Infectious Diseases 1: Cases

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 Disclosure

- I have the following financial relationships with the manufacturers of any commercial products and/or provider of commercial services discussed in this CME activity: speakers bureau for sanofi pasteur and Merck
Infectious Diseases 1: Cases

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Disclosure

- “It is my obligation to disclose to you (the audience) that I am on the Speakers Bureau for sanofi pasteur and Merck. However, I acknowledge that today’s activity is certified for CME credit and thus cannot be promotional. I will give a balanced presentation using the best available evidence to support my conclusions and recommendations.”
Infectious Diseases I: Cases

- Discussion
  - “off label” use of FDA approved vaccines
  - “off label” use of FDA approved antimicrobials
Infectious Diseases I: Cases

Objectives

- Bite wounds
  - be familiar with common pathogens, management
- Rash
  - formulate an appropriate differential diagnosis
- Lymphadenopathy
  - be familiar with etiologies, management
- Cough
  - discuss differential diagnosis and management
Case 1: Dog Bite

- 5 year old girl
  - dog bite to face 3 days before presentation
  - fever and facial pain
**Pasteurella multocida**

- Dog or cat bite wound
- Clinical features
  - rapid development of cellulitis
    » within 24 hours
  - swelling, erythema, tenderness, serous or sanguinopurulent discharge
  - chills, fevers
  - complications: septic arthritis, osteomyelitis, sepsis, meningitis
Bite Wounds**

- General care
  - clean
  - debridement
- Update routine immunizations
  - tetanus
- Human bite
  - update HBV
  - assess HIV risk
Bite Wounds: Rabies Risk**

- **High risk**
  - bats (even suspected minor contact), skunks, raccoons, foxes, most other carnivores, woodchucks, in rabies endemic area
    - may euthanize and test if available
  - rapid/suspected rabid dog, cat, ferret
    - may observe 10 days if healthy and available

- **Risk assessment**
  - rabies endemicity
Bite Wounds: Rabies Risk**

- **Unknown risk**
  - escaped dog or cat
    » consult public health officials

- **Low risk**
  - livestock, small rodents, lagomorphs
Bite Wounds: Rabies Prophylaxis**

- High risk wounds
  - administer RIG and rabies vaccine

- RIG
  - infiltrate wounds

- Rabies vaccine
  - 4 dose series
  - (pre-exposure prophylaxis)
Bite Wounds: Antimicrobial Therapy

- Increased infection risk
  - moderate-severe wounds
  - puncture wounds
  - facial, hand, foot, genital bites
  - immunocompromised subjects

- Infecting organisms
  - dog or cat: *S. aureus*, streptococci, *Pasteurella multocida*, *Capnocytophaga canimorsus*
  - human: *S. aureus*, streptococci, *Eikenella corrodens*
Bite Wounds: Antimicrobial Therapy**

- **Antibiotic prophylaxis/treatment**
  - po: amoxicillin-clavulanate
    - alternative: extended-spectrum cephalosporin (e.g., cefpodoxime) or TMP-SMX, plus clindamycin
  - parenteral: ampicillin-sulbactam
    - or piperacillin-tazobactam
Case 2: Rash

- 16 year old girl
  - 1 week of fever, malaise
  - rash on arms
  - bumps behind ears
  - achy hands
Parvovirus B19: Erythema Infectiosum**

- Older children, adults
  - arthralgia and arthritis
    »knees, fingers
  - posterior auricular or suboccipital adenopathy

- Younger children
  - 7-10 days fever, malaise, myalgia
  - appearance of rash
    »“slapped cheek”, maculopapular lacy rash on trunk and extremities
Parvovirus B19: Complications**

- Immune compromised
  - HIV, immune suppression
    » severe anemia (chronic erythroid hypoplasia)
  - sickle cell or other hemolytic anemia
    » transient aplastic crisis, 7-10 days

- Pregnancy
  - fetal hydrops
  - IUGR
  - fetal death (2-6%)
Case 3: Lymphadenopathy

- 6 year old girl
  - eyelid lesion
  - preauricular adenopathy 1 week later
Case 3: Lymphadenopathy

- Further history
  - kitten acquired 2 months ago
Cat-Scratch Disease: Clinical Features**

- Papule inoculation site
- Regional lymphadenopathy
  - axillary, cervical, submental, epitrochlear, inguinal
- Complications
  - granulomatous lesions
    » liver/spleen, osteomyelitis
  - encephalopathy, meningitis
  - endocarditis
Cat-Scratch Disease: Epidemiology**

- Kitten (<1 year of age)
  - cat transmission from fleas
    - more common in outdoor kittens
  - human transmission bite or lick
- Incubation period
  - 1-2 weeks from scratch to primary lesion
  - 1-7 weeks from primary lesion to adenopathy
Cat-Scratch Disease: Management**

- **Diagnosis**
  - serology
  - other: PCR, pathology (necrotizing granulomas)

- **Treatment**
  - disease generally self-limited
  - consider antimicrobial therapy for acutely ill, severe symptoms, disseminated disease
    - azithromycin, quinolones, trimethoprim-sulfamethoxazole, rifampin
Case 4: Lymphadenopathy

- 13 month old boy
  - gradual onset submental swelling over weeks
  - otherwise well
    » no fever
    » normal growth and development
Clinical course

- work up
  » TST 11 mm
  » interferon-gamma release assay negative

- progression
  » more swollen, overlying purplish hue
  » drainage
Nontuberculous Mycobacterial Adenitis**

- Age: 1-5 years
- Anatomic site: most commonly submental or submandibular
- Progression: slow
- Diagnosis: culture
- Management
  - surgical excision (avoid aspiration)
  - consider antibiotic therapy
    » clarithromycin or azithromycin, plus rifampin
Cervical Adenitis: Clinical Evaluation**

- **Age of onset**
  - 1-5 years of age: nontuberculous mycobacteria
  - school age: group A Strep, S. aureus

- **Epidemiologic history**
  - tb contact
  - cat contact

- **Clinical course**
  - acute: group A Strep, S. aureus
  - subacute: nontuberculous mycobacteria, cat-scratch disease
**Lymphadenitis: Physical Findings**

- **Anatomic location**
  - submandibular, submental: nontuberculous mycobacteria
  - anterior cervical: group A Strep, S. aureus, tuberculosis
  - posterior auricular, suboccipital: Parvovirus B19, rubella, tinea capitis
  - multiple nodes, posterior cervical: viral
    » eg, EBV, community-associated respiratory viruses
  - cat-scratch disease: site of inoculation

- **Tenderness**
  - yes: bacterial
  - nontender: nontuberculous mycobacteria, cat-scratch disease
Case 5: Cough

- 5 month old
  - 1 week rhinorrhea
  - 2 weeks cough
    » distressful
    » perioral cyanosis
    » occasional post tussive emesis
Case 5: Cough

- Additional information
  - mother, father and 4 year old sibling also with cough beginning 3 weeks ago
  - children not immunized

- Laboratory work up
  - CBC: WBC 21.1
    » 15% polys, 81% lymphocytes, 4% monocytes
  - CXR
Pertussis Clinical Features**

- **Incubation period:** 7-10 days
- **Stages**
  - **catarrhal:** cough and rhinorrhea
    » 1-2 weeks
  - **paroxysmal:** paroxysms, inspiratory whoop (infants), posttussive emesis
    » 2-8 weeks
  - **convalescent:** gradual waning of symptoms
    » weeks- months
  - **fever generally absent**
PERTUSSIS. Incidence* of reported cases, by age — United States, 2014

* Per 100,000 population.
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Pertussis Diagnosis**

- PCR
- Culture
- (Direct fluorescent antibody [DFA] not recommended)
- (Serology)
- Clinical
  - paroxysmal cough, post tussive vomiting, whoop
  - lymphocytosis
Pertussis Treatment**

- **Macrolides**
  - azithromycin (5 days)
    » preferred <1 month of age, preferred in pregnancy
  - alternatives: erythromycin (14 days), clarithromycin (7 days), trimethoprim-sulfamethoxazole (14 days)

- **Benefits**
  - limits spread
  - ameliorates cough if administered in catarrhal stage
Pertussis Chemoprophylaxis**

- Indications
  - household and other close contacts
    » e.g., child care

- Choices
  - same as for treatment
Changes You May Wish To Make In Practice

- Ensure that primary care providers are aware of:
  - bite wound pathogens and appropriate management
  - formulating a differential diagnosis for rash
  - the epidemiology and clinical presentation of infectious causes of lymphadenopathy
  - the clinical presentation and management of pertussis
PREP 2017: Infectious Diseases Cases

Dean Blumberg, MD

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- I have a Speakers' Bureau relationship with Sanofi Pasteur.

Case 1: Dog bite

A previously healthy 5 year old girl experiences a dog bite to the face 3 days before presentation. When evaluated, she has fever and facial pain.

Questions:

1. What is the most likely infecting pathogen in this case? Why?
2. What is the general approach to bite wound management?
3. How do you assess the risk of rabies?
4. If rabies prophylaxis is indicated, what is the regimen?
5. What types of bite wounds are at highest risk of infection and merit consideration for antibiotic prophylaxis?
6. What antibiotics are appropriate for prophylaxis for bite wounds? What if the patient has antibiotic allergies?

Case 2: Rash

A previously healthy 16 year old girl presents with 1 week of fever and malaise, along with a rash on her arms. Examination is also significant for posterior auricular adenopathy and hand tenderness.

Questions:

1. What other questions do you have regarding the history?
2. What is the most likely diagnosis?
3. Which patients are at risk for complications from this infection? What are the complications?
4. What are the dangers of infection during pregnancy?

Case 3: Lymphadenopathy

A 6 year old girl develops an eyelid lesion, then presents with preauricular adenopathy 1 week later.

Questions:

1. What other questions do you have regarding history?
2. With this further information, what is the most likely diagnosis?
3. What is the usual clinical presentation of this infection? What lymph nodes are typically affected?
4. What are the possible complications?
5. Describe the epidemiology of this infection?
6. How is the diagnosis confirmed?
7. When is treatment indicated? What is the treatment?

Case 4: Lymphadenopathy

A 13 month old boy has gradual onset submental swelling over weeks. He is otherwise well, has no fever, and has normal growth and development.

Questions:

1. What further work up would you do?
2. What is the most likely diagnosis?
3. What is the typical presentation of this infection?
4. How is the diagnosis confirmed?
5. What is the appropriate management of this infection? Is a referral appropriate; if so to what subspecialty?
6. Is there a role for antimicrobial therapy?
7. For cervical adenitis, how do pathogens differ by age of presentation?
8. What epidemiologic clues are important for cervical adenitis?
9. How does the pace of the clinical course of cervical adenitis differ by pathogen?
10. For each anatomic location, describe the likely pathogens causing lymphadenopathy.

Case 5: Cough

A 5 month old has 1 week of rhinorrhea and 2 weeks cough. The cough is distressful resulting in perioral cyanosis and occasional post tussive emesis.

Questions:

1. What additional history do you want?
2. What initial laboratory tests would be most helpful?
3. What is the most likely diagnosis?
4. Describe the stages of this disease.
5. How does the infection rate differ by age?
6. In general, who is the most likely source for infants with this infection?
7. How is the diagnosis confirmed?
8. What is the appropriate treatment of this infection? What if the patient is <1 month of age? What if the patient is pregnant? What if the patient is allergic to or intolerant of first-line therapy?
9. For who is chemoprophylaxis indicated? What agents are appropriate for chemoprophylaxis?
NARRATIVES ARE PROVIDED AS A REFERENCE FOR THE CASE PRESENTATION SESSIONS.

IN ORDER FOR YOU TO ACHIEVE THE MOST BENEFIT FROM THESE SESSIONS, WE ASK THAT YOU DO NOT REFER TO THE NARRATIVES PRIOR TO ATTENDING THE CASE PRESENTATION SESSIONS.
Case 1: Dog bite

A previously healthy 5 year old girl experiences a dog bite to the face 3 days before presentation. When evaluated, she has fever and facial pain.

Questions:

1. What is the most likely infecting pathogen in this case? Why?

   Given the rapidity of onset, erythema, tenderness and fever, the most likely pathogens are *Pasteurella multocida* and group A Strep; the former is more common after a dog bite.

2. What is the general approach to bite wound management?

   Wounds should be cleaned, and devitalized tissue should be debrided. Routine immunizations should be updated including for tetanus, and hepatitis B (for human bites). HIV risk should be assessed for human bites.

3. How do you assess the risk of rabies?

   High risk bites include those from bats (even suspected minor contact); rapid or suspected rabid dog, cat, ferret; and skunks, raccoons, foxes, most other carnivores, woodchucks, in rabies endemic area. An unknown risk occurs from bites from escaped dogs or cats; in this case, consult public health officials regarding the risk. Low risk bites include those from livestock, rodents, and lagomorphs.

4. If rabies prophylaxis is indicated, what is the regimen?

   For high risk wounds, administer RIG and rabies vaccine. Use RIG to infiltrate wounds. Rabies vaccine is administered in a 4 dose series.

5. What types of bite wounds are at highest risk of infection and merit consideration for antibiotic prophylaxis?

   Wounds at increased risk of infection include moderate-severe wounds; puncture wounds; facial, hand, foot, genital bites; and those occurring in immunocompromised subjects.

6. What antibiotics are appropriate for prophylaxis for bite wounds? What if the patient has antibiotic allergies?

   For oral therapy, amoxicillin-clavulanate covers all expected pathogens with the exception of MRSA. Alternative agents include an extended-spectrum cephalosporin (e.g., cefpodoxime) or trimethoprim-sulfamethoxazole, plus clindamycin. If parenteral therapy is indicated, then ampicillin-sulbactam is appropriate.
**Case 2: Rash**

A previously healthy 16 year old girl presents with 1 week of fever and malaise, along with a rash on her arms. Examination is also significant for posterior auricular adenopathy and hand tenderness.

Questions:

1. What other questions do you have regarding the history?

   This may be a vaccine-preventable disease, so immunization history may be useful. History of ill contacts may suggest a community associated infection.

2. What is the most likely diagnosis?

   The characteristics of the rash (lacy), posterior auricular adenopathy and hand arthritis are suggestive of Parvovirus B19 at this age. Rubella is another consideration, but less likely since she is immunized.

   In younger children, infection presents with 7-10 days of fever, malaise, myalgia; and then the appearance of the rash. At this age, the rash may have a “slapped cheek” appearance, in addition to a maculopapular lacy rash on the trunk and extremities. For older children and adults, illness may present with arthralgia and arthritis (most commonly involving the knees and fingers), as well as posterior auricular or suboccipital adenopathy.

3. Which patients are at risk for complications from this infection? What are the complications?

   Immune compromised patients, those with HIV or immune suppression are at risk for severe anemia (chronic erythroid hypoplasia). Those with sickle cell or other hemolytic anemia may experience transient aplastic crisis lasting 7-10 days.

4. What are the dangers of infection during pregnancy?

   Infection during pregnancy may result in intrauterine infection causing fetal hydrops, intrauterine growth retardation, and even fetal death (in 2-6% of cases).

**Case 3: Lymphadenopathy**

A 6 year old girl develops an eyelid lesion, then presents with preauricular adenopathy 1 week later.

Questions:

1. What other questions do you have regarding history?

   History of trauma to the area, ill contacts, pet contact may all be useful.
2. With this further information, what is the most likely diagnosis?

The papule is likely the inoculation site for cat-scratch disease with localized preauricular lymphadenopathy.

3. What is the usual clinical presentation of this infection? What lymph nodes are typically affected?

A papule may occur at the inoculation site, followed by regional lymphadenopathy which depends on the site of inoculation: axillary, cervical, submental, epitrochlear, inguinal nodes may be affected.

4. What are the possible complications?

Complications may involve the development of granulomatous lesions which may disseminate to the liver/spleen, or bone causing osteomyelitis. Central nervous system involvement may result in encephalopathy or meningitis. Endocarditis is an additional complication.

5. Describe the epidemiology of this infection?

Kittens (<1 year of age) are infected from fleas. Therefore, outdoor kittens are more commonly infected, since they are at higher risk of flea bites compared to exclusively indoor kittens. Human transmission occurs via a kitten bite or lick. The incubation period is 1-2 weeks from scratch to primary lesion, and 1-7 weeks from primary lesion to adenopathy.

6. How is the diagnosis confirmed?

The diagnosis is most commonly made by serology (positive IgM, or highly positive IgG). If tissue is obtained, then PCR and pathology (necrotizing granulomas) are useful.

7. When is treatment indicated? What is the treatment?

Cat-scratch disease is generally self-limited, and usually no treatment is indicated. Consider antimicrobial therapy for acutely ill patients, those with severe symptoms, and in the presence of disseminated disease. Several antibiotics may have activity, including azithromycin, quinolones, trimethoprim-sulfamethoxazole, and rifampin.

Case 4: Lymphadenopathy

A 13 month old boy has gradual onset submental swelling over weeks. He is otherwise well, has no fever, and has normal growth and development.

Questions:
1. What further work up would you do?

The age, clinical presentation, and anatomic location suggest the pathogen is atypical mycobacteria. Low level positive TST (ppd) is often seen, as a cross reaction with related antigens. Interferon-gamma release assays are useful differentiating between true positive TST (ppd) and cross reactions.

2. What is the most likely diagnosis?

A nontuberculous mycobacterial infection is the likely cause at this age, anatomic location, and subacute clinical presentation and progression.

3. What is the typical presentation of this infection?

Age of onset is generally 1-5 years of age. The most commonly involved sites are submental or submandibular nodes. Progression is usually subacute or slow, resulting in an overlying purplish hue, and may be complicated by drainage and fistula formation.

4. How is the diagnosis confirmed?

A cross reactive TST (ppd) may be suggestive of infection. Diagnosis is confirmed by biopsy and culture, or may be suggested by pathology.

5. What is the appropriate management of this infection? Is a referral appropriate; if so to what subspecialty?

Surgical excision is curative, but may not be possible depending on the anatomic site; submandibular involvement is often near the facial nerve resulting in risk of Bell’s palsy during surgery. In general it is best to avoid aspiration or partial node excision, as this may increase the risk of fistula formation and resulting scarring.

6. Is there a role for antimicrobial therapy?

Antibiotic therapy may be considered to decrease the organism load and accompanying inflammation. The usual agents used are clarithromycin or azithromycin, plus rifampin.

7. For cervical adenitis, how do pathogens differ by age of presentation?

At 1-5 years of age, nontuberculous mycobacteria are relatively common. For school age children (>5 years of age), group A Strep and S. aureus are more common pathogens.

8. What epidemiologic clues are important for cervical adenitis?

It may be useful to explore if the patient has had contact with a case of tuberculosis or is at increased risk for tuberculosis exposure. Kitten contact subjects the patient to risk of cat-scratch disease. If there are ill contacts with pharyngitis at school or in the community, this may suggest increased risk of group A Strep infection.
9. How does the pace of the clinical course of cervical adenitis differ by pathogen?

Group A Strep and S. aureus adenitis are usually relatively acute illnesses. In contrast, nontuberculous mycobacteria and cat-scratch disease usually result in more subacute presentations.

10. For each anatomic location, describe the likely pathogens causing lymphadenopathy.

Submandibular or submental adenopathy is generally caused by nontuberculous mycobacteria. Anterior cervical adenopathy is more commonly due to group A Strep, S. aureus, or tuberculosis. Posterior auricular or suboccipital adenopathy is associated with Parvovirus B19 or rubella infection. If multiple nodes are involved, or posterior cervical adenopathy occurs, viral causes are common including EBV, or community-associated respiratory viruses.

Case 5: Cough

A 5 month old has 1 week rhinorrhea and 2 weeks cough. The cough is distressful resulting in perioral cyanosis and occasional post tussive emesis.

Questions:

1. What additional history do you want?

   History of ill contacts is always useful. If a vaccine-preventable disease is being considered, then immunization history is valuable.

2. What initial laboratory tests would be most helpful?

   CBC may suggest a vaccine-preventable disease, or an acute bacterial or viral infection. CXR may reveal pneumonia.

3. What is the most likely diagnosis?

   Age, immunization status, whoop, clinical course, and lymphocytosis suggest pertussis.

4. Describe the stages of this disease.

   After an incubation period of 7-10 days, the catarrhal stage occurs with cough and rhinorrhea; this generally lasts 1-2 weeks. Gradually the paroxysmal stage develops resulting in paroxysms of coughing, inspiratory whoop (generally seen only in infants), and post tussive emesis. The paroxysmal stage may last from 2-8 weeks. It is followed by the convalescent stage consisting of gradual waning of symptoms and lasting weeks- months.

5. How does the infection rate differ by age?
Infection rates are relatively high in infants, and then a surge in disease is also seen in school-age children. Although adult cases occur, they are reported less commonly.

6. In general, who is the most likely source for infants with this infection?

Family members (household contacts) are the most common source of pertussis for infants.

7. How is the diagnosis confirmed?

Culture and PCR are the best diagnostic assays. Due to unreliability (both false positives and false negatives, direct fluorescent antibody (DFA) assays are no longer recommended. Serology may be useful if performed in a reliable laboratory: highly elevated or rising titers of pertussis toxin IgG suggest recent infection. Finally, a clinical diagnosis is sometimes made in the presence of paroxysmal cough, post tussive vomiting, and whoop, especially if supported by lymphocytosis.

8. What is the appropriate treatment of this infection? What if the patient is <1 month of age? What if the patient is pregnant? What if the patient is allergic to or intolerant of first-line therapy?

Macrolides are the drugs of choice. Azithromycin (5 day course) is preferred in pregnancy and preferred <1 month of age. Alternatives include erythromycin (14 day course) or clarithromycin (7 day course). For those allergic or intolerant of macrolides, trimethoprim-sulfamethoxazole may be considered (14 day course).

9. For who is chemoprophylaxis indicated? What agents are appropriate for chemoprophylaxis?

Chemoprophylaxis is indicated for household and other close contacts (e.g., child care). The antibiotic agents are the same as for treatment.