The Rise in Syphilis and the Role of the Emergency Department

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Disclosures/Conflicts of Interest

• None
Case Presentation

• 75 year old woman who presents to ED with progressive left vision loss.

• Symptoms started about 1 month prior, was seen at an outside facility where she was found to have left sided choroidal infarcts on exam – at the time she also endorsed headaches and was found to have elevated inflammatory markers – so the diagnosis of giant cell arteritis (GCA) was made

• Patient was treated with 1 gram IV methylprednisolone, followed by 75 mg daily of prednisone x 1 month (to present)

Case Presentation

• At some point did undergo a temporal artery biopsy, which was negative for findings suggestive of GCA

• Reported that initially visual symptoms improved with steroids, but over the last several days she noticed significant decrease in vision in the left eye

• Ophthalmologic exam was notable for active choroiditis with new uveitis/vitritis in the left eye. Admitted to the hospital for further evaluation
Case Presentation

• Further history reveals that the patient currently lives at home by herself in Ohio. She has 2 cats at home and no other animal exposures
• Currently retired (worked in retail in the past)
• No recent travel, no history of any international travel
• Has 2 adult children who live out of state
• No tobacco, alcohol or other drug use
• Not currently sexually active

Case Presentation

• Physical exam was unremarkable other evidence of a very faint, healing rash on the trunk and upper arms
• On further questioning, the patient reports that several weeks ago she developed a severe rash over her entire body – went to an urgent care and was diagnosed with a bad allergic reaction. States the rash has been improving slowly over time.
Case Presentation

• Patient reported she had a male new sexual partner about 6 months prior, although they are no longer in contact
• Barrier protection used but not every time
• She reports that the prior partner had several other sexual partners (both men and women); she was screened for HIV a few months ago after her partner notified her that he may have had unprotected sexual contact with a person with HIV
• No prior history of gonorrhea, chlamydia, syphilis or HSV

Case Presentation

• HIV 1/2 Ab/p24 Ag: Non-reactive
• Urine/oral chlamydia/gonorrhea NAAT: Negative
• Syphilis IgM/IgG: REACTIVE
• RPR: 1:512
• Lumbar puncture: WBC 15, RBC <3, Protein 62, glucose 75
• CSF VDRL: Reactive 1:2
Taking a sexual history

**BOX 1. The Five P’s approach for health care providers obtaining sexual histories: partners, practices, protection from sexually transmitted infections, past history of sexually transmitted infections, and pregnancy intention**

1. Partners
   - "Are you currently having sex of any kind?"
   - "What is the gender(s) of your partner(s)?"

2. Practices
   - "To understand any risks for sexually transmitted infections (STIs), I need to ask more specific questions about the kind of sex you have had recently."
   - "What kind of sexual contact do you have or have you had?"
   - "Do you have vaginal sex, meaning ‘penis in vagina’ sex?"
   - "Do you have anal sex, meaning ‘penis in rectum/anus’ sex?"
   - "Do you have oral sex, meaning ‘mouth on penis/vagina’?"

3. Protection from STIs
   - "Do you and your partner(s) discuss prevention of STIs and human immunodeficiency virus (HIV)?"
   - "Do you and your partner(s) discuss getting tested?"
   - For condoms:
     - "What protection methods do you use? In what situations do you use condoms?"

4. Past history of STIs
   - "Have you ever been tested for STIs and HIV?"
   - "Have you ever been diagnosed with an STI in the past?"
   - "Have any of your partners had an STI?"

Additional questions for identifying HIV and viral hepatitis risk:
- "Have you or any of your partner(s) ever injected drugs?"
- "Is there anything about your sexual health that you have questions about?"

5. Pregnancy intention
   - "Do you think you would like to have (more) children in the future?"
   - "How important is it to you to prevent pregnancy (until then)?"
   - "Are you or your partner using contraception or practicing any form of birth control?"
   - "Would you like to talk about ways to prevent pregnancy?"

Source: CDC Sexually Transmitted Infections Treatment Guidelines, 2021

Taking a sexual history

- Establish rapport and make your patient feel comfortable before asking sensitive questions
- Use neutral and inclusive terms (e.g. partner) and pose your questions in a non-judgmental manner
- Avoid making assumptions about your patients’ sexual orientation, gender identity or sexual behaviors based on age, appearance, marital status, or other factors
Syphilis: a review

- Syphilis is caused by the spirochete *Treponema pallidum*
- Major mode of transmission is via sexual contact
- Vertical transmission can occur (congenital syphilis)
- Can cause a wide variety of clinical manifestations, including periods of clinical latency (asymptomatic) if left untreated

Source: U.S. Centers for Disease Control and Prevention
**Syphilis: a review**

*Primary and Secondary Syphilis — Distribution of Cases by Sex and Sex of Sex Partners, United States, 2019*

![Syphilis chart](image)

Source: U.S. Centers for Disease Control and Prevention

**Congenital Syphilis**

*Congenital Syphilis — Reported Cases by Vital Status and Clinical Signs and Symptoms of Infection, United States, 2015–2019*

![Congenital Syphilis chart](image)

Source: U.S. Centers for Disease Control and Prevention
Congenital Syphilis

Primary syphilis

- Painless ulcer (chancre) appears at site of inoculation – can go unnoticed depending on the location.
- Regional lymphadenopathy can occur (inguinal, cervical)
- Chancre is highly infectious and may resolve without treatment within 1-6 weeks
Primary syphilis

Source: Centers for Disease Control and Prevention Public Health Image Library

Secondary syphilis

• Typically occurs about 4-8 weeks after onset of primary chancre, more likely to prompt medical evaluation
• The classic symptom is a diffuse maculopapular rash, which commonly involves the palms, soles, chest and back
• Lymphadenopathy, malaise, fever, mucous patches (genitals, mouth), patchy alopecia, and condyloma lata can occur as well
Secondary syphilis

Source: Negusse Ocbamichael, PA; Public Health—Seattle & King County STD Clinic

Secondary syphilis

Source: Negusse Ocbamichael, PA; Public Health—Seattle & King County STD Clinic
Source: Centers for Disease Control and Prevention Public Health Image Library
Tertiary Syphilis

- Form of late syphilis – can occur decades after initial infection if treatment is not administered
- Gummatous disease (granulomatous disease of skin, subcutaneous tissues, bones or viscera)
- Cardiovascular syphilis (involvement of vasa vasorum – aortic aneurysm, aortic insufficiency)

Source: Centers for Disease Control and Prevention Public Health Image Library
Latent syphilis

• Early latent syphilis (infection of less than 1 year duration)
• Late latent syphilis (infection greater than 1 year duration)
• Latent syphilis of unknown duration

Neurosyphilis, ocular syphilis, otosyphilis

• CNS involvement can occur during any stage of infection
• Early neurosyphilis - cranial nerve dysfunction, meningitis, meningovascular syphilis, stroke and/or acute altered mental status
• Late neurosyphilis – general paresis/tabes dorsalis (less common)
• Ocular syphilis (anterior, posterior or pan-uveitis), can occur with or without other associated neurologic manifestations
• Otosyphilis: usually presents with tinnitus, vertigo, sensorineural hearing loss
Screening for syphilis

<table>
<thead>
<tr>
<th>Syphilis</th>
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<tbody>
<tr>
<td><strong>Women and Men</strong></td>
<td>• Screen asymptomatic adults at increased risk (history of incarceration or commercial sex work, geography, race/ethnicity, and being a male younger than 29 year) for syphilis infection.2-7</td>
<td></td>
</tr>
<tr>
<td><strong>Pregnant Women</strong></td>
<td>• All pregnant women at the first prenatal visit6</td>
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<td>• Retest at 28 weeks gestation and at delivery if at high risk (lives in a community with high syphilis morbidity or is at risk for syphilis acquisition during pregnancy (using drugs, STIs during pregnancy, multiple partners, a new partner, partner with STIs).2</td>
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<tr>
<td><strong>Men Who Have Sex With Men (MSM)</strong></td>
<td>• At least annually for sexually active MSM2</td>
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<tr>
<td></td>
<td>• Every 3 to 6 months if at increased risk2</td>
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<tr>
<td><strong>Transgender and Gender Diverse People</strong></td>
<td>• Consider screening at least annually based on reported sexual behaviors and exposure2</td>
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<tr>
<td><strong>Persons with HIV</strong></td>
<td>• For sexually active individuals, screen at first HIV evaluation, and at least annually thereafter.8-10</td>
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<td>• More frequent screening might be appropriate depending on individual risk behaviors and the local epidemiology8</td>
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Source: CDC Sexually Transmitted Infections Treatment Guidelines, 2021

Screening for syphilis

• Laboratory testing - Reverse sequence algorithm
• Treponemal specific tests: Syphilis IgM/IgG, T. pallidum particle agglutination assay (TP-PA)
• Non-treponemal specific tests: rapid plasma reagin (RPR)
**Diagnosis**

- **Quantitative RPR or VDRL**
  - (+) Syphilis (past or present)
  - (-) No evidence of syphilis

- **EIA or CIA**
  - (+) Syphilis IgM/IgG
  - (-) No evidence of syphilis

**Treatment**

- **Early syphilis (primary, secondary, early latent):** 2.4 million units Benzathine penicillin G IM in a single dose
  - Alternative for penicillin allergic, non-pregnant adults: doxycycline 100 mg twice daily x 14 days
Treatment

- Late syphilis (late latent syphilis, latent syphilis of unknown duration, tertiary syphilis if CNS disease excluded): 2.4 million units Benzathine penicillin G IM weekly x 3 doses
  - Alternative for penicillin allergic, non-pregnant adults: doxycycline 100 mg twice daily x 28 days

Treatment

- Neurosyphilis: Aqueous crystalline penicillin G 18-24 million units per day, administered as 3-4 MU IV every 4 hours or continuous infusion given for 10-14 days
  - Alternative procaine penicillin G 2.4 million units IM once daily plus probenecid 500 mg orally 4 times/day for 10-14 days
Other treatment considerations

• All people with syphilis should be screened for HIV
• Syphilis exposure has been associated with an increased risk of future HIV acquisition, particularly in men—counseling on safer sex practices and HIV Pre-Exposure Prophylaxis (PrEP)
• Sexual partners should be treated


References

Syphilis and co-existent sexually transmitted diseases

Syphilis re-infection?
Sexually Transmitted Diseases

Sommer E. Lindsey, MD, FACEP
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Department of Emergency Medicine
The Ohio State University Wexner Medical Center

Background

National Data

• Sexually transmitted infections are on the rise
• Syphilis
  – 35,063 new cases since 2014, 71% increase
    – Several demographics have shown increased case numbers
    – Gonorrhea and syphilis increase the likelihood of transmission of HIV
STI testing in Urban Emergency Departments

Ideal Population

- Indigent population
- Uninsured
- No Primary Care
- ED is point of healthcare access
- High risk populations:
  - Minorities
  - Transient/homeless
  - IVDU
  - prostitution
  - multiple partners with diverse sexual orientation
- Perfect opportunity to screen for syphilis in a population that is under tested and under treated

Primary and Secondary Syphilis — Rates of Reported Cases by State and Territory, United States, 2018

Source: CDC

* Per 100,000.
NOTE: Section A1.11 in the Appendix for more information on interpreting reported rates in US territories.
Franklin County

- Ranks 21st amongst counties in nation in number of new cases of syphilis
- Half of all new cases of syphilis in just 28 counties nationally
  - Less than 1% counties nationwide
- One of 48 counties identified nationally as HIV hot spot

Source: CDC

Emergency department visits: trends

<table>
<thead>
<tr>
<th>YEAR</th>
<th>NHAMCS ESTIMATED ED VISITS (MILLIONS)</th>
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<tbody>
<tr>
<td>2001</td>
<td>107.5</td>
</tr>
<tr>
<td>2002</td>
<td>110.2</td>
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<tr>
<td>2003</td>
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<td>2004</td>
<td>110.2</td>
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<td>2005</td>
<td>115.3</td>
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<td>2006</td>
<td>119.2</td>
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<td>2007</td>
<td>116.8</td>
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<td>2008</td>
<td>120.8</td>
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<td>2012</td>
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<tr>
<td>2014</td>
<td>141.4</td>
</tr>
<tr>
<td>2015</td>
<td>136.9</td>
</tr>
<tr>
<td>2016</td>
<td>145.6</td>
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Source: CDC

Order practice prior to initiation of study

STI Testing in the OSU East Emergency Department 2012-2017

Why didn’t we do this sooner?

- It’s Complicated

Source: CDC

https://www.kff.org/hiv/aids/fact-sheet/hiv-testing-in-the-united-states/
Why didn’t we do this sooner?

- Practitioners unaware of syphilis surge
- Who is responsible for follow-up on these results?
- Interpretation of results
- Tracking patients down
- Collaboration with outpatient clinics
- Linkage to care and initiation of PrEP
- Insurance coverage: US Preventative Services Task Force
  - Medicaid mostly cover routine screening or “medically necessary” testing

Source: CDC

The test has been there. Why aren’t you ordering it?

- Survey of all EM faculty, residents, NPs at OSU Main and East
- Questions address hesitation to ordering HIV/syphilis testing from ED

Source: CDC
If you have not screened every high risk eligible patient for HIV or syphilis, what led to your decision?

- I didn't remember to discuss screening
- I am not familiar with screening guidelines
- I do not want to be liable if the test is positive
- I am not sure of the specific tests that must be ordered
- I don't believe in screening high risk patients in the ED setting
- Other

How willing would you be to order an HIV/syphilis test if the follow-up on a positive result was off-loaded from the ED and there was a system in place to get these patients expedited follow up care?

- Very willing
- Somewhat willing
- Neutral
- Somewhat hesitant
- Not willing at all

Number of Responses
**Solution: Guarantee follow-up outside the ED**

- ID generated list daily
  - All patients tested for HIV/syphilis and their results
- Interpretation of results
- Contacting patient
  - CPH and ODH help
- Arranging for treatment or continued surveillance
- PrEP
- STI ID Attending on call pager on WebExchange


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**ED STI Protocol**

**Management of STIs**

**Patient examination:**
- Previous STIs including HIV status, barrier protection, sex of partners, number of partners, rectal, oral, vaginal intercourse

**STI orders:**
- **Female:** gonorrhea and chlamydia (cervix)
  - Affirm (wet prep-BV, yeast, trich)
  - Syphilis (STAT not next day lab)
  - Rapid HIV (blood)
- **Male:** gonorrhea and chlamydia (urine/urethra)
  - Urine micro (trich)
  - Syphilis (STAT not next day lab)
  - Rapid HIV (blood)
ED STI Protocol  Management of STIs

May provide presumptive treatment for gonorrhea and chlamydia based upon history, exam, and/or high-risk status while in the ED.

If HIV or syphilis +, notification will be sent to Infectious Disease and the health department for follow up (by lab, not the ED provider). ID will then contact the patient regarding treatment options/locations, follow-up, and PrEP initiation for high risk patients.

ED STI Protocol  Management of STIs

Current CDC treatment Recommendations:
- Chlamydia: Zithromax 1000 mg PO x1 OR Doxycycline 100mg BID x7 days
- Gonorrhea: Rocephin 250mg IM x1 PLUS Zithromax 1000 mg PO x1
- Trichomoniasis: Flagyl 2000 mg PO x1 OR Flagyl 500mg BID x7 days
- Syphilis: Benzathine (PCN G) 2.4 million units IM x1

Update: Gonorrhea 500mg IM x 1 for 300 lbs or less, 1 gram IM x 1 for greater than 300 lbs
ED protocol

- STI-related complaint/Concern for STI based on clinical presentation
- History
  - Number sexual partners
  - Known HIV or syphilis diagnosis?
  - Barrier methods used
  - Sexual contact
    - Need for oral, rectal, and/or vaginal swabs
- Test for GC/Chlamydia (oral, urine, rectal, urethral, vaginal swabs), HIV (serum), syphilis (serum)
- Rapid HIV, with p24 antigen and syphilis AB with reflex RPR

Source: CDC

ED Order Set

- Order set
  - Type “STI” in order set box on IHIS

Please select gender appropriate orders for STI screening

- CHLAM & GONORRHEA: AMP CERVIX
- VAGINITIS DNA PROCES
- CHLAM & GONORRHEA: AMP, URINE
- CHLAM & GONORRHEA: AMP, ORAL
- CHLAM & GONORRHEA: AMP, RECTAL
- SYPHILIS AB W/REFLEX RPR
- RAPID HIV-1/HIV-2 AB WITH P24 ANTIGEN
- HIV VIRAL LOAD RNA PCR QUANT (Use in addition to rapid HIV test if acute HIV suspected)
- azithromycin (ZITHROMAX) tablet
- ofloxacin (ROCEPHIN) injection
- metronidazole (Flagyl) tablet
- omeprazone (ZOFTRAN-ODT) disintegrating tablet
- STAT, ONE TIME For 1 Occurrences CERVIX
- Urgent, ONE TIME For 1 Occurrences VAGINA
- STAT, ONE TIME For 1 Occurrences URINE FIRST CATCH
- STAT, ONE TIME For 1 Occurrences THROAT
- STAT, ONE TIME For 1 Occurrences RECTUM
- STAT, ONE TIME For 1 Occurrences
- STAT, ONE TIME For 1 Occurrences
- STAT, ONE TIME For 1 Occurrences
- STAT, ONE TIME For 1 Occurrences

1,000 mg, Oral, ONCE For 1 Doses
250 mg, Intramuscular, ONCE For 1 Doses
2,000 mg, Oral, ONCE For 1 Doses
4 mg, Oral, ONCE For 1 Doses

Source: CDC

UPDATE: Rapid Gonorrhea and Chlamydia testing now available. ALSO added pregnancy test and UA to streamline ordering.
Data since initiation of project

![Graph showing data since initiation of project]

Source: CDC

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STI Testing in the OSU East Emergency Department 2012-2017

![Bar chart showing number of STI tests]

Source: CDC
HIV and syphilis tests ordered from OSU EDs

![Chart showing HIV and Syphilis tests ordered from OSU EDs]

SYPHILIS

- Between Nov 1 2018 and Nov 30 2019 there were 57 positive syphilis antibody tests
  - 24 positive tests in women
  - 33 positive tests in men

- Totals:
  - 27/57 Previously treated infections
  - 19/57 Late latent infections (6 fully treated, 4 partially treated, 9 untreated)
  - 2/57 Secondary syphilis (2/2 fully treated)
  - 1/57 Primary syphilis (1/1 fully treated)
  - 8/57 false positives
  - 16 positive and/or inadequately treated cases found
    - 1% of those tested had a positive result and inadequate/no treatment

Source: CDC
Moving Forward

- Protocol for STI testing in EDs nationally
- Exemplar of interdepartmental collaboration with OSU Infectious Disease and collaboration with Columbus Public Health
- Model for quick linkage to care and initiation of PrEP
  - PrEP can reduce risk of HIV acquisition through sex by 90%
  - Navigators in ED who will assist patients with LTC and PrEP
- Social Work resources
- Nurse case manager, establish primary care

Source: CDC

Goals

- PrEP referral in STI order set to specific sites
  - ID clinic, THW, FACES, Equitas, primary care, patient choice
- HPV vaccine in appropriate patients
- Introduce model to other area healthcare systems
- Retrospective analysis of how early detection/treatment of HIV reduces number of ED visits/year
- Study demographics of patient populations being tested
  - Visits to ED/year
  - Race
  - Age
  - Gender
  - Sexual Orientation
  - Insurance status

Source: CDC