      • Nose: scaring, stenosis, deformity, narrowing of nasal passages
      • Larynx: glottic, subglottic stenosis
RHINOSCLEROMA
RHINOSCLEROMA

• **Diagnosis**
  - Tissue cultures
    - MacConkey agar
  - Biopsy
    - plasma cells and large vacuolated Mikulicz cells with clear cytoplasm that contains bacilli and Russell bodies (which are transformed plasma cells).

• **Treatment**
  - Surgical debridement + tetracycline (or ciprofloxacin) x 3-9 months
  - Long term follow-up; high relapse rates
FUNGAL INFECTIONS

GRANULOMATOUS SYSTEMIC MYCOSIS
HISTOPLASMA CAPSULATUM

• Dimorphic fungus
• Endemic to Ohio and Mississippi river valleys
  • soil enriched with bird, chicken or bat excrement.
• Inhaled as a spore once ingested by macrophages it converts to a yeast
• Clinical Manifestations
  • **Acute Pulmonary:** Asymptomatic in 90% of patients; Self limiting
  • **Chronic Pulmonary:** occurs in patients with underlying lung disease  
    focal consolidation, cavitation of lung parenchyma
  • **Progressive Disseminated:** immunosuppressed patients
    • Fever, weight loss, dyspnea, cough
    • GI (mimics IBS)
    • Liver, spleen enlargement
    • Ulcers of mucous membranes
    • Septic shock
    • Death
HISTOPLASMA CAPSULATUM

Acute Pulmonary Infection
- Asymptomatic
- Buckshot Calcifications

Chronic Pulmonary Infection
- Cavitation of lung parenchyma
HISTOPLASMOSIS

- Head and Neck manifestations:
  - Most commonly oral cavity and oropharyngeal ulcers
    - Ulcers begin as flat, plaque like, non tender and become painful after ulceration
  - Mediastinal granulomatosis- nodes coalesce and form large lesions
  - Fibrosing Mediastinitis-healing
  - Cutaneous lesions
HISTOPLASMOSIS

- **Diagnosis:**
  - Urine and Serum Ag
  - Biopsy:
    - H&E-noncaseating granulomatous inflammation
    - Gomori methenamine silver staining

- **Treatment:**
  - Immunocompetent
    - Itraconazole
  - Immunocompromised/advanced disease
    - Amphoterecin B
**BLASTOMYCES DERMADEMATIDIS**

- **Dismorphic fungus found in moist soil**
  - Ohio and Mississippi
- **Clinical manifestations**
  - **Pulmonary:** Chronic Infection (Most common)
  - Extrapulmonary occurs in conjunction with pulmonary disease
  - **Cutaneous** (Most common)
    - Verrucous/ulcerative
  - **Laryngeal** (2%)
    - Hoarseness, dyspnea, odynophagia, cough
    - Diffuse erythema/ulcerations and/or Fungating lesions
      - Commonly mistaken for SCC; biopsy is critical
      - TVF’s most common subsite
BLASTOMYCOSIS

Mulberry-like appearance
BLASTOMYCOsis

**Diagnosis:**
- Sputum or tissue biopsy
  - Acute + chronic Inflammation, microabcess, giant cell formation
  - Hallmark sign: pseudoepitheliomatosus hyperplasia
- Gomori staining-Broad-based budding
- Culture

**Treatment:**
- Itraconazole
- Amphotericin B
**Coccidioides immitis**

- **Endemic to southwest US; found in soil of dry desert climates, “Valley fever”**
- **Primary pulmonary infection**
  - Inhaled of arthroconidia then form spherules with lung parenchyma
- **Clinical Manifestations:**
  - 60% are asymptomatic/flu-like symptoms
  - Extrapulmonary/Disseminated disease (0.5%)
    - Immunocompromised; dark-skinned people; pregnant
    - Skin, lymph nodes, bone, CNS, etc (except GI)
COCCIDIOIDOMYCOSIS

- Head and Neck Manifestations
  - Laryngeal manifestations
    - Submucosal Nodules, edema
      - Hoarseness, dyspnea, stridor
  - Cervical lymphadenopathy
  - Cutaneous Manifestations
    - Erythema nodosum or erythema multiforme
COCCIDIOIDOMYCOSIS

- **Diagnosis**
  - Culture
  - Biopsy
    - Granuloma + spherule with endospores
  - Serology*
    - Very specific and sensitive

- **Treatment**
  - Itraconazole
  - Amphotericin B
RHINOSPORIDIOSIS

- Caused by *Rhinosporidium seebri*
  - *Fungus? Aquatic Protistan of fish?*
  - India, Sri Lanka
  - Contaminated water/soil
  - Inoculation of spores into traumatized epithelium
- Most commonly affects the nose/nasopharynx (85%) and conjunctiva or lacrimal sac (15%)
  - Also involves skin, sinuses, palate, tonsil, larynx, parotid, genitalia
RHINOSPORIDIOSIS

• Clinical manifestations
  • Nasal obstruction, chronic epistaxis watery or purulent rhinorrhea
  • Friable, polypoid, vascular nasal mass
    • Lesions have pin-size yellow spots that bulge through epithelium gives it “strawberry appearance”
  • Mass is slow growing and painless
RHINOSPORIDIOSIS

- **Diagnosis**
  - Biopsy
    - Pseudoepitheliomatous hyperplasia, thick walled sporangia with numerous endospores
  - FNA
  - Culture
    - Nasal secretions

- **Treatment**
  - Surgical excision with cauterization at the base
ASPERGILLUS

- **Mold**
  - Septate hyphae that branch at 45 degrees
  - Illness results from an immunological response or tissue invasion
    - Lungs, Sinuses, CNS most commonly involved

- **Allergic Bronchopulmonary**
  - Pre-existing asthma -> bronchospasm

- **Fungus Ball (non-invasive)**
  - Recurrent sinusitis (single sinus)
    - Maxillary and sphenoid sinuses most commonly involved

- **Diagnosis**
  - CT/MRI of paranasal sinuses
    - Heterogeneous opacification (double density)
  - Biopsy/Culture (Sabouraud’s agar stain)

- **Treatment:** FESS (surgical removal)
  - Peanut-butter like appearance
• **Allergic fungal sinusitis**
  - Fungus becomes an antigen for an allergic response resulting in allergic mucin, mucosal thickening and nasal polyps
  - Patients are immunocompetent +/- hx of asthma, atopy
  - Symptoms of chronic rhinosinusitis + Allergy
  - More than one sinus affected

• **Diagnosis**
  - Allergy evaluation for molds/fungus (RAST, skin testing)
  - Allergic mucin (nasal eosinophilia), polyps
  - Nasal endoscopy
  - Tissue culture
    - Fungal hyphae without invasion
  - CT/MRI paranasal sinuses

• **Treatment**
  - FESS, steroids (intranasal +/- systemic), IT and antihistamines
**Aspergillus**

- **Acute invasive Fungal Sinusitis**
  - Fungal rapidly invades soft tissue and bone-Aspergillus
    - Mucormycosis – more invasive (vascular occlusion, thrombosis, infarction, necrosis)
  - **Affects immunocompromised patients** (DM, DKA, HIV, Chemotherapy,)
    - Fatal in 50% of patients with CNS
  - **Manifestations**
    - Fevers, orbital swelling, facial pain, congestion
    - Mucor-Necrotic black turbinates/soft palate, CNS involvement
  - **Diagnosis**
    - Same
  - **Treatment**
    - Surgical debridement + Amphotericin B (IV)+ stabilizing underlying disease

- Non-septated
- 90 degree broad-branching hypae
ASPERGILLUS

- Chronic invasive Fungal Sinusitis
  - Slow/indolent course
  - Locally invasive-soft tissue and bone
- Diagnosis
  - Same
- Treatment
  - Surgery (Debridement) + amphotericin B
- Granulomatous Invasive Fungal Sinusitis
  - Aspergillus falvus
    - Sudan, India, Saudi Arabia
    - Normal immune system
  - Diagnosis: Granulomas
  - Treatment: Surgery + antifungals
AUTOIMMUNE/VASCULITIS
SARCOIDOSIS

• Unknown etiology
  • Environmental/Microbial exposure?
    • Insecticides, mildew, molds, Mycobacteria
  • Genetics?
    • Butyrophilin-like 2 gene (BTNL 2)

• Epidemiology
  • 10-80 cases per 100,000
  • African Americans women
  • 20-40 years old
Sarcoidosis

• The clinical characteristics
  • bilateral hilar lymphadenopathy on chest radiography, erythema nodosum, uveitis, and maculopapular skin lesions

• Acute Sarcoidosis (Löfgren Syndrome)
  • Sudden onset with undergoing spontaneous remission within 2 years

• Chronic Sarcoidosis
  • Gradual onset, organ specific symptoms, and tendency to symptomatic relapse

• Head and Neck manifestations occur in 9% of patients
SARCOIDOSIS

- Nasal /Sinus Manifestations:
  - Rare
- Symptoms
  - Nasal obstruction, rhinorrhea, hyposmia, anosmia
- Clinical Findings
  - Dry, friable nasal mucosa with crusting
  - Septum/Turbinates typically present with white/yellow submucosal nodules/ granulomas or polypoid changes
  - Sinuses-Mucosal thickening/opacification
**SARC OIDOSIS**

- **Laryngeal manifestations**
  - 1-5%
  - **Symptoms**
    - Hoarseness, dyspnea, stridor, dysphagia, cough
  - **Findings:**
    - Supraglottis most commonly affected
      - Epiglottis (most common subsite) followed by arytenoids, AE folds and false vocal folds.
    - Classic appearance “Turban-like thickening” this is due to the pale, pink, diffuse induration and swelling of the supraglottis
    - Punctate nodules, ulcerations and masses are also seen
Sarcoidosis

- Cutaneous Manifestations
  - Papules, plaques, erythema nodosum, Darier-Roussey nodules (subcutaneous nodules)
  - Lupus pernio
    - Violaceous plaques and nodules covering the nose, nasal alae, malar areas, nasal labial folds and around the eyes.
SARCOIDOSIS

• Salivary gland involvement:
  • 5-10% of patients
  • Bilateral parotid swelling is most common
    • Non-tender, firm, smooth
  • Lacrimal gland swelling
• Heerfordt’s Syndrome (Uveoparotid fever)
  • Chronic febrile course, bilateral parotid gland swelling, uveitis and facial nerve palsy
SARCOIDOSIS

- **Diagnosis**
  - Bilateral Hilar adenopathy
  - Biopsy
    - Non-caseating granuloma
      - Epithelioid histiocytes
      - Surrounded by lymphocytes
  - Labs
    - Elevated ACE and calcium serum/urinary
  - Gallium Scan
SARCOIDOSIS

Non-caseating granuloma
Epithelioid histiocytes surrounded by lymphocytes
Sarcoidosis

- Positive gallium scan
  - Increased activity in parotid/lacrimal gland
    - Panda sign
  - Increased activity of perihilar adenopathy
    - Lamda sign
SARCOIDOSIS

• **Treatment**
  • **Corticosteroids**
    • Prednisone (10-40 mg/daily)
    • Intranasal steroids
  • **Methotrexate**
  • **Antimalarial Drugs**
    • Hydroxychloroquine and chloroquine
    • First line for dominant skin, nasal mucosa, sinus sarcoidosis
WEGENER’S GRANULOMATOSIS

• Recently known as Granulomatosis with polyangiitis

• Epidemiology
  • Prevalence: 3 in 100,000
  • Men and Women equally affected
  • Average age 40-55 years old
  • Most common amongst whites

• Systemic disease characterized by necrotizing granulomatosis and small vessel vasculitis.
  • Classic Triad of WG involvement:
    • Upper and lower respiratory tracts
      • Nasal/Paranasal - Most common manifestation in limited WG
      • Larynx/trachea
      • Lungs (most commonly involved 90%)
    • Renal involvement
      • Segmental /proliferative glomerulonephritis
      • Disseminated vasculitis
WEGENER’S GRANULOMATOSIS

• Head and Neck Manifestations
  • Nasal/Paranasal involvement
    • Occurs in 95% of patients and in 30% it can be the only manifestation (limited WG)
    • Patients present with a several week history of an URI
      • Nasal congestion, rhinorrhea, anosmia, chronic/recurrent sinusitis
      • Later: Nasal pain over the dorsum, serosanguinous rhinorrhea, epiphora
  • Exam:
    • Nasal crusting, friable mucosal affecting nasal turbinates
    • Septal perforations --> Saddle nose deformity
    • Obstruction of nasolacrimal duct
WEGNER’S GRANULOMATOSIS

- **Oral Cavity:**
  - Rare Manifestation
    - 6-13% may present as initial site of the disease
    - Ulcers, gingival hyperplasia (Strawberry gums)
- **Larynx/trachea**
  - Subglottic stenosis, tracheal stenosis
    - Occurs in the presence of systemic disease
  - Hoarseness, cough, stridor/wheezing (confused with asthma), dyspnea
WEGENER’S GRANULOMATOSIS

- **Ear**
  - Swelling, tenderness of the auricle
  - Otitis Media with effusion (24%)
    - Secondary to ETD-nasopharyngeal inflammation, luminal granulomata
  - CHL
  - SNHL, Vertigo
    - Cochlear vasculitis

- **Orbit:**
  - Nasolacrimal duct obstruction → epiphora
  - Orbital pseudotumor
  - Periorbital edema
  - Chemosis
  - Proptosis (15%)
WEGENER’S GRANULOMATOSIS

• Lungs
  • Dyspnea, cough, hemoptysis
  • Cavitating granulomatous lesions
    • Pulmonary parenchyma and bronchi
  • Chest xray: single or multiple (<10) cavitary nodules of 5-100mm in diameter

• Renal
  • 20 % have renal disease at time of dx
  • 80% progress to glomerulonephritis
    • U/A: Hematuria, proteinuria, red cell casts,
    • hypertension, edema

• Cutaneous
  • Ulcers of distal extremities
  • Wart-like lesions around the elbows
  • Pyoderma gangrenosum like lesions
  • Petechia
  • Crusted plaques
Diagnosis

- Serum c-ANCA, and PR3
  - Caused by antibodies against proteinase-3
  - Specificity 98%, Sensitivity is variable 90% (active systemic disease), 60% (active local disease), 30% (remission)
  - Can be used to monitor disease activity/relapse

Biopsy

- Nasal biopsy is the most common
  - All nasal crusting must be removed to ensure a good tissue sample from septum, nasal floor, and turbinates
  - Culture/ Stains
  - Necrotizing granulomas with vasculitis

Chest Xray

Urinalysis
WEGENER’S GRANULOMATOSIS

• **Treatment**
  
  • **Initial goal is to induce remission**
    
    • Cyclophosphamide (2mg/kg/day)x 6-12 months + high dose Prednisone (1mg/kg/day) x 1 month and taper
      
      • May use Methotrexate or Azathioprine (both are less toxic)
        
        • Local disease
    
    • Trimethoprim-sulfamethoxazole
      
      • Maintenance therapy
    
    • Rituximab, Etanercept, Lefunomide
      
      • Investigational therapies
  
  • **Sinonasal Disease**
    
    • Low-dose systemic steroids, NS irrigations, +/- Abx
    
    • FESS, repair of saddle nose deformity and septal perforation
WEGENER’S GRANULOMATOSIS

- **Laryngeal Disease (subglottic stenosis)**
  - Medical management
    - Immunosuppressents and high dose steroids
  - Acute Airway obstruction
    - Trach
  - **Subglottic stenosis**
    - Dilation + Intrallesional steroids or topical mitomycin c
    - CO2 laser
      - Gouveris et al. Better long term results with CO2 laser + intrallesional triamcinalone + topical mitomycin c and post-op immunosuppressants + PPI
  - Stents
  - Resection and end to end anastamosis
Wegener's Granulomatosis

Easy to diagnose and treat -- if you think of it.

Wegener's is infamous for its subtle presentation, and its lethality if (and only if) missed.

Caused by autoantibodies against proteinase 3.

Positive anti-neutrophil cytoplasm test (c-ANCA).

Granulomas and patchy necrosis in arteries and veins.

Sore eye?

Sore ear (outer? middle? inner?)

Stuffy nose?

Chest x-ray blip?

Sore joint?

Trace of blood?

Lung cavities

Permanent kidney failure

8 bleeds

Gangrene

Destruction of the face
RHEUMATOID ARTHRITIS

- Autoimmune disease causing inflammation of synovial joints
- 3:1, Women: Men
- Head and Neck Manifestations
  - TMJ dysfunction
  - Laryngeal
    - Cricoarytenoid joint involvement with ankylosis
      - Hoarseness, pain, odynophagia
      - Vocal cord impairment -> stridor, dyspnea -> +/- trach
  - Submucosal nodules of the vocal folds
    - Necrotizing granuloma
    - Hoarseness

A. CA erosion, closed glottic space, TVC fixed in Adduction
B. erosion of CA joint

Bilateral intracordal nodules
RHEUMATOID ARTHRITIS

- Otologic
  - CHL secondary to ossicular joint involvement
    - Rare
- Xerostomia
- Diagnosis:
  - Morning stiffness, symmetric polyarthritis, subcutaneous nodules (Rheumatoid nodules)
  - RF, ESR
  - CXR (Nodules, pleural effusion, fibrosis)
  - Biopsy
    - Nodules will show Necrotizing granulomas
- Treatment
  - NSAIDS, ASA
  - Prednisone
  - Methotrexate, azathioprine, pencillamine
  - Hydroxychloroquine
LUPUS ERYTHEMATOUS

- Idiopathic autoimmune vasculitis
  - Tissue damage occurs by deposition of autoantibodies and immune complexes
- 1 in 1,000; 9:1 Female: Male
  - Child bearing age, African American
- Main systemic manifestations:
  - Photosensitive skin eruptions, pleurisy, pericarditis, pneumonitis, myocarditis, nephritis, hypercoagulability, anemia, intractable headaches and CNS involvement
- Head and neck manifestations
  - Malar rash “butterfly rash”
  - Oral Cavity
    - Ulcers, macules
  - Laryngeal
    - Cricoarytenoid arthritis, TVF thickening, or paralysis, subglottic stenosis
    - Hoarseness, dysphonia, pian
  - Nasal cavity - anterior nasal perforations
- Xerostomia
  - Acute parotid enlargement
LUPUS ERYTHEMATOUS

- Neuropathy
- SNHL
- LAD
- Discoid lupus
  - Cutaneous lesions (face, neck, scalp), oral lesions, no visceral involvement
  - Elevated erythematous plaques $\rightarrow$ scar on resolution
- Diagnosis
  - Presence of 4 of the 11 manifestations listed, characterized by exacerbation and remission
  - ANA (non-specific), anti-dsDNA (specific), anti-Smith (specific)
- Treatment;
  - NSAIDs, Prednisone, avoid sun exposure, methotrexate
  - +/- retinoids for skin lesions
RELAPSING POLYCHONDРИTIS

- Rare inflammatory disease of cartilaginous structures
  - Ears, eyes, nose, larynx, trachea, bronchi, costal cartilages, articular joints
  - Relapsing-remitting
- Incidence is approximately 3.5 cases per million
  - Males and females equally affected
  - Peak onset 40-50 years old
- Some patients have been reported to have antibodies to Type II and Type IV collagen
  - Assay not widely available; poor sensitivities/specificities
- 30% of patients with RP have an associated autoimmune disease
  - Systemic vasculitis- Wegener’s granulomatosis
  - Connective tissue disorder- RA, SLE
  - Myelodysplastic syndrome
RELAPSING POLYCHONDRITE

• **External ear**
  - Erythema, tenderness of auricle and EAC, **SPARES** the earlobe
    - Earliest and most common manifestation
    - Can result in cauliflower ear
    - Often mistaken for cellulitis

• **Inner ear**
  - SNHL, Tinnitus, Vertigo
    - Vasculitis of labyrinthine artery
RELAPSING POLYCHONDRITE

• **Nasal cartilage:**
  • Recurrent Nasal inflammation
    • Saddle nose deformity
    • Septal perforation
    • Epistaxis

• **Eyes:**
  • Scleritis, episcleritis and conjunctivitis are most common
  • Periorbital edema, proptosis, chemosis
• **Laryngotracheobronchial tree**
  • Hoarseness, coughing, wheezing, stridor, dyspnea, tenderness of anterior cervical trachea, thyroid cartilage and larynx
  • Recurrent Inflammation leads to subglottic stenosis
  • Destruction and fibrosis can lead to airway collapse/obstruction
RELAPSING POLYCHONDРИTIS

- **Diagnosis criteria:**
  - presence of at least three of the following:
    - bilateral auricular chondritis
    - nonerosive seronegative polyarthritis
    - nasal chondritis
    - ocular inflammation
    - respiratory chondritis
    - audiovestibular damage
  - McAdam’s criteria revised Damiani and Levine
    - three McAdam criteria (as above) or
    - one McAdam criterion and positive histology or
    - two McAdam criteria and response to corticosteroids or dapsone.
- Cartilage biopsy not required
- Elevated antibodies to type II and IV collagen
- Exclusion of other diseases
RELAPSING POLYCHONDritis

- **Treatment**
  - High dose Glucocorticoids
    - Prednisone 0.5-1 mg/kg/d
    - Acute inflammation
  - Dapsone, colchicine, NSAIDs
    - Empirically used
  - Methotrexate, Cyclophosphamide
    - Maintenance therapy
  - Surgery
  - Symptoms typically resolve on 5-10 days
RELAPSING POLYCHONDРИTIS

Relapsing Polychondritis

Easy to diagnose and treat -- if you think of it.

Relapsing polychondritis is not-at-all subtle, but the correct diagnosis is often difficult to make.

Because the disease is migratory and transient, patients may seem to be hypochondriacs or even malingerers, and proper therapy with prednisone or dapsone is delayed.
CHURG-STRAUSS SYNDROME

- Unknown etiology
- Men > Female, onset 50’s
- Affects small to medium sized vessels and causes allergic granulomatosis
- Three phases:
  - **Prodromal stage** - adult onset asthma, allergic rhinitis with nasal polyposis, recurrent sinusitis
  - **Second stage** - peripheral blood and tissue eosinophilia (chronic eosinophilic pneumonia or gastroenteritis)
  - **Third stage** - systemic vasculitis (Renal, GI, Cardiac, CNS)
CHURG-STRAUSS

- **Nasal/Paranasal involvement**
  - Nasal crusting and polyposis
  - Recurrent sinusitis
  - Septal perforation is rare
  - Presence of asthma and nasal polyps distinguishes it from WG

- **Middle ear**
  - Granulation tissue with eosinophilic infiltration
  - Chronic ear drainage, suppurative OM
  - CHL, SNHL

- **Diagnosis**
  - Asthma, eosinophilia, and vasculitis with necrotizing granulomas
  - Leukocytosis with > 10% eosinophils
  - p-ANCA is found in 70% of patients, MPO-ANCA
  - Elevated serum IgE

- **Treatment**
  - Prednisone
  - Cyclophosphamide
CHURG STRAUSS SYNDROME

- The following criteria are based on the American college of rheumatology
  - Asthma
  - Eosinophilia > 10%
  - Neuropathy
  - Migratory pulmonary infiltrates
  - Parasinonasal abnormalities
  - Tissue eosinophils
- The presence of 4/6 finding results in a diagnostic sensitivity of 85%, with a specificity of 99%
NEOPLASTIC
NASAL NK/T-CELL LYMPHOMA

• Previously known as lethal midline granuloma
• Originates from NK or T cells
  • form of extranodal non-Hodgkin’s lymphoma
• Etiology
  • Unknown, EBV may play a role
• Most common in Men
• Clinical Manifestations:
  • Systemic signs
  • Nasal obstruction, purulent rhinorrhea, serosanguineous discharge→ septal perforation
  • Unilateral mucosal ulceration with extension into the palate, maxillary sinus, and upper lip
  • Destruction of mid face
  • mucosa is pale and friable, with crusting
  • Oronasal fistulas
NASAL NK/T-CELL LYMPHOMA

• **Diagnosis**
  • Biopsy
    • Sheets of polymorphonuclear cells with angiocentric lymphoid invasion, no granulomas or palisading histiocytes
  • CT/MRI Sinus

• **Treatment**
  • Radiation therapy
  • Chemotherapy + Radiation therapy
COCAINE-INDUCED MIDLINE DESTRUCTIVE LESION

- Nasal inhalation of cocaine can cause necrosis and destruction of nasal and paranasal structures and can easily be confused with (limited) WG
  - facial pain, epistaxis, nasal crusting, septal perforation, destruction of medial maxillary wall, inferior and medial turbinates,
  - No systemic symptoms
  - p-ANCA (+), PR-3 (+), NE (+)
    - c-ANCA is specific for WG; p-ANCA is nonspecific, (10% WG)
- Histology:
  - Extensive necrosis, acute/chronic inflammatory changes
  - Absence of necrotizing granulomas, multinucleated giant cells, vasculitis distinguishes it from WG
- Treatment:
  - Stop use of cocaine
  - Topical steroids
  - Antibiotics
COCAINE-INDUCED MIDLINE DESTRUCTIVE LESION
LANGERHANS CELL HISTIOCYTOSIS

- Granulomatous Disease of unknown etiology
- Histology
  - proliferation of Langerhans cells, eosinophils, macrophages, and lymphocytes
- Electron microscopy
  - Birbeck granules in cytoplasm of LCs
- Immunohistochemistry staining: S100 (+)
- Children > Adults
- Previously divided into disease subsets (eosinophilic granuloma, Hand-Schüller-Christian Disease, and Letterer-Siwe disease.)
LANGERHANS CELL HISTIOCYTOSIS

- **Eosinophilic granuloma**
  - Ages 5-9
  - Solitary osteolytic lesion
  - Mandible, maxilla, skull (Frontal, temporal bones)
    - Femur, pelvis, scapula, vertebrae, ribs
  - Benign course, good prognosis
  - Treatment: Local curettage +/- low-dose radiation (60 Gy)

- **Hand-Schuller-Christian disease**
  - Ages <5 year old
  - Multifocal lesions (visceral, osseous, cutaneous, soft tissue)
  - Constitutional symptoms
  - Triad: osteolytic skull lesions, exophthalmos, diabetes insipidous
    - Diabetes insipidus from erosion of Sphenoid sinus to sella turcica
  - TX: low-dose radiation therapy
LANGERHANS CELL HISTIOCYTOSIS

• Letterer-Siwe Disease
  • Disseminated disease (spleno-, hepatomegaly, dermatitis, proptosis)
  • Ages < 2 years old
  • Poor prognosis, high mortality rate
  • Tx: Chemotherapy (corticosteroids + Vincristine + Methotrexate) + Radiation

• Head and Neck Manifestations
  • Otorrhea, granulation tissue/aural polyps in EAC, acute mastoiditis, CHL
  • FN paralysis, vertigo, SNHL is rare

• Diagnosis
  • Biopsy
  • Imaging: Plain x-rays CT, MRI with gad
LANGERHANS CELL HISTIOCYTOSIS
NECROTIZING SIALOMETAPLASIA

- Benign, self healing inflammatory process of minor salivary glands
  - Ischemic injury
- Etiology: unknown, associated with trauma and radiation therapy, Men >> Women
- Head and Neck Manifestations
  - Painless ulceration or swelling usually over the hard palate
    - Unilateral lesion
- Diagnosis: Biopsy
  - Pseudoepitheliomatous hyperplasia
  - Commonly misdiagnosed as SCCa, Mucoepidermoid
- Treatment: self-limiting
NECROTIZING SIALOMETAPLASIA
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