CITYWIDE CASE

Benjamin Bluen ID Fellow PGY-5

Our Patient

- 70's male pt admitted Hospital for LLE pain and swelling.
- Ongoing for 2 months and gradually worsening
- Initially possible gout, arthrocentesis outpatient by rheumatologist w/o crystals
- Intra-articular steroid injection + Medrol dose pack
- Minimal improvement
- Nocturnal cough, clear productive, improved with famotidine

Additional HPI

No sick contacts

- Traveled to Philippines 2 months prior to onset of symptoms for 1 week, stayed with family, no known animal exposures
- Went to spa for pedicure one month prior to symptom onset
- No pets
- Previously in usual state of health

First Admission

- Admitted a few months ago A-fib with RVR
- TEE/CV, given Apixaban
- Noted to have LLE midcalf to ankle pain and swelling as "chronic issue"
- D/c'd on Medrol dose pack, gout?
- Also given 7 day course of Cephalexin 500mg PO BID for empiric SSTI

Second Admission

- LLE Minimal improvement, still "nonpurulent" cellulitis + fever to 102
- IV Vancomycin then Cefazolin x10 days total with mild improvement
- MRI LLE with myositis anterior, posterior compartments, vascular?
- Angiogram: Left distal tibial artery chronic occlusion with collaterals



Further Information

- PMHx: HTN, HLD, Gout, A-fib, DM2
- ESRD initiated HD 5 months prior
 - RUE AVF
 - Well tolerated HD sessions
- From Philippines, came to US 30 yrs prior worked as accountant
- SHx: nonsmoker, no EtOH, no drugs, lives with wife
- FMHx: mother + father with colon CA

Medications

- Omeprazole
- Digoxin
- Combivent
- Insulin Rapid and Long Acting
- Atorvastatin
- Famotidine

- Apixiban
- MVI
- EPO @ HD
- Sevelamer
- Cholecalciferol

Physical Exam Admission #3

- Temp 97.6, HR 67, BP 96/57, RR 16, Sat 96% RA
- HEENT: nc/at, no thrush
- Neck: w/o jvp elevation, supple
- Cardiac: RRR, nl s1 and s2
- Resp: Decreased bs @ bases
- Abd: soft, nt/nd, bs+
- Extremities: LLE with nonpitting edema



- MSK: left ankle tenderness, no other inflamed joints, full ROM, RUE AVF + bruit + thrill
- Skin: 2x2cm slightly tender nodule with mild surrounding erythema LLE sup to ankle

Laboratory Studies

- WBC 7.1, 65% Neutrophils
- Hb 9.4
- Plt 257
- Na 137
- K 3.9

- CI 97
- HC03 29
- BUN 32
- **Cr 4.89**

Imaging



Imaging



Third Admission

- LLE Multiple nodular fluid collections with mild surrounding erythema
- US 3/31: Collection developing 5.0x1.8cm immediately superior to ankle
- OR 4/7: Abundant purulent material sent for gs/cx from OR
- Continued Vancomycin per primary team



Questions?

- 70's M ESRD on HD, gout, with nodular lesions on LLE and CT with b/I LL nodular opacities developing over course of ~2 months.
- Additional information?
- Thoughts?



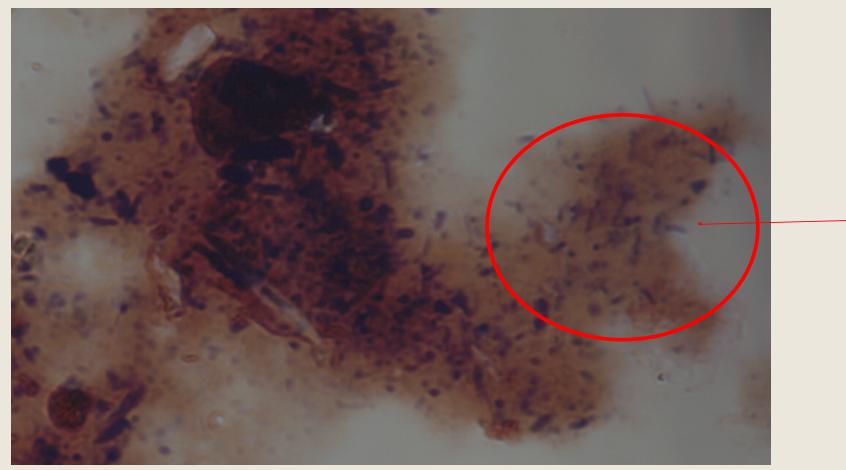
Differential Diagnosis

- Actinomyces
- Nocardia
- Non-tuberculous mycobacteria
- Leshmaniasis
- Sporotrichosis

- Cutaneous Meliodosis
- Auto-immune
- Malignancy
- Sweet syndrome

Gram Stain

OR tissue culture + beaded gram positive rods



Further Course

- ID c/s recommended change abx to TMP-SMX high dose PO
 - Possible nocardiasis, awaiting ID, sensitivity
- Additional nodular lesions ascending superiorly, TMP-SMX held
- I/D all with gram stain + beaded GPR, sent for AFB culture. AFB smear positive
- I/D left shoulder SSTI with also beaded GPR
- Culture from OR resulted in....

Final Result

Mycobacterium abscessus subspecies abscessus

Final Result

Antibiotic	MIC	Interpretation
Amikacin	8	Sensitive
Doxycycline	>16	Resistant
Minocycline	>32	Resistant
Moxifloxacin, Ciprofloxacin	4	Resistant
Tigecycline	0.12	Sensitive
Clarithromycin	16	Resistant
TMP-SMX	4/76	Resistant
Imipenem	64	Resistant
Linezolid	4	Sensitive

Workup and Treatment

- Patient eventually placed on:
 1.) IV Amikacin post-HD
 2.) IV Imipenem via Hickman
 3.) PO Linezolid
- Thrombocytopenia resulted, improved with once daily Linezolid
- AFB blood cxs negative
- No further skin lesions developing to date

Mycobacterium abscessus complex

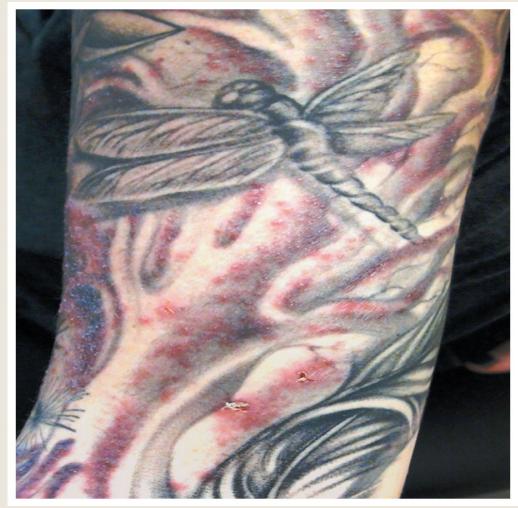
- First description Mycobacterium abscessus by Moore + Frerichs, 1953
- Rapidly growing mycobacteria comprising of 3 subspecies
 - Mycobacterium abscessus
 - Mycobacterium massiliense
 - Mycobacterium bollettii
- Ubiquitous in soil and water, dust, soil, rocks
- PNA and SSTI, disseminate to CNS, joints in immunocompromised
- Often treatment challenging, optimal antibiotic treatment unknown

Risk Factors

- Cosmetic Procedures
- Injection, liquid solution
- Dialysis
- Immunosuppression
- Trauma
- Surgical wound



Horii KA, Jackson MA. N Engl J Med 2010



Kennedy et al. N Engl J Med 2012; 367: 1020-1024

Treatment

- Challenging, susceptibility based, multidrug resistant
- Often combined medical + surgical treatment
- Inducible –erm gene macrolide resistance
 - Functional in abscessus
 - Nonfunctional in massiliense, favorable treatment
 - Present in bollettii
- Higher rates of antimicrobial clearance in *M. abscessus* pulmonary infection with macrolide-susceptible isolate

Treatment of *Mycobacterium abscessus* Infection

Novosad SA et al, M abscessus study team Emerg Infect Disease Network 2013

Extrapulmonary disease, 21		
No IV agents	9 (43)	1 (11)
Clarithromycin, other, 1		
Clarithromycin, doxycycline, 1		
Moxifloxacin, tobramycin drops, azithromycin drops, other, 1		
Azithromycin, linezolid, 1		
Tobramycin drops, azithromycin, moxifloxacin drops, azithromycin topical, 1		
Levofloxacin, doxycycline, 1		
Ciprofloxacin, minocycline, 1		
Clarithromycin, minocycline, 1		
Azithromycin, moxifloxacin, 1		
Single IV agent	5 (24)	2 (40)
Amikacin, azithromycin, clofazimine, 1		
Cefoxitin, azithromycin, 1		
Amikacin, ethambutol, 1		
Imipenem, azithromycin, moxifloxacin, 1		
Imipenem, azithromycin, ciprofloxacin, 1		
Dual IV agents	6 (29)	5 (83)
Amikacin-based regimens	6 (29)	5 (83)
Amikacin, macrolide and one IV agent, in addition to amikacin	5 (24)	4 (80)
Amikacin, azithromycin, imipenem, 2		
Amikacin, clarithromycin, cefoxitin, 1		
Amikacin, clarithromycin, imipenem, 2		
Amikacin, macrolide, 1 IV agent, in addition to amikacin, and other oral agents	1 (5)	1 (100)
Amikacin, clarithromycin, cefoxitin, moxifloxacin, linezolid, 1		
Triple IV agents	1 (5)	1 (100)
Amikacin, macrolide, 2 IV agents, in addition to amikacin, and oral agent	1 (5)	1 (100)
Amikacin, clarithromycin, imipenem, tigecycline, clofazimine, 1		
+D/ introveneur		

*IV, intravenous.

†Therapy was started for 34 patients, but 1 initial regimen was unknown.

Take Home Points

- Mycobacterium abscessus complex includes 3 different subspecies
- Rapidly growing mycobacteria
- Often multidrug resistant
- Treatment based upon sensitivities, macrolide preferred as sensitivity allows, individualized
- Medication toxicity
- Optimal treatment unknown

CITYWIDE

Kedesha Sibliss, MD PGY 5 ID Fellow September 19, 2017

Chief complaint

- 50's YO AAM with left wrist pain and swelling
- Reason for consult: Eval and treat for septic arthritis of left wrist

HPI

6 wks PTA:

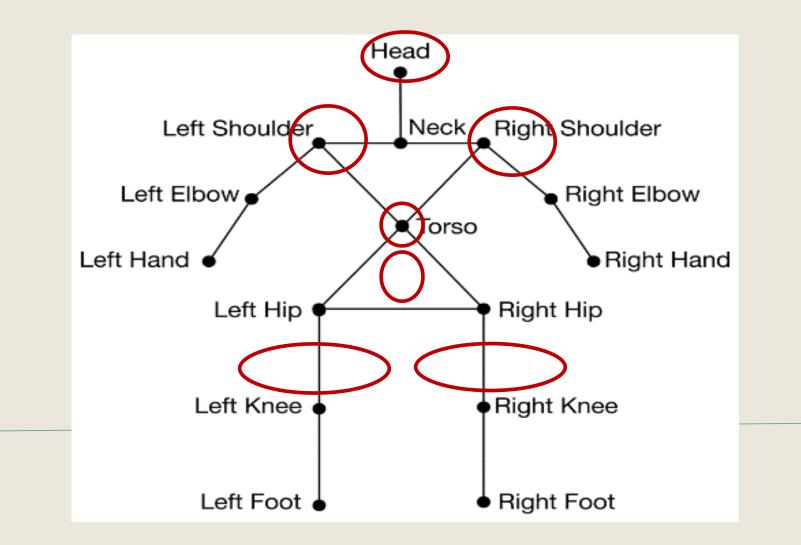
URI, fever, chills, productive cough and fatigue, a/w diarrhea and nausea <u>1 wk PTA:</u> left wrist and right thumb pain with swelling

<u>2 wks PTA</u> Weakness in bilateral shoulders, associated with back pain and thigh numbness and sensation of weakness

Additional HPI

- Denies travel out of state or out of country
- Owns a children's daycare although denies sick contacts.
- Denies sexual activity in one year. Although has history of high risk sexual behavior one year ago (involving multiple people including men- unprotected).
- Denies past STIs, never been HIV tested.
- Denies IVDU or other illicit drug use, social alcohol use only.
- No pets at home.
- Lives alone.

Review of systems



Medical History

PMH: HTN, GERD

- Surg Hx: septoplasty 2010, foot neuroma excision 2015
- FMH: Dad- HTN, Mom- arthritis / DM
- Social Hx: per HPI

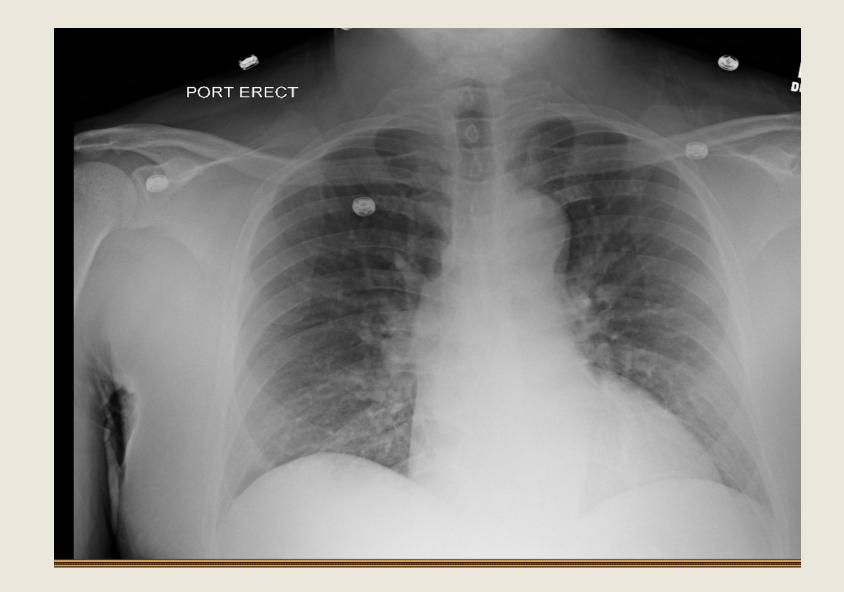
Physical Examination

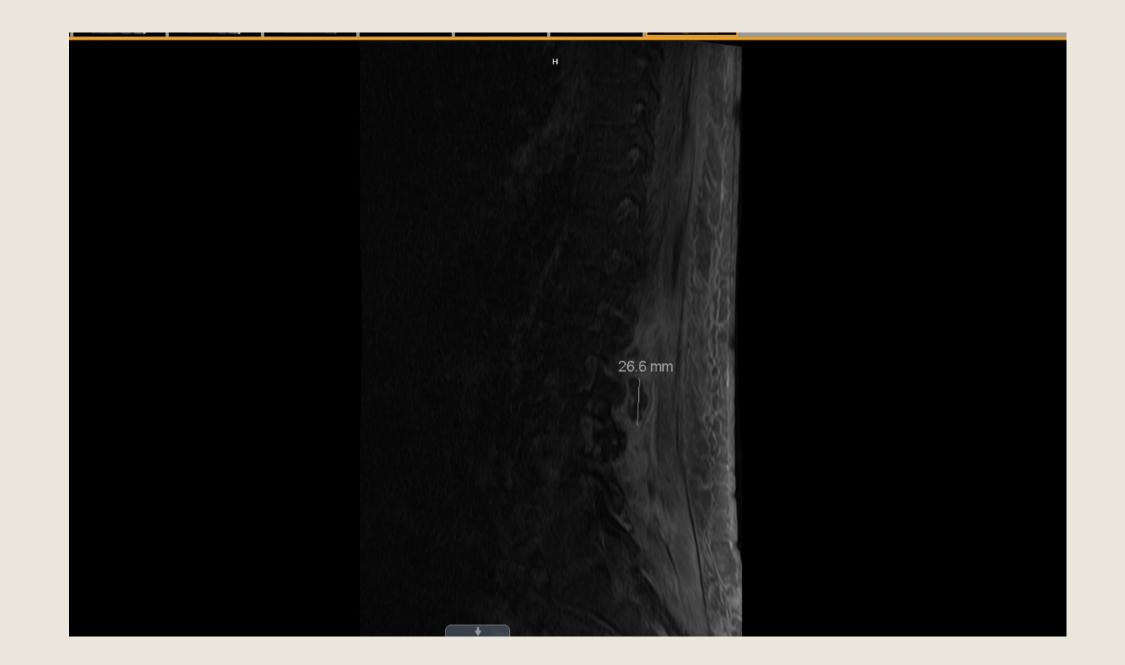
- Vitals: T100.0, P 91, RR16, BP 163/99, 02 sat 94% ambient air
- **GEN:** pleasant appearing AAM, NAD
- HEENT: PERL, normal conjunctiva, anicteric, moist oral mucosa, no oropharyngeal erythema/edema, no petechial rash, no oral ulcers, no sinus tenderness
- **Nodes** No lymphadenopathy
- Cardiopulmonary exam: WNL
- Abdomen Normal bowel sounds, abdomen soft and nontender, no HSM
- EXTREM: cannot make fist with left hand, diffuse swelling, , + synovitis + ttp , limited ROM

Axial skeleton

- + mild TTP of the paraspinal muscles in lumbar region
- NEURO
- Alert and oriented x 3, CN 2-12 grossly intact.
 - Motor strength:
 - RUE: 5/5
 - LUE: 5/5
 - RLE: 4/5 (thigh)
 - LLE: 4/5 (thigh)
 - Sensation: intact in all 4 extremities

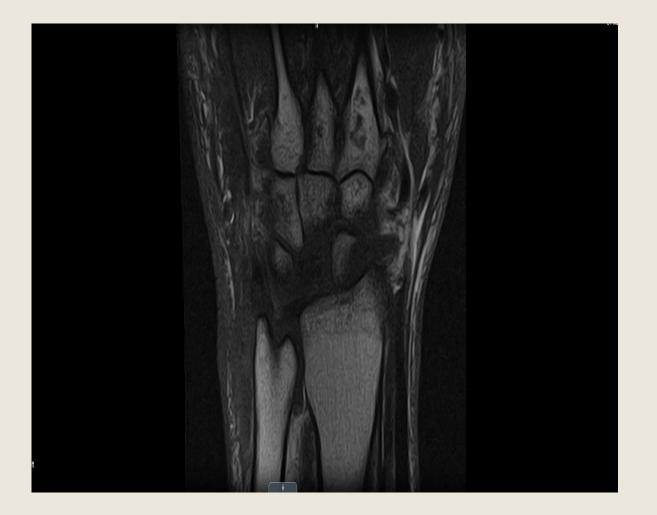
Wbc	14.4 (H)
Hgb	8.3 (L)
Platelets	487
Sodium level	131 (L)
Potassium	3.4
Chloride	97
Co2	20
BUN	28 (H)
Creatinine	1.13
Total protein	6.6
Albumin Ivl	2.6
ТВ	0.67
Alk phos	92
AST/ALT	27/44





Wrist MRI

- Extensive myositis and cellulitis of the wrist.
- No cortical erosion is seen within bones to suggest osteomyelitis.
- Trace fluid within the wrist joint, nonspecific.



Initial Assessment

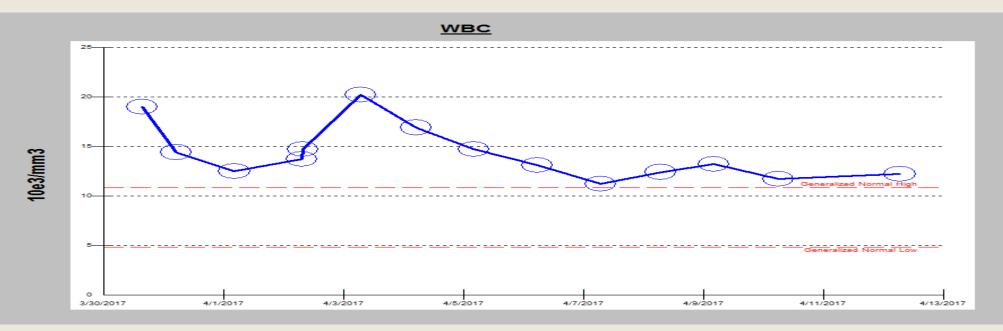
50 year old male presenting with 6 week history of URI symptoms, fever, GI upset (nausea/vomiting/diarrhea), and with a 2-3 week onset of muscles weakness in shoulders, back and bilateral thighs and a subsequent onset of left wrist and right thumb pain and swelling. Found to have epidural and sacroiliac abscess.

Differential/ Discussion

- The presentation here is not classic for septic arthritis , multiple other symptoms can present as described including :
 - campylobacter infection,
 - Reactive arthritis from URI or GI sources,
 - Dissemination of gonococcal infection,
- Possible viral causes include:
 - Parvovirus (works in daycare),
 - adenovirus (resp symptoms),
 - enteroviruses (GI symptoms).
- Less likely based on systemic symptoms is crystal arthropathies.

What additional workup would you send at this point?

Brief hospital course



- Call received from OSH with ³⁄₄ BCX strep pneumonia (S) CFTX, PCN
- wrist arthrocentesis performed was negative
- Pt switched to Ceftriaxone 2g
- L3-L5 laminectomy MRI also shows sacroiliac joint collection. Echo (TTE) no vegetation
- DC to rehab

Follow up outpatient

- Repeat CT pelvis showed resolving abscess anterior to sacroiliac joint
- Afebrile
- WBC 8.2
- Hemoglobin 9

Why did this immunocompetent 50's year old male contract invasive Pneumococcal disease?

INVASIVE PNEUMOCOCCAL **DISEASE IN** IMMUNOCOMPETENT MALE PRESENTING AS SEPTIC ARTHRITIS

What is invasive Pneumococcal disease?

An infection confirmed by the isolation of *Streptococcus pneumoniae* from a normally sterile site (eg, blood or cerebrospinal fluid but not sputum)

Who gets Invasive Pneumococcal disease

The highest incidence occurs in adults \geq 65 years of age, in children <2 years of age, and in those with certain underlying conditions, such as HIV infection.

What about the vaccines?

<u>CDC recommends pneumococcal</u> <u>conjugate vaccination for:</u>

- All babies and children younger than 2 years old
- All adults 65 years or older
- People 2 through 64 years old with certain medical conditions

<u>CDC recommends pneumococcal</u> polysaccharide vaccination for:

- All adults 65 years or older
- People 2 through 64 years old with certain medical conditions
- Adults 19 through 64 years old who smoke cigarettes

Evolution of the Pneumococcal Vaccine Prevnar/PCV

- PCV 7 for children was introduced in 2000
 - There was a resultant decrease in invasive pneumococcal infection during that time in children and in adults (herd immunity)
 - There was a 64% decrease in PCN resistant organisms
 - Increase in "replacement strains"
 - Serotypes covered: 4, 6B,9V,14, 18C, 19F, 23 F
 - increased incidence of 19A serotypes developed
- PCV 13 replaced PCV7 in 2010
 - Serotypes covered: 4, 6B,9V,14, 18C, 19F, 23 F, 1,3,5,7, 6A, 19A

Evolution of the Pneumococcal Vaccine Pneumovax/PPSV

- In 1977 the pneumococcal vaccine protected against 14 different strains was licensed
- In 1983 it was expanded to protect against 23 strains

Comparison of serotypes in pneumococcal vaccines

Conjugate vaccines				Polysaccharide vaccine	
PCV7 (Prevnar 7)	PCV10* (Synflorix)	PCV13 (Prevnar 13)	PCV151	PPSV23 (Pneumovax 23)	
4	4	4	4	4	2
6B	6B	6B	6B	6B	8
9V	9V	9V	9V	9V	9N
14	14	14	14	14	10A
18C	18C	18C	18C	18C	11A
19F	19F	19F	19F	19F	12F
23F	23F	23F	23F	23F	15B
					17F
	1	1	1	1	20
	5	5	5	5	22F
		з	з	з	33F
	7F	7F	7F	7F	
		19A	19A	19A	
		6A	6A		
			22F		
			33F		

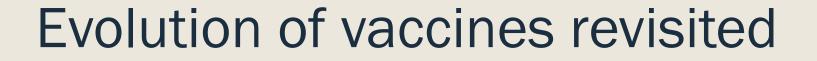
Risk factors for infection

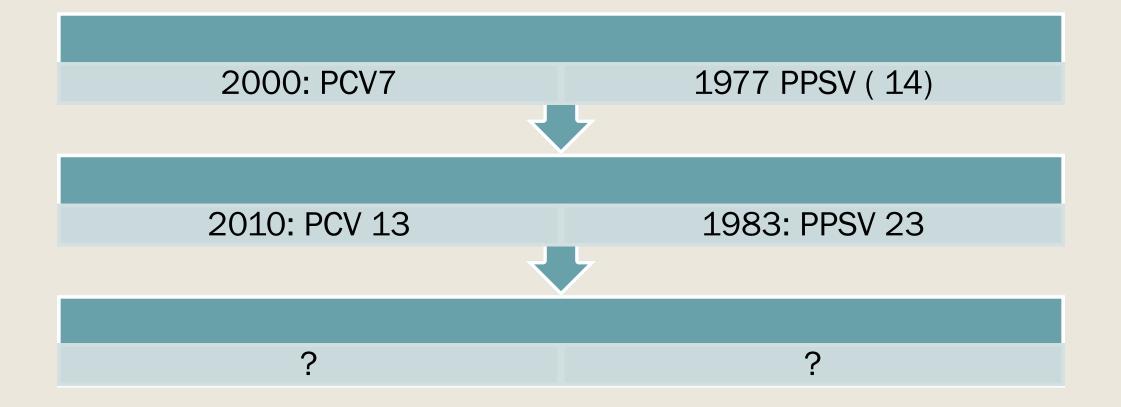
Non-modifiable

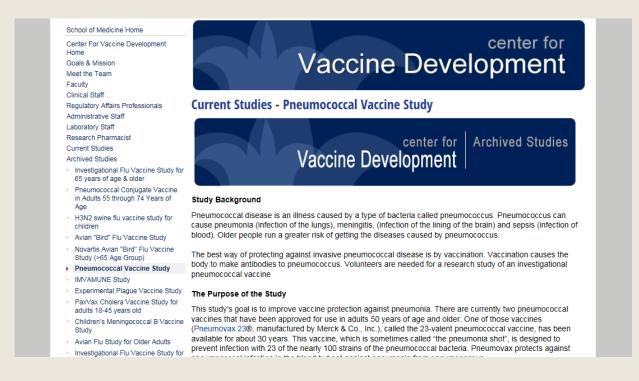
- Age <2, >65
- Certain racial/ethnic groups, including people of African descent, Alaskan Natives, and American Indians
- Male sex
- Modifiable/ comorbidities
 - Chronic CVD, Pulm disease, renal disease
 - Social: cocaine, ETOH, smoking
 - Cochlear implant
 - CSF leak
 - *DM*

Risk factors for infection cont..

- Risk of invasive disease is increased with concomitant resp viral illness
- Immunocompromised patients
 - HIV
 - Recent transplant (within 4 months)
 - Functional asplenia
 - Treatment with alkylating agents, antimetabolites, or systemic glucocorticoids







The Purpose of the Study

1) This study's goal is to improve vaccine protection against pneumonia.

2) To evaluate whether giving two injections of Prevnar 13 to adults who have been previously vaccinated with Pneumovax 23 improves the antibody response to the pneumococcal strains in Prevnar 13. Everyone in this study will receive Prevnar vaccine, either one or two doses.

Do you think there is value in serotyping strains of invasive pneumococcal disease?

Citywide Presentation Caytlin Deering, DO PGY5

Initial Presentation

80's year old male referred for evaluation in the Infectious Diseases Clinic (5 years ago) with cough of 19 months duration

Past Medical History

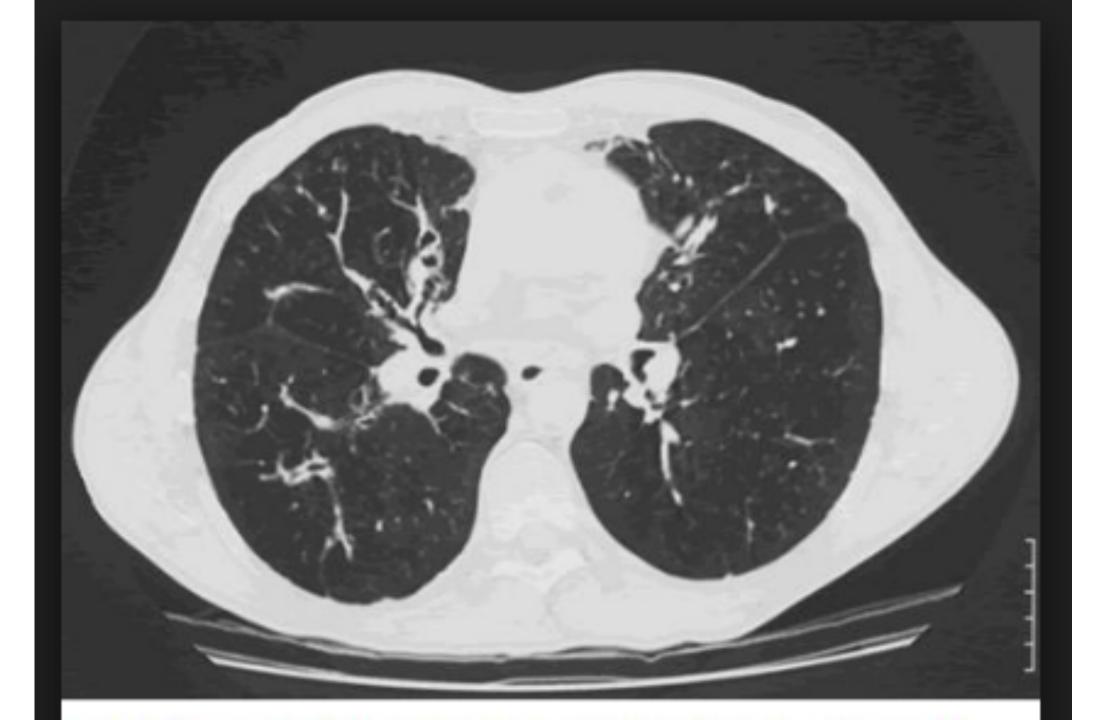
PMH/PSH: Myleodysplastic Syndrome, C. difficile infection, hypothyroidism, GERD, Hypertension, Lung Biopsy (6 years ago) Family History: Diabetes, Lung Cancer **Social History:** Lives in Philadelphia suburbs. Remote smoking history, no alcohol or illicit drugs. No travel. **Medications:** levothyroxine, multivitamin, pantoprazole, metoprolol, azacitadine (Vidaza) **Allergies:** Penicillin (urticarial rash) **Positive Review of Systems:** cough, 5 pound weight loss, anorexia, constipation, nausea after chemotherapy, fatigue

History of Present Illness

- Non-productive cough started in 6 years ago
- 5 years ago, CT scan of the chest
 - Bronchoscopy with BAL, no biopsy
 - Sputum culture positive for *Curvularia*
- 5 years ago, admitted for *Clostridium difficile* infection
 - Lung biopsy performed

"Dilated bronchials with allergic mucous," abundant eosinophils, fungal hyphal elements. No invasion into the lung parenchyma.

No antifungal therapy given.



History of Present Illness

- *3* years agothe cough increased
 - Repeat CT scans had shown bronchial dilatation, mucous plugging, bronchiectasis, and <u>various levels of inflammation</u>
- bronchoscopy
 - *Curvularia* was isolated from sputum culture

Exam and Pertinent Laboratory Data

Afebrile, normotensive. BMI 18.94 General: Alert, well appearing, in no acute distress, thin HEENT: Normocephalic, PERRLA, no scleral icterus. No oral thrush or dental decay. CV: RRR without murmur. No peripheral edema. RESP: Good air entry, few scattered rhonchi ABD: Soft, without HSM SKIN: No rash HEME: No lymphadenopathy, no bruising

WBC 5.3, 37% eosinophils

80's year old male with MDS presents with cough of 19 months. Imaging shows bronchiectasis with mucous plugging, and lung biopsy showed dilated bronchials with allergic mucous and fungal elements. Multiple sputum cultures have been positive for Curvularia.



Differential Diagnoses

Allergic Bronchopulmonary Aspergillosis Lung Abscess Tuberculosis Recurrent Aspiration Curvularia infection or colonization

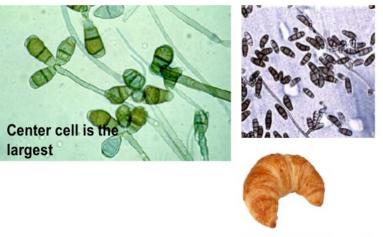
Asthma Bronchiectasis Cystic Fibrosis Neoplasm Rheumatologic Disease Myelodysplastic Syndrome Toxin Exposure Medication Side Effect

Initial Assessment and Plan

Non-invasive Curvularia infection

- >15 months of symptoms
- Curvularia "equivalent" of ABPA (ABPM, or ABPC)
- No therapy initiated

Curvularia lunata



IgE level 1949 IU/mL

Started on <u>prednisone</u> and <u>itraconazole</u> for 4 month course. Cough improved. CBC showed WBC 4.7, Hg 8.6, PLT 112. Eosinophils were not checked.

Phaeohyphomycosis

Phaeohyphomycosis

- Dermatiaceous, darkly pigmented fungi (melanin in cell wall)
 - More than 100 species
 - Soil organism, worldwide
 - Common laboratory contaminant
 - Affects immunocompetent and immunocompromised
- Inhalation or cutaneous inoculation

Allergic Disease

- Fungal Sinusitis
 - chronic sinus symptoms
 - antibiotic failure
- Commonly caused by *Bipolaris* and *Curvularia*
- Treatment: Remove mucin, give steroids. Itraconazole use not routine.
- Allergic Bronchopulmonary Mycosis
 - Similar to ABPA
 - Most caused by genera *Bipolaris* and *Curvularia*
 - Large spores (20–30 μ m x 8–12 μ m) (aspergillus is 2–3 μ m)
 - Asthma, bronchiectasis
 - Eosinophilia, elevated IgE
 - Criteria for ABPM diagnosis not well established

Critical Reviews in Microbiology

http://informahealthcare.com/mcb ISSN: 1040-841X (print), 1549-7828 (electronic)

Crit Rev Microbiol, 2014; 40(1): 30–48 © 2014 Informa Healthcare USA, Inc. DOI: 10.3109/1040841X.2012.754401



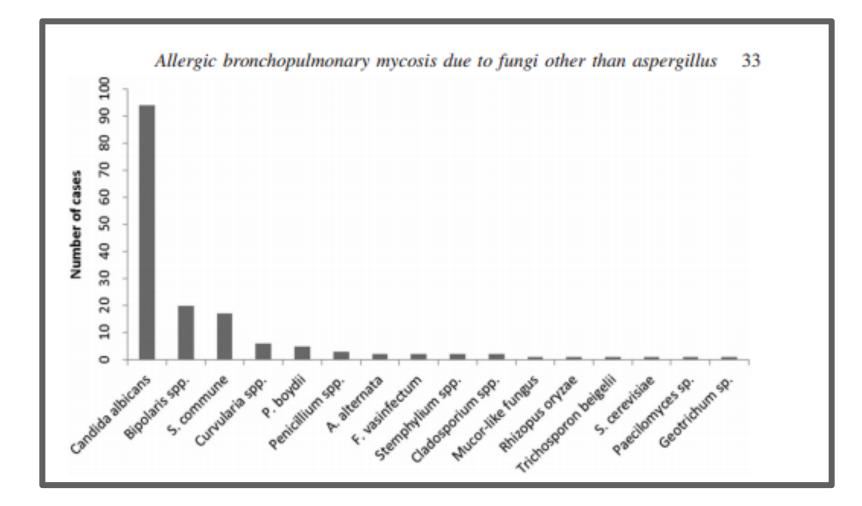
healthcare

REVIEW ARTICLE

Allergic bronchopulmonary mycosis due to fungi other than Aspergillus: a global overview

Anuradha Chowdhary¹, Kshitij Agarwal², Shallu Kathuria¹, Shailendra Nath Gaur², Harbans Singh Randhawa¹, and Jacques F. Meis^{3,4}

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Management

- Suppress immune response
- Control eosinophilic bronchitis
- Remove mucous plugs
- Eliminate fungus from the environment

<u>Systemic steroids may not prevent exacerbations or decline in</u> <u>lung function.</u>

- Reduce IgE 35-50% over 6-8 months
- Achieve remission