Interactive Case Studies in Clinical Microbiology

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Case #1

32 year old female who presents with abdominal pain that began at approximately 1:00am

Cramping pain (2/10), localized in the left upper quadrant

Pain was worse earlier this morning. Does not radiate

No other associated gastrointestinal symptoms (Nausea/Vomiting/Diarrhea

Patient reports not having any fevers, no one at home with similar symptoms

Took home pregnancy test this morning that was positive, LMP ~6/14/18

Some more history…

Patient is a physician assistant in a dermatology

Ate dinner last night: salmon fillet and vegetables

Coughed and removed small fish bone

Began examining fillet for more bones…
Medical progression

- Patient admitted to inpatient medical floor
- Complaining of persistent, crampy abdominal pain (3/10)
- Had one episode of non-bloody, non-bilious emesis
- Therapeutic endoscopy

Esophagogastroduodenoscopy (EGD)
Examination of the esophagus, stomach and duodenum

EGD/Biopsy Findings

- 2cm x 1mm worm noted in the proximal antrum (greater curvature) with burrowing into the stomach mucosa removed using cold forceps
- Area at burrowing site biopsied
- Mild diffuse erythema seen throughout stomach
- Mild patchy erythema in the duodenal bulb
- Localized eosinophilia around biopsy, no evidence of larvae
Anisakiasis

- Caused by the accidental ingestion of nematode larvae of Anisakis simplex, Anisakis physeteris, Anisakis pegreffii, or Pseudoterranova species
- Worldwide incidence
- High incidence where raw fish are consumed
  - Japan
  - Pacific coast of South America
  - The Netherlands

Clinical manifestations of Anisakiasis

- Symptoms begin 1-8 hours after ingestion of the contaminated fish or squid
- Larvae furrow into the gastric and intestinal mucosa and begin maturation
- Acute epigastric pain, nausea, and vomiting are the most common clinical symptoms
- Pruritus and tingling may develop in the posterior oropharynx

Diagnosis

- Typically made clinically based on history of consumption of undercooked food
- Recovery of larvae during EGD or surgery
- Serology

Treatment for Anisakiasis

- Humans are incompatible hosts, and the larvae die within a few days of ingestion
- Physical removal of larvae is curative
- Some patients have been treated with albendazole 400mg twice daily for 3-21 days, but data are limited

Prevention

- Larvae are destroyed by:
  - Cooking to > 63°C (> 145°F)
  - Freezing at ~20°C (~4°F) or below for 7 days
  - Freezing at ~35°C (~31°F) or below until solid, then storing at that temperature for ≥ 24 hours
  - Larvae may resist pickling, salting, and smoking

Case #2—No Way

- 79yo male with a history of stage IV lung cancer, coronary artery disease with defibrillator placement, and stroke
- At home receiving hospice care
- Presents to ED from home with abdominal pain and shortness of breath for 4 days
- Not relieved by home hospice interventions
- Pain is located on left side of abdomen—family reports that patient has known metastatic extension in this area
- He takes oral liquid morphine at home but this has not controlled his pain or shortness of breath

- Remaining image content is not relevant to the provided text.
Prior to Admission

- In the last week has been needing more home oxygen
- Productive cough with green sputum
- Reports a tactile fever
- Started at home on ciprofloxacin without improvement
- Receives care at another facility, but overall unsatisfied with care there

In the ED

- Febrile to 100.7
- Tachycardic (rapid heart rate)
- Tachypneic (rapid breathing)
- Placed on oxygen
- Started on ceftriaxone and azithromycin for suspected pneumonia and UTI.

Imaging

- Chest Xray with bilateral upper lobe pulmonary masses as well as multiple pulmonary nodules consistent with reported history of lung cancer
- Right perihilar consolidation extending to right middle lobe noted as well
- No prior CXR available for comparison.

Initial Treatment and Diagnostic Testing

- Extend antibiotic coverage to IV vancomycin/cefepime/metronidazole for empiric coverage
- Blood, urine, sputum cultures ordered
- Respiratory pathogens panel was positive for RSV.
- Patient is stable and being transferred out of ICU

Review of Gram stain from Sputum

- [Image of Gram stain with labeled bacteria]
Micro Lab Data

- Specimen collection Day 0 4pm
- Day 2 am
- Sputum culture—rejected as >10 squamous epithelial cells per low powered field
- Blood cultures—NG 2 days
- Urine Culture—beaded branching Gram positive rods

Micro Lab Follow Up

Day 3
- Urine—presumptive Nocardia sp.
- Sputum—set up for culture
- Blood—positive beaded branching GPR

16s rDNA gene sequencing based identification = Nocardia cyriacigeorgica

Nocardiosis = Disseminated Nocardia infection

- >90 species; 1/3 associated with human disease
- Most commonly in immunocompromised patients
- CNS is most common site of systemic dissemination, followed by skin
- Immunocompromised—Infection typically starts in the lung

Nocardia sp.

- Nocardia sp. are positive by modified acid fast stain
- Also Rhodococcus, Tsukamurella, Gordonia
- Presumptive identification using staining
- Identification (or preliminary identification) using MS*
- Sequence based identification is required for final species-level identification*
- Susceptibility testing required in most cases
- Can takes extra time to grow in the lab—ask providers to notify the lab to look for this if on the differential diagnosis
MALDI-TOF MS and Nocardia ID

- Spectra were analyzed using versions 5 and 6 of the BDAL Biotyper Research Use Only (RUO) library.
- Optimal species-level identifications were achieved using BDAL v6 at a score cutoff of ≥1.8 after direct extraction (49/60, 82%).
- Biotyper platform with BDAL v6 accurately identified 12/16 species of Nocardia.
- Sample processing steps such as boiling or mechanical disruption by bead beating did not improve the frequency of correct identifications.

Follow up

- Patient medically ready for discharge
- Transferred home by family; resume hospice care
- Transitioned to oral antibiotics—TMP/SXT
- No additional follow up at our facility

Case #3

- 31 y/o female who presents to ED with high-grade fever, generalized musculoskeletal pain, abdominal pain, headache, and multiple episodes of watery diarrhea/ emesis.
- Just returned from vacation to Playa del Carmen, Mexico.
- Patient appears in acute distress.
- Vitals upon examination are as follows:
  - BP: 142/68, HR: 124, Temp: 102.3°F, RR: 22, SpO2: 98%
- While in Mexico...
  - Ate local foods, including fruits, vegetables, seafood, and street vendor foods
  - Drank bottled water mostly, beverages with ice
  - Participated in outdoor excursions, swimming in fresh water and salt water, cliff jumping, cave diving, scuba diving (30-40 feet) day before returning home.
  - Reported several mosquito bites during trip.

Take Home Points

- Nocardia can be preliminarily identified by a positive modified acid fast stain that demonstrates long delicate filamentous rods.
- Taxonomy is changing so it’s a good idea to confirm the identification and get a susceptibility test.
- New technology may improve time to identification.

BioMérieux Vitek MS

- Spectra for the database were acquired using the direct smear method or the extraction method.
- Extraction method includes bead beating.
- Next release of VITEK MS update (IVD Version 3.0).
- 94% accurate identification to the species level on a set of 164 isolates.
ED Assessment

Review of Systems
- Constitutional: Positive for chills, fever, and malaise/fatigue
- Skin: Positive for rash
- Eyes: Negative for blurred vision and double vision
- Cardiovascular: Negative for chest pain, edema
- Respiratory: Negative for cough, sputum production, shortness of breath and wheezing
- Gastrointestinal: Positive for abdominal pain, diarrhea, nausea, and vomiting
- Genitourinary: Negative for dysuria
- Musculoskeletal: Positive for back pain, joint pain, and myalgias
- Neurological: Positive for weakness and headaches

Physical Examination
- Appears distressed
- Head/Ear/Neck/Eyes (HEENT): Normal, dry mucosa, normal gums
- Cardiovascular: Tachycardic, no murmur
- Pulmonary/Chest: Normal breath sounds, no respiratory distress
- Abdomen: Soft, not distended, no rebound or guarding, normal bowel sounds
- MSK: Normal range of motion
- Skin: Rash. Diffuse sunburn present, no lesions

Diagnostic lab testing

Common causes of Travelers’ diarrhea

1. Bacterial causes
   - Enterotoxigenic E. coli
   - Salmonella
   - Campylobacter
   - Shigella
2. Viral causes
   - Rotaviruses common
   - Norovirus
3. Parasitic causes
   - Cryptosporidium
   - Giardia
   - Cyclospora

Stool Culture
- BAP: heavy growth of wet, grey, beta-hemolytic colonies; heavy growth of grey, non-hemolytic colonies
- MAC: pink and colorless colonies
- HEK: heavy growth of orange/yellow colonies, moderate growth of green colonies with blackened center
**Microbiologic workup**

- Stool cx: No enteric pathogens isolated
- Cryptosporidium/Giardia stool antigen negative
- Stool O&P: No ova or parasites seen x 1
- Thin/thick PB smear: No malaria seen
- Negative toxin gene for *C. difficile* by PCR

**Downtrending WBC**

- Persistent fevers
- Blood cultures collected, incubating
- Now with leukopenia, thrombocytopenia

**Acute Dengue Fever**

- NS1 Antigen Index: 28.52 (H)
  - Reference Interval: <1.00
- DENV 1 or 3 RNA: Detected
- DENV 2 or 4 RNA: Not Detected

**Dengue Virus (DENV) Infection**

- Febrile illness caused by infection with one of four DENV (1-4)
- Transmitted by the *Aedes* aegypti or *Aedes* albopictus mosquitoes
- 390 million infections worldwide per year

**Dengue clinical presentations**
Differentiating among flaviviruses

Preventing arboviral infections
- Avoid travel to endemic regions
- Prevent mosquito bites
- Cover exposed skin
- Use EPA-registered insect repellents (DEET, picaridin)
- Use mosquito netting over bed
- Remove stagnant water in and around homes

Case #4—Not So Cute
- 20yo male patient presents to clinic with ankle wound and a sore throat
- Got the abrasion while traveling in Cambodia 3 weeks ago
- Traveling in South East Asia for the past 8 weeks
- Persistently oozing green fluid
- Used an antibiotic ointment he got over the counter in Cambodia
- FEVERS 2 weeks ago when he contracted Dengue Fever

Wound Infection
- 3 cm diameter wounds over the lateral malleolus scabbed over with minimal purulent drainage from the periphery and minimal surrounding erythema
- Xray rules out osteomyelitis
- Culture sent to lab

Microbiologic Workup
Gram stain: Very Few WBCs, Moderate GPCs, Few GPR
Moderate *Staphylococcus aureus* (Staphaurex)
Many Group A Streptococci (Lancefield typing)
Moderate *Corynebacterium* species (Gram stain, catalase)
MALDI Says?

1. Staphylococcus aureus
2. Streptococcus pyogenes
3. Corynebacterium diphtheriae

Cutaneous diphtheria

- Rare in US
- Endemic in tropical countries
- Characterized by shallow non-healing skin ulcers
- Often associated with infected insect bites
- Frequently co-infected with pathogens such as S. aureus and S. pyogenes
- Lesions are a reservoir for infection and can be associated with both cutaneous and respiratory disease

Additional Testing

1. Toxigenicity Testing
   - PCR for tox gene
   - Elek Test
   - Demonstration of toxin production is required for confirmed case

2. Biotyping
   - intermedium, bellive, mitis, or gravis
   - Differentiated by hemolysis, colonial morphology, and fermentation reactions.
   - Urease
   - Pyrazinamidase
   - Catalase
   - Nitrate reduction: varies by biotype

3. Additional Testing
   - Serologic testing
   - Molecular typing
   - AST

Elek Test

Treatment

- For cutaneous diphtheria, antitoxin is rarely required
- Attention should focus on wound hygiene and antimicrobial agent treatment
- The antibiotic of choice for treatment of cutaneous diphtheria is erythromycin or penicillin.
- Any person with clinical symptoms of respiratory diphtheria should receive diphtheria antitoxin (DAT) as soon as it can be made available without waiting for bacteriologic confirmation of the diagnosis.
Follow Up

- Patient moved out of state and was lost to follow up—vaccination history unknown
- Results received from CDC lab
  - *C. diphtheriae* biovar gravis
  - Non-toxigenic strain by Elek Test
- Patient was initially on TMP-SXT, but Penicillin added
- Patient reported sore throat? GAS RADT was neg.

Take Home Points

- Cutaneous diphtheria is easy to miss because the clinical appearance is nonspecific and other pathogens often co-infect the lesions
- CDC performs confirmatory testing
- ID can change therapy and infection prevention follow up

Case #5 – History of Present Illness

- 33 year old female with complicated past medical history
- Initially presented to rheumatology clinic in April 2018 with oral ulcers, arthritis, and rash
- Was reportedly well until September 2017 when she had an episode of severe lower abdominal pain with bilateral LE swelling and vaginal bleeding. Seen by OB/GYN and treated with ibuprofen with resolution of symptoms
- December 2017 developed a sore throat x 2-3 weeks with dry cough
- Treated with azithromycin but developed hives so switched to another antibiotic
- CT chest performed in February 2018, diagnosed with pulmonary embolism and begun on rivaroxaban

Case #5 – History of Present Illness (cont.)

- Following therapy with rivaroxaban, developed painful ulcers in the mouth
- In March 2018 noticed worsening pain and swelling in right ankle and right wrist
- Developed pustules in upper extremities and on her back
- The lesions were thought to be caused by Behçet disease
- Prescribed prednisone 30mg with a slow taper
- Rivaroxaban switched to dabigatran due to side effects
- Evaluated by dentist, had a tooth extracted and given antibiotics with pain relief but no resolution of ulcers

Skin Lesions:

- May
  - Progression of skin lesions
  - Superficial skin biopsy = no microorganisms
  - Aerobic swab culture = moderate growth of MRSE, moderate diphtheroids, light *C. albicans*

- Early June
  - Skin Lesions: May
Infectious Disease Consult: End of June

- No travel outside the country >2 years
- Lives in NW Indiana
- Office manager for a small financial group
- Enlarging raised lesion on her face, over her left upper cheek which was intermittently painful and draining pus

Skin biopsy from back lesion

“Verruca Vulgaris, inflamed and with overlying hemorrhagic neutrophilic scale crust with bacterial colonies. No deep fungal or atypical mycobacterial microorganisms identified with GMS, PAS, and Fites stains”

2-week follow up

- After 2 weeks on itraconazole, she noted significant decrease in size of most of her skin lesions, including her face, back and R finger
- Her facial lesion in particular is much smaller and flatter with no redness or drainage
**Blastomyces dermatitidis**

- Ubiquitous in the soil, environment
- Inhalation of microconidia and conversion into the yeast form leads to pneumonia
- Skin disease is the second most common manifestation
- Characteristic cutaneous finding is a verrucous lesion, with irregular borders
  - Lesion may mimic squamous cell carcinoma
- Ulcerative lesions bleed easily and have well-demarcated, heaped-up borders
- Multorgan disease occurs in approximately 20 percent of patients

**Case #6—Something’s Fishy**

- 24yo female patient from Illinois presents to urgent care after several days of gastrointestinal symptoms including bloating, stomach cramps, nausea, vomiting, tiredness, muscle aches and low-grade fever.
- During her summer babysitting job she’s been eating Goldfish crackers, Ritz Bitz crackers, Honey Smacks cereal, pre-cut melon, as well as eating at McDonalds.

**Summer of Salmonella and Cyclospora in Illinois**

- Salmonella Typhimurium—Fareway chicken salad
- Salmonella Adelaide—pre-cut melon
- Salmonella Mbandaka—Honey Smacks Cereal
- Salmonella Reading—raw turkey products
- Salmonella Braenderup—shell eggs
- Salmonella Sandiego—Hytine pasta salad
- Salmonella—back yard chicken flocks
- Salmonella Typhimurium—coconut, chicken salad
- Salmonella Montevideo—raw sprouts

- Cyclospora—veggie trays and McDonald’s salads ~620 cases

**Voluntary Recall of Pepperidge Farm Products**

Including:
- Goldfish Crackers
- Ritz Bitz
- Whey powder contaminated with Salmonella
- No linked cases so far
Microbiologic Workup

Stool Culture: No Salmonella or Shigella isolated
O&P exam: Negative
Not ordered: Shiga toxin testing, Norovirus testing
GI Panel: Cyclospora detected

Culture Independent Diagnostic Testing (CIDT)
- Campylobacter (jejuni, coli and upsaliensis)
- Clostridium difficile (Toxin A/B)
- Enterococcus faecalis
- Enterococcus faecium
- Enterobacter aerogenes, sobrinus and chouanniae
- Escherichia coli/Shigella
- E. coli O157:H7
- F. coli (ETEC)
- F. tularensis
- Giardia lamblia
- Helicobacter pylori
- Listeria monocytogenes
- Salmonella
- Shigella
- Vibrio (parahaemolyticus, vulnificus and cholerae)
- Vibrio cholerae
- Yersinia enterocolitica

Culture Independent Diagnostic Testing (CIDT)
- Campylobacter (jejuni, coli and upsaliensis)
- Clostridium difficile (Toxin A/B)
- Enterococcus faecalis
- Enterococcus faecium
- Enterobacter aerogenes, sobrinus and chouanniae
- Escherichia coli/Shigella
- E. coli O157:H7
- F. coli (ETEC)
- F. tularensis
- Giardia lamblia
- Helicobacter pylori
- Listeria monocytogenes
- Salmonella
- Shigella
- Vibrio (parahaemolyticus, vulnificus and cholerae)
- Vibrio cholerae
- Yersinia enterocolitica

Cyclosporiasis
- Caused by Cyclospora cayatensis
- Consuming food or water contaminated with the parasite
- Not spread person to person as organism is not infective when passed in the stool
- Sporulate after days to weeks in the environment at 22-32°C
- Ingested and invade epithelial cells of small intestine
- Symptoms begin about 7 days after ingestion; bloating, stomach cramps, nausea, vomiting, tiredness, muscle aches and low-grade fever
- Treatment with TMP-SXT

LUMC Data
Using BioFire GI Panel since 2016:
- About 10 cases of Cyclospora per year
- Over past 4 weeks = 71 cases detected
- Average 1-2 cases per week
- This Week = 6 cases

BioFire Film Array
Gastointestinal Panel

Take Home Points
- Cyclospora can be challenging to identify using routine light microscopy techniques
- Additional testing not routinely requested by clinicians
- CIDT may play a significant role in early detection and identification of outbreaks with pathogens like Cyclospora
• 55 year old male with significant past medical history
• Quadriplegia due to cervical spine injury 02/2016
• Requires total care, resides in a skilled nursing facility (SNF)
  • Tracheostomy, foley catheter, gastrostomy tube, colostomy
  • Chronic sacral and decubitus ulcers
• History of recurrent UTIs with MDR pathogens
• Admitted from SNF due to malfunctioning gastrostomy tube and hypotension due to poor enteral intake

Case #7

• On hospital day 3, infectious disease consulted to manage infection and make antibiotic recommendations
  • Chronic foley (previous VR E. faecium in 02/2018)
  • Bacteremia – Klebsiella pneumoniae

**CULTURE URINE**

**CULTURE FUNGUS**

**MALDI-TOF (Vitek MS) identified the yeast as Candida haemulonii. You should:**

- Report out C. haemulonii: 6%
- Report as Candida non albicans: 80%
- Panic and alert your local public health department: 14%
**Candida auris** often misidentified

- *Candida haemulonii*
- *Candida duobushaemulonii*
- *Candida guilliermondii*
- *Candida catenulata*
- *Candida famata*
- *Candida sake*
- *Candida spp.*
- *Rhodotorula glutinis*


Clinical cases of *Candida auris* reported by state, United States, as of June 30, 2018.

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Thank you!

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