

## Citywide case conference

DUCOM

**Division of Infectious Diseases** 



### Case 1

Presented by Nabil Zeineddine 2<sup>nd</sup> year ID fellow



#### Case Presentation

- 60's years old male
- CC: right calf and ankle pain

Increasing right ankle and calf pain and swelling over the past 2 months, with fever for the past 2 weeks. Unable to bear weight on his right lower extremity

Symptoms started with onset of nodular erythematous rash over shin and calf.



#### Case presentation

• PMH:

Psoriatic arthritis

HTN

• PSH:

Cholecystectomy

Right shoulder surgery

• Social history:

From Chile, moved to USA 25 years ago

Retired bus driver

No alcohol use, drug use. Non smoker



#### Home medications

- Medrol 14 mg daily
- Ca + vit D
- Ibuprofen
- HCTZ 25 mg daily
- TMP/S M,W,F



#### Case Presentation

ROS

- General: + fever. No chills, no weight loss
- Lungs: no SOB, no cough
- GU: no dysuria, no frequency
- Abdomen: no diarrhea, nausea, vomiting
- Neuro: no HA, dizziness
- Skin: psoriatic skin lesions



#### Case presentation

- Temp 101 F, BP 132/75mmHg, HR 85/min
- General: Awake, oriented, not in acute distress
- HEENT: no conjunctivitis, no oral lesions, no cervical LAD, supple neck
- CV: RRR
- Lungs: CTAB
- Abdomen: non distended, +bs, non tender
- Skin: multiple psoriatic plaques over elbows, neck and abdomen nodules and central necrosis over right anterior shin and calf
- MSK: right ankle swollen, limited ROM







#### Lab data



136	99	13		
3.4	26	0.72		

AST 40 ALT 33 A phos 87 T bili 0.8 mg/dl UA 1-5 wbc, 2+ proteins



#### Case presentation

- CT scan of right lower extremity done
- Biopsy of the skin lesions done as OP before admission
- Specimen submitted for GS and Cx, afb, GMS and fungal culture

#### CT ankle







## CT scan showing abscess of the calf

• Abscess was tapped and specimen sent for GS and Cx, GMS stain and fungal Cx, afb

Questions? Thoughts?

#### GMS stain

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#### Hospital course

- Patient initially placed on vanco and piperacillin-tazobactam with no improvement. His skin lesions were debrided.
- All cultures resulted as Scedosporium apiospermum
- Blood Cx negative
- Patient underwent right BKA



#### Case presentation

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Scedosporium apiospermum					
Antifungal	MIC				
Fluconazole	16 ug/ml				
5-FU	> 64 ug/ml				
Itraconazole	4 ug/ml				
Voriconazole	0.5 ug/ml				
Amphotericin B	2 ug/ml				
Posaconazole	0.5 ug/ml				
Isavuconazole	4 ug/ml				

UT Health San Antonio Department of Pathology and Laboratory Medicine



#### Scedosporium complex

- Ubiquitous in the environment, frequency correlated to organic pollution
- *S. apiospermum* have a global distribution including Europe, Australia, South America, and the United States
- Infection often results from inhalation of spores from the environment into the lungs or paranasal sinuses or through direct inoculation, as in a skin puncture



#### Epidemiology

- The incidence of Scedosporium infection increased from 0.82 cases per 100,000 patient-inpatient days (in 1993-1998) to 1.33 cases per 100,000 patient-inpatient days (in 1999-2005).
- Dissemination occurs in about 2/3 of patients. The 12-week mortality rates 70% and 100% for S. apiospermum and S. prolificans infection, respectively.

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#### Unique species

- <u>S. apiospermum</u>
- S. aurantiacum
- S. dehoogii

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- P. minutispora
- Lamentospora prolificans



#### Scedosporium

- Hyphal forms appear as branching septate hyphae with a single terminal conidia, which is uninucleate and cylindrical in shape
- Asexual form = Scedosporium spp
- Sexual form = *Pseudallescheria boydii*



#### Scedosporium

- Hyphal forms appear as branching septate hyphae with a single terminal conidia, which is uninucleate and cylindrical in shape
- Asexual form = Scedosporium spp
- Sexual form = *Pseudallescheria boydii*

#### S. apiospermum

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 cylindrical uninucleate conidiogenous cell with conidium attached



# *P. Boydii* (cleistothecia)

• Spherical sexual structures that characterize *P. boydii*.







Anatomical origins (sites of infection) of 370 isolates submitted to the Fungus Testing Laboratory at the University of Texas Health Science System at San Antonio from January 2000 to May 2007.



#### Fungemia

- Fungemia is more common with *L. prolificans* than with *S. apiospermum* complex
- Positive blood cultures reported in 70 percent of *L. prolificans* cases.



#### Treatment

- Voriconazole as a first line.
- Combination of voriconazole with terbinafine is listed as a treatment option as there is demonstration of *in vitro* synergy.

The European Society of Clinical Microbiology and Infectious Diseases (ESCMID) and the European Confederation of Medical Mycology (ECMM) joint guidelines





Species	No. ofDrug combination (drug A +strainsdrug B)		Drugs alone		Drugs in combination		Interaction <sup><u>b</u></sup> (% of strains)
			Drug A	Drug B	Drug A	Drug B	
S. prolificans	20	Terbinafine + itraconazole	32 (4->64)	>32 (>32)	1 (0.5-4)	1 (0.5-16)	SYN (85), ADD (15)
	5	Terbinafine + voriconazole	>64 (>64)	8 (4-16)	9.51 (2- 32)	0.71 (0.03-2)	SYN (100)
	5	Terbinafine + miconazole	>64 (>64)	64 (8->64)	2 (1-4)	2 (0.13-8)	SYN (100)
	30	Amphotericin B + pentamidine	32 (4-32)	64 (8-128)	2 (1-4)	8 (2-32)	SYN (93), ADD (7)
	4	Voriconazole + micafungin	4 (2-4)	256 (256)	1 (1-2)	0.5 (13-64)	SYN (75), ADD (15)
	17	Amphotericin B + micafungin	>8 (1->8)	>32 (>32)	4 (0.5-8)	16 (0.06-16)	SYN (84), ADD (16)
S. apiospermum	3	Voriconazole + micafungin	0.13 (0.13- 0.25)	32 (0.25- 128)	0.06 (0.06)	0.25 (0.13- 0.5)	SYN (66), ADD (33)
	19	Amphotericin B + micafungin	8 (0.5->8)	2 (1->32)	1 (0.12-8)	1 (0.12-8)	SYN (31), ADD (69)
	8	Amphotericin B + miconazole	1 (0.25-2)	0.25 (0.13- 0.5)	NA <sup><u>a</u></sup>	NA	SYN (13), ADD (63)
	8	Amphotericin B + itraconazole	1 (0.25-2)	0.25 (0.03- 0.5)	NA	NA	SYN (25), ADD (13)
	8	Amphotericin B + fluconazole	1 (0.25-2)	16 (4-32)	NA	NA	SYN (38), ADD (50)



## Thank you



### Case 2

Presented by Melissa Tiyouh 2<sup>nd</sup> year ID fellow



**CC**: S/p cardiac arrest



#### HPI

60'syo African American man brought by EMS after cardiac arrest on the field.

➤Witnessed by bystander and CPR initiated.

- Patient received a single shock by AED. ROSC achieved. Intubated in the field.
- ≻In the ER, found to have STE in leads V1-V4, AVL.
- ➤Taken to Cath lab and underwent RHC/LHC which showed chronic total occlusion (100%) of LAD and ramus, not amenable to PCI.
- ➤Intra-aortic balloon pump placed.



#### Of note...

- Seen in the ER 2 ½ months ago for R hand wound from human bite during an altercation.
- ➢Had unremarkable hand XR. Given Tdap booster and discharged with Augmentin for 10days.



#### ROS

Unable to obtain



#### **PMH**: Schizophrenia, Cocaine use, heavy drinking, HCV (Untreated), OA

Allergies: NKDA

Meds: Olanzapine 20mg QHS

**PSH**: L wrist surgery

FH: HTN, DM (mother)

**Social Hx**: Cocaine and heavy alcohol use, unknown IVDU. Lives in senior home.



#### Physical exam

Vitals: 96.3F, HR=105, BP= 149/65, RR=24, 100% on Vent

- Gen: Intubated and sedated
- HEENT: NC/AT, anicteric sclera, pupils equal and reactive
- Neck: No JVD, no cervical lymphadenopathy
- Lungs: transmitted mechanical sounds anteriorly
- CVS: tachycardic, no murmurs, rubs, gallops
- Abd: Soft, non-tender, non-distended.
- **GU**: indwelling foley
- Ext: moved all extremities with pain stimulation
- Skin: no visible wounds or ulcers
- Lines: LFA sheath, RFV and RFA Swan Ganz catheter



#### Labs

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- WBC 6.6
- Hb 13/Hct 36
- Platelets 288
- K 4.0, CO2 **17**, Glu 154
- Bun 12, Cr **1.25**
- Albumin 3.9
- Alk Phos 49, ALT 58, AST 134, Tbili 0.82

- Lactate 1.2
- Trop **0.044**
- BNP 430
- CK 142
- Procalcitonin 1.5


### More labs

- Ethanol level undetected
- UDS + cocaine
- Urinalysis trace LE, neg nitrite, 1-5WBC
- HCV ab reactive. PCR 1.5million



# **Hospital Course**

- Admitted to CCU
- Completed 24hrs hypothermia protocol
- CTH with no hemorrhage or infarct.
- Developed hypotension 80/50s >2 sets of Blood cultures, urine and sputum culture. Obtained 15hrs after admission.

## CXR





# Day 2

- IABP and femoral sheath removed.
- 1/4 aerobic blood culture positive for GNR.
- Started on Cefepime 1g Q6H.
- GNR negative by nucleic acid test for:
  - Acinetobacter species
  - Citrobacter species
  - Enterobacter species
  - Proteus species
  - Escherichia coli
  - Klebsiella pneumoniae
  - Klebsiella oxytoca
  - Pseudomonas aeruginosa.



# Day 3

- Developed refractory hypotension.
- LIJ central line and L. radial A-line placed.
- Started on Norepinephrine.
- Sputum culture Strep pneumoniae and H. Influenzae.
- CCU team added Vancomycin and Metronidazole.
- Repeated Blood and urine culture.







# Day 5

- Developed low grade fevers 100 100.8F
- ID consulted



#### So far...

 60's yo man with cocaine and alcohol use admitted s/p cardiac arrest. Found to have chronic vessel occlusions. Developed septic shock. Found to have Pneumococcal & H. Influenzae pneumonia and GNR bacteremia of unknown source.



## ID evaluation

- Still intubated. Sedated but arousable
- Still on Levophed
- WBC 7.6, neut 57%, bands 31%
- Cr 0.83, AST 38, ALT 24
- Repeat blood and urine cultures negative
- Recommended CT chest/abdomen/pelvis





## CT Chest



# CT abd/pelvis



# CT abd

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# CT abd



# CT abd





### Course continued...

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- Underwent percutaneous cholecystostomy.
- Bilious fluid culture negative.





# Any thoughts?



# Burkholderia Cepacia



# Susceptibilities

	Burkholderia species	
Drug	MICM Inter	MICM Dilut
Amikacin	S	8
Aztreonam	S	4
Cefepime	S	<=2
Gentamicin	l	8
Imipenem	R	>=16
Levofloxacin	S	<=1
Meropenem	S	2
Pip/Tazo	S	<=8
Tobramycin	S	4



# Burkholderia Cepacia Complex



#### Introduction

- Burkholderia cepacia complex (Bcc) aerobic gram negative bacilli. Non-lactose fermenting.
- Found in soil, water, animals, plants and humans.
- Typically not pathogenic for healthy humans.
- Known opportunistic pathogen in CF and CGD patients.
- Very rare and limited data on community acquired infection in non-CF patients.



#### Common human species identified:

• B. cepacia

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- B. multivorans
- B. cenocepacia
- B. gladioli
- B. vietnamiensis
- B. pseudomallei
- B. fungorum
- B. dolosa

Appl Environ Microbiol. May 2008; 74 (10): 3121-3129



#### Bcc misidentification

- Pseudomonas aeruginosa
- Stenotrophomonas maltophilia
- Achromobacter xylosoxidans
- Alcaligenes xylosoxidans



### Transmission

- Person-to-person contact less common
- Contact with contaminated surfaces.
- Exposure to *B. cepacia* in the environment.
- Contaminated medicines and devices.



# Cepacia Syndrome

- Severe progressive respiratory failure
- High fever
- Leukocytosis
- Elevated CRP, ESR
- Bcc strains are usually resistant to antibiotics
- High case fatality rate



## Melioidosis

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- Also called Whitmore's disease.
- Caused by the *Burkholderia pseudomallei*.
- Predominately in Southeast Asia and Northern Australia.
- Can be a bioterrorism agent.



## **CDC** reports

- March 2004 manufacturer's recall of Nasal Spray contaminated with *Bcc*.
- August 2004 Bcc linked to nosocomial infections among ICU patients with exposure to sublingual probes.
- 2005 clusters of pneumonia and other infections caused by *B. cepacia* associated with contaminated mouthwash.



#### CDC

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• September 2016 - multistate outbreak of *Bcc* bloodstream Infections associated with contaminated prefilled saline flush syringes.

State	Number of affected facilities	Number of cases*	Number of deaths** among cases
Delaware	2	4	0
Maryland	3	12	0
New Jersey	20	59	0
New York	24	58	5
Pennsylvania	10	30	2
Totals	59	163	7



#### CDC

- August 2017 Multistate Outbreak of *Bcc* Infections associated with liquid Docusate Sodium.
- Restricted to oral docusate products manufactured by PharmaTech and distributed by six firms – Rugby, Major, Bayshore, Metron, Centurion, and Virtus.



#### Dr. El Chakhtoura and associates.

- Reviewed >1,000 VA hospitals, clinics, and long-term care facilities from 1999 to 2015.
- 248 cases of Bcc blood infections.
- 98% were older men (mean age 68 years).
- 44% had DM, 23% on hemodialysis.
- 41% on mechanical ventilation.
- 62% were nosocomial, 41% associated with a central venous line. 20% with pneumonia.
- 9% were community acquired, mostly associated with pneumonia and IVDU.

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#### Back to our case

- Pt completely recovered with Meropenem course.
- Refused further work up of pancreatic mass.
- Source of Bcc bacteremia likely environmental, cross infection or exposure from Senior living home.
- Unlikely from acalculous cholecystitis or pancreatic mass.



#### Take home points

- Bcc is an emerging cause of health care associated infections.
- Commonly affects CF, CGD and Immuno-compromised patients.
- Bcc are intrinsically resistant to aminoglycosides and some beta-lactam antibiotics.
- Healthcare facilities should consider isolation policies for Bcc infection in both CF and non-CF patients.



# References

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- A 17-Year Nationwide Study of Burkholderia cepacia Complex Bloodstream Infections Among Patients in the United States Veterans Health Administration, El Chakhtoura NG.
- Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases (Eighth Edition), 2015



# THANK YOU!

# Case 3

Presented by Marinela Ingilizova 2<sup>nd</sup> year ID fellow



20's y/o Male originally from Brazil with no significant PMH presents with swelling of hands and feet, arthralgia, redness swelling and pain over his ear lobes, episodic epistaxis that was getting worse . He also mentions skin lesions over his face, upper and lower extremities for over a year, worsening with sun exposure.

3 weeks ago he had similar presentation, his work up revealed negative "rheumatologic work up ", skin biopsy was done with pending results he was discharged on prednisone and appointment for dermatology was made; however shortly after stopping the steroids his symptoms returned and he decided to came back for re-evaluation.


PMH - none

PSH - unremarkable

SH - denies tobacco, alcohol or recreational drug

use

Travel - born in Brazil, immigrated in US 2 years back Occupation - construction worker, previously worked in a farm in Brazil Pets - has a dog



**ROS** : feeling generally well no weight loss has occasional changes in vision and headaches, appetite is good, has nosebleeds skin lesions present for over 1 year, worse with sunlight, has paresthesis over arms, legs, area of the rash

#### ΡΕ

Vitals 120/80 RR 16 HR 72 T 98 sat 99 on RA Alert oriented x 3 No jaundice No oral thrush or active nosebleeds Has facial edema more pronounced over the eyebrows cheeks nose loss of hair lateral eyebrows, bilateral malar area S1 s2 no rubs or gallops PP+ CTAB Abdomen soft non tender borderline enlarged spleen Significant swelling of the upper extremities bilaterally No palpable lymphadenopathy

Neurological exam is non focal

Skin – facial swelling, upper extremities with diffuse erythematous edematous plaques and hypopigmentation over the lower extremities





# Labs

Cr 0.84 AST 16 ALT 26 alk phos 62 HIV negative WBC 4,1 HH 12.5/30 PLT 205 Negative RPR negative RF, ANA , cANCA, pANCA , lyme serology UA no protein WBC or RBC

# RADS

CXR grossly normal CT scan C/A/P Mild splenomegaly, prominent left axillary LN otherwise unremarkable

# No Cx data



# Differential Diagnosis ???



# Pathology

Left lower extremity biopsy :

- Abundant necrotizing aggregates
- Acid fast organisms present
- Chronic inflammation extending to the fat including nerves
- Warthin-Starry stain positive for abundant rod shaped organisms



Leprosy is very old disease, described in literature of ancient civilizations.

Many people have been ostracized by communities and even their family.

People suffering from this disease can be disfigured and permanently disabled If not treated.

At present, 2 million people around the world are disabled due to leprosy.

Reportable disease



# Etiology

Mycobacterium leprae

Acid fast rod shaped bacillus

Very slow growth

Multiplies every 13 days

Obligate intracellular pathogen

Lacks several genes needed for independent survival

95% of population is considered non susceptible to the disease



# Transmission

No exact mechanism is known (possibly direct inoculation /droplet)

Prolonged close contact with untreated individual

No vertical transmission during pregnancy

No sexual transmission



#### Prevention

Early diagnosis and treatment (patients are considered no longer contagious after 1 day of effective therapy)

Annual exams for close contacts for 5 years



### Presentation

Discolored painless flat hypopigmented symmetric lesions Thick stiff dry skin Edema/erythema of skin (painful or painless) Chronic non healing ulcers

Nosebleeds/Nasal bridge deformities

Blindness/Corneal ulcers/Staphyloma

Redness and pain around the affected site

Foot drop/Claw hand/palpable swelling along nerves

Resorption of digits









# **Classification:**

• Paucibacillary (Tuberculoid)

Few hypopigmented or hyperpigmented macules with loss of sensation,

Due to the immune response we can observe nerve swelling

• Multibacillary (lepromatous)

Generalized or diffuse involvement of the skin, nerve thickening, potential to involve other organs – eyes, nose, testes, bone

• Borderline (Dimorphus) Tuberculoid but more numerous



# Diagnosis

Multiple biopsies from the skin lesions

AFB smear

PCR

One of the fallowing In Pandemic area:

- Hypopigmented / reddish skin lesions with definite loss of sensation
- peripheral nerve damage (loss of sensation or weakness)
- Skin smear + for Acid Fast Rod shaped Bacilli

#### Geographical distribution of new leprosy cases, 2015



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Source: World Health Organization/ National leprosy programmes Map: Global leprosy programme © WHO 2016. All rights reserved







#### Treatment

Dapsone 100 mg daily Rifampicin 600 mg once a month

Clofazimine 100 mg daily added for multibaucillary

Ofloxacin, Clarithromycin, Minocycline also used

Treatment is the same in HIV positive and HIV negative patients

Treatment should be provided during pregnancy



# **Complications of therapy**

Reversal reactions – increased cell mediated immunity (worsening neuritis and edematous lesions, claw hand, foot drop)

Erythema Nodosum Leprosum immune complex mediated (erythematous nodules, fever, synovitis, iridocyclitis, glomerulenephritis, secondary amyloidosis)

If steroids are needed for over 4 months – prophylactic Clofazimine 50 mg q day is advised

Tx is analgesics, steroids and if persistent Clofazimine, Thalidomide, Infliximab, Etanaercept



National Hansen's disease Program Baton Rouge, Louisiana



Thank you!