1:30 – 2:30 pm

Challenging Cases in Infectious Disease

SPEAKER
Paul E. Sax, MD

Presenter Disclosure Information

The following relationships exist related to this presentation:

- Paul E. Sax, MD: No financial relationships to disclose.

Off-Label/Investigational Discussion

- In accordance with pmiCME policy, faculty have been asked to disclose discussion of unlabeled or unapproved use(s) of drugs or devices during the course of their presentations.

Challenging Cases in Infectious Diseases

Paul E. Sax, M.D.
Clinical Director, Division of Infectious Diseases
Brigham and Women's Hospital
Professor of Medicine
Harvard Medical School

Challenging ID Cases

- Cases selected based on those commonly encountered in outpatient primary care practice
- Frequent source of "curbsides"
- Participation required!

Case

- 82 year old man, subacute mild cognitive decline
- As part of w/u, has syphilis testing:
  - TP-EIA positive; RPR 1:1; TP-PA positive
- General PE normal
- No prior treatment for syphilis

Syphilis Alphabet Soup

- RPR
- VDRL
- TRUST
- MHA-TP
- TP-PA
- FTA-ABS
- TP-EIA

Use of Syphilis Tests

Screening
- RPR
- VDRL
- TRUST
- TP-EIA

Confirmatory
- FTA-ABS
- MHA-TP
- TP-PA

Syphilis: Non-Treponemal Tests

- VDRL, RPR
- Detect non-specific AB directed at cardiolipin-lecithin-cholesterol antigens ("reaginic" AB)
- False-positives common, usually low titer
- Used for: screening, following response to treatment

Treponemal Tests

- FTA-ABS, MHA-TP, TPPA, and treponemal-EIA (TP-EIA)
- Detect *specific* AB directed at *T. pallidum* antigens; however, false + rarely occur
- Recorded as reactive or non-reactive
- FTA-ABS, MHA-TP, TPPA used for confirmation of reactive RPRs
- TP-EIA increasingly used for screening in high volume settings

Don't Fall For This Trap

Hi Paul,
Quick question – I sent an RPR on a patient who has mild dementia and it came back positive. I don't really think she has neurosyphilis.
What should I do?
Thanks,
Scott

Case

- 75 year-old woman with questions about the zoster vaccine
- Husband has CLL and is receiving chemo
- She is concerned about transmitting vaccine virus to him

Zoster Vaccine

- Live attenuated virus
- 14X strength c/w varicella vaccine
- Indicated for immunocompetent adults > 60

Zoster Vaccine: Who's Immunocompromised?

- Neoplasms affecting the bone marrow or lymphatic system
  - Post treatment: assess on case-by-case basis
- Acquired or congenital defects in cellular immune function
- HIV with symptoms or CD4 < 200/15%
- Immunosuppressive therapy
  - Prednisone ≥ 20 mg/d for ≥ 2 weeks
  - Recombinant human immune mediators and immune modulators (e.g. TNF blockers)

MMWR 2008;57:1-30.

Varicella: Who Can be Considered Immune?

- History of chicken pox
- Healthcare-provider diagnosis of zoster
- Lab evidence of immunity
- Prior receipt of varicella vaccine (2 doses)
- **US-born before 1980**
  - Date of birth does not apply to immunocompromised, pregnant women, or healthcare workers

MMWR 2008;57:1-30.

A Typical VZV Curbside Exchange …

Subject: Cellcept and Varicella

Paul,

I have a patient on cellcept for dermatomyositis. Her son has just been diagnosed with chickenpox. She had it at age 11. Would you consider prophylactic Acyclovir? or assume she has immunity given that she had it before? If so how much Acyclovir? For how long?

Tony

Subject: RE: Cellcept and Varicella

Tony,

If she had chicken pox as a child, you do not need to worry. In the rare cases where people get it twice, the 2nd case is usually very mild.

Regards, Paul

A Typical VZV Curbside Exchange …

Subject: Cellcept and Varicella

Cellcept doesn' t change your mind? I' m a worrier!!!

Subject: RE: Cellcept and Varicella

We have lots of immunosuppressed patients out there (organ transplants, AIDS, biologics, etc) who get exposed to chicken pox, and if they're immune, nothing happens. (I assume she has not had a bone marrow transplant from a non-immune person!)

But of you're worried, and you'd rather do "something than nothing," you are free to give her acyclovir -- it's incredibly safe. You'll have to make up some dose/course.

Paul

Zoster Vaccine: Other Common Questions

- Should it be given to those with a prior history of zoster?
- Given FDA approval, should it be given to those younger than 60?
- Given lack of proven efficacy, should it be given to those older than 80?
- Should it be given to HIV+ patients? If so, which ones?
- When are supply, cost, and distribution issues going to be resolved?

Case

- 64 year-old medical transcriptionist, calls you regarding upcoming dental work
- Six months prior, underwent elective hip replacement for OA, uncomplicated; tolerated perioperative cefazolin
- She requests prescription for antibiotics based on her dentist's and orthopedist's recommendation

Dental Prophylaxis for Endocarditis: The Logic Behind It … But a Major Data Gap

- Dental procedures may induce bacteremia with oral flora
- These bacterial species commonly cause endocarditis, a serious condition
- Animal models demonstrate the efficacy of antibiotic prophylaxis
- But … no controlled data have ever demonstrated reduction in endocarditis from prophylaxis

DeSimone DC, et al. Circulation 2012 Jul 3; 126:60.

Endocarditis Prevention Guidelines: Procedures

1. Dental: gingival manipulation, perforation of mucosa
2. Respiratory mucosa
3. Infected skin/soft tissue

Not recommended for GU or GI procedures

Prevention of Infective Endocarditis, *Circulation*, May 7, 2007; circ.ahajournals.org

Endocarditis Prevention Guidelines: Cardiac Conditions

1. Prosthetic valve
2. Prior infective endocarditis
3. Congenital heart disease with shunts, conduits, patches
4. Cardiac transplant with valvulopathy

Prevention of Infective Endocarditis, *Circulation*, May 7, 2007; circ.ahajournals.org

Dental Prophylaxis and Prosthetic Joint Infections (PJI)

- Most common microbiologic causes of PJI: Staph aureus, coag-neg Staph, beta strep
- "Oral flora" account for approx 1-2% of cases
- Dental procedures linked to PJI only by case reports, very limited animal data
- CEA have repeatedly failed to demonstrate the utility of prophylaxis for this purpose

Wahl MJ. Clin Infect Dis 1995;20:1420-5.

However ...

"The less the evidence there is, the more antibiotic we give."

--Unknown Surgeon

Hi Paul,
Sorry to bother you. I have a pt who is 5 years s/p knee replacement, recently s/p C diff infection. Needs a colonoscopy. Has been advised by her orthopedic surgeon to be pretreated with antibiotics prior to having a colonoscopy. She is understandably concerned about causing another bout of C. Diff. Should I treat her with empiric Flagyl after she gets the amoxicillin?
Thanks.

Conditions to "Consider" Giving Antibiotics Before Dental Work to Prevent PJI

- Joint replacement < 2 years prior
- Inflammatory arthropathies (e.g. RA)
- Immunosuppression
- Diabetes
- History prior PJI
- Malnutrition
- Hemophilia

J Am Dent Asoc. 2003;134:895-9.

AAOS 2009: Give Prophylactic Antibiotics Indefinitely s/p Total Joint Replacements

http://www.aaos.org/about/papers/advistmt/1033.asp

- *"The practitioner might consider discontinuing the practice of routinely prescribing prophylactic antibiotics for patients with hip and knee prosthetic joint implants undergoing dental procedures."*

J Bone Joint Surg Am 2013; 95:745

Dental Procedures: Risk Factor for Prosthetic Joint Infection?

- 339 case patients (knee or hip infection) and 339 control subjects at Mayo Clinic
- Findings
  - No increased risk for those undergoing dental procedures
  - No reduced risk for those receiving antibiotic prophylaxis
- Editorial: "Time to focus on the data" – reconsider antibiotics, but improve dental hygiene

Berbari, Clin Infect Dis 2010;50:8–16; Zimmrli Clin Infect Dis 2010;50:17–19.

Bottom Line on Prophylactic Antibiotics for Dental Work

If you're asked about it, and it's not for prevention of endocarditis, don't do it!

Case

- 36 year-old advertising executive with loose stools, bloating x 1 month
- Dates symptom onset to an extensive business trip to Asia, including Indonesia, China, and Nepal; pt convinced he has a "parasite"
- PE: No weight loss. Stool O/P exam: many *Endolimax nana*

Parasites are confusing …

Hi Paul, 63 y/o female with h/o HTN and DM, presents for evaluation of "severe" anal itching x 2 weeks. Itching is worse at night and she does not believe it is diet related or associated with defecation. She is concerned she might have whip worm because her dog was recently dx with this. She reports stomach grumbling and excessive gas, but states she has always had this problem.

After her exam I think cause is a hemorrhoid. Can whip worm be transferred from dogs to humans? Is it safe for her to take her dog's medicine? (I think she has already done this.) Also, I have always understood that whip worm typically presents with bloody diarrhea. Is this correct? Thanks, Brenda

Pathogenic Intestinal Protozoa

- Definite
  - *Entamoeba histolytica* -- travelers, invasion
  - *Giardia lamblia* -- most common
  - *Dientamoeba fragilis* -- eos, Rx tetracycline
  - Cryptosporidia, microsporidia, isospora, cyclospora -- need special stains
- Possible
  - *Blastocystis hominis* -- conflicting data, Rx metronidazole 750 TID x 10 days

Start D, Int J Parasitol. 2007 Jan;37(1):11-20; Boorom KF, Parasit Vectors. 2008; 1: 40.

Non-pathogenic Intestinal Protozoa

- Amoebae
  - *Entamoeba hartmanni*
  - *Entamoeba coli*
  - *Entamoeba polecki*
  - *Endolimax nana*
  - *Iodomoeba butschlii*
  - *(Entamoeba dispar)*
- Flagellates
  - *Trichomonas hominis*
  - *Chilomastix mesnili*

Aucott JN, et al. Infect Dis Clin North Am 1993; 7:467-85. Start D, Int J Parasitol. 2007 Jan;37(1):11-20; Boorom KF, Parasit Vectors. 2008; 1: 40.

Non-pathogenic Intestinal Protozoa and Ongoing Diarrhea after Travel

- Presence of organisms indicate fecal contamination of food and/or water – no treatment necessary if symptoms improve
- In severely symptomatic patients (especially with weight loss), consider:
  - Antigen studies – in particular for giardia, cryptosporidia
  - Special stains for cryptosporidia, microsporidia, isospora, cyclospora
  - Post-infectious lactase deficiency
  - Bacterial overgrowth
- Diagnosis of exclusion (but common): Post-infectious irritable bowel

71 year old man, says he has the "flu"

- Generally healthy, on no medications; avid golfer and gardener
- Comes in in late June with 5 days of fevers, chills, headaches, poor appetite
- Has not been seen for any medical issues for 5 years; forced to come in by spouse
- PE: Looks tired but OTW well. T 101 (after acetaminophen). Remainder of exam normal, no neck stiffness or rash.

Older is Colder

- With older age:
  - Lower "normal" temperature
  - Less diurnal variation
  - Fewer "benign" febrile illnesses
- Management of acute fevers in older adults needs to always consider host, exposures, epidemiology

J Am Med Dir Assoc. 2007 Jun;8(5):335-7; J Am Geriatr Soc. 2005 Dec;53(12):2170-2.

Tick-Related Illnesses: Diagnostic Considerations and Lab Evaluation

- Northeast/Mid-Atlantic region: Lyme Disease, anaplasmosis, babesiosis; less commonly Rocky Mountain Spotted Fever, Powassan
- Generally include some combination of these tests
  - CBC with differential, "malaria smear"
  - Chemistry panel
  - Lyme antibody
  - Babesia PCR
  - Anaplasma PCR
- Low threshold for empiric doxycycline

Serologic Testing for Lyme Disease

- Two-step procedure
  - ELISA or immunoflourescence assay done first
  - Positives referred for Western blot confirmation
- Criteria for positive Western blot:
  - IgM 2/3 bands +: (22-25), 39 and 41
  - IgG 5/10 bands +: 18, 23, 28, 30, 39, 41, 45, 58,66, 93

Clin Infect Dis 2007;43:1089–134.

Serologic Testing for Lyme: Key Points

- Only 20-40% of patients with erythema migrans have positive serologies – no need to send test!
- If symptoms are > 4 weeks duration and *only* IgM is positive, it is likely a false positive
- >90% of patients with disseminated or late-Lyme are seropositive
- No "test of cure" available; serologies may stay positive for months-years
- Urine antigen, blood PCR, lymphocyte transformation commercially available, but not validated

Clin Infect Dis 2007;43:1089–134; Kalish et al. Clin Infect Dis 2001 15;33:780-5
MMWR. 2005;54:125; Lancet Infect Dis 2011;11:713-19.

Case

- 21 year-old college student, flies home early from Dominican Republic with fever, rash
- Symptom onset was abrupt; associated with chills, headache, arthralgias
- Exam: T 102, diffuse rash, lymphadenopathy
- WBC 2900, PLT 110K, HCT 39, malaria smear negative

Fever and Rash in Returning Traveler: Diagnoses to Consider

- Dengue
- Acute EBV
- Acute HIV
- Measles, rubella
- Typhoid
- Parvovirus, enteroviruses
- Chikungunya
- Lassa fever
- Marburg virus
- Syphilis
- Rickettsial infections
- Leptospirosis
- Drug reaction
- Other

Slide courtesy J Maguire

Chikungunya

- "That which bends up"'
- Dengue-like viral illness, transmitted by same vectors
- Rare patients have incapacitating arthralgia/arthritis lasting weeks or months
- Cases widespread through tropics – though may be declining in some areas

Dengue and Chikungunya

- In suspected cases, diagnostic test of choice is antibody – may be negative early in illness
- No antiviral therapy available
- Prevention
  - Insect repellants (DEET) on skin and clothing
  - Dengue vaccine promising
- How to counsel travelers? Especially travelers with a prior case of dengue?