The Great Imitator Revealed: Syphilis

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Learning Objectives

After attending this presentation, learners will be able to:

▪ List the differential diagnosis of an anogenital ulcer
▪ Describe the preferred treatment for syphilis by stage
▪ Cite at least 3 means of syphilis prevention

Case

44 year old man with new painless lesion near his anus

Had a new sex partner 2 weeks ago
Anogenital Ulcer
Differential Diagnosis

Sexually transmitted diseases
• Primary syphilis
• Genital herpes
• Chancroid

Other
• Fixed drug reactions
• Staph/ strep infections
• Autoimmune conditions
• Trauma
• Malignancy

1000x darkfield microscopy

Treponema pallidum pallidum, bacterial spirochete

Primary syphilis – penile chancre
ARS Question 1: What is best treatment?

1. Amoxicillin 500 mg PO TID x 10 days
2. Benzathine PCN-G 2.4 MU x 1
3. Benzathine PCN-G 2.4 MU x 3
4. Doxycycline 100 mg PO BID x 14 days
5. Ceftriaxone 250 mg IM once

Injectable Penicillin G Benzathine Treatment of Choice for Primary Syphilis

- Single intramuscular injection penicillin G benzathine 2.4 MU
- Prophylactic treatment:
  - Syphilis case contacts < 90 days
  - Notify partners up to 3 months

Penicillin G benzathine cures syphilis

N=328, 52% HIV+, Tanzania

Riedner, G. et al. NEJM, 2005

Penicillin G benzathine cures syphilis

CDC STD Treatment Guidelines, 2015
Case

- 24 yo male with new onset of rash on chest and back, recently started on ART (ABC/3TC/DTG), has one regular partner
Differential Diagnosis: Generalized Rash

- Trunk rash
  - Secondary syphilis
  - Viral exanthem, including acute HIV infection
  - Pityriasis rosea
  - Drug eruption
  - Lichen planus
  - Psoriasis
  - Sarcoidosis
- Palmoplantar rash
  - Secondary syphilis
  - Erythema multiforme
  - Rocky Mountain spotted fever

Secondary syphilis: split papules, “moth-eaten” alopecia, mucous patches, and condyloma lata

Case

- RPR 1:16
- TPPA positive
ARS Question 2: What is best treatment?

1. Amoxicillin 500 mg PO TID x 10 days
2. Benzathine PCN-G 2.4 MU x 1
3. Benzathine PCN-G 2.4 MU x 3
4. Doxycycline 100 mg PO BID x 14 days
5. Doxycycline 100 mg PO BID x 28 days

Injectable Penicillin G Benzathine
Treatment of Choice for Secondary Syphilis

- Single intramuscular penicillin G benzathine
- Prophylactic treatment:
  - Syphilis case contacts < 90 days
  - Notify partners up to 6 months

CDC STD Treatment Guidelines, 2015

Epidemiology

CDC: STD rates skyrocketing in United States

Syphilis rates are on the rise, and dating apps may be playing a role, experts say

Syphilis Rises Sharply Among Newborns
Along with an increase in adult infections, the rate of infants born with the disease has reached a 20-year high.
New Cases of Syphilis at Highest Rate Since 1994

Primary and Secondary Syphilis — Reported Cases by Sex and Sexual Behavior, 37 States*, 2013–2017

Congenital Syphilis — Reported Cases by Year of Birth and Rates of Reported Cases of Primary and Secondary Syphilis Among Women Aged 15–44 Years, United States, 2008–2017
Case

- 32 HIV-infected male, on HAART for 2 years, virologically suppressed
- New to your office with RPR reactive at 1:32, TPPA reactive
- Asymptomatic without any lesions or rash

ARS Question 3: What stage is this case?

1. Primary
2. Secondary
3. Latent, early
4. Latent, late
5. Latent, unknown duration

ARS Question 4: What is best treatment?

1. Amoxicillin 500 mg PO TID x 10 days
2. Benzathine PCN-G 2.4 MU x 1
3. Benzathine PCN-G 2.4 MU x 3
4. Doxycycline 100 mg PO BID x 14 days
5. Doxycycline 100 mg PO BID x 28 days
Injectable Penicillin G Benzathine
Treatment of Choice for Latent Syphilis, Unknown Duration

- Intramuscular injection 2.4 MU benzathine penicillin weekly x 3
- Prophylactic treatment:
  - Syphilis case contacts < 90 days
  - Notify partners up to 12 months

CDC STD Treatment Guidelines, 2015

Latent syphilis

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All Those Syphilis Tests

- Non-treponemal tests (RPR, VDRL)
  - Detects antibody to cardiolipin
  - Rise and fall with infection and treatment over time
  - 4-fold change in titer (1:2 to 1:8 or 1:64 to 1:16) is significant
  - Specificity = 98% (false-positives in IDU, autoimmune, etc)

Klausner, Current STD Diagnosis and Management 2007
**All Those Syphilis Tests**

- Treponemal tests (TPPA, FTA-Abs, TP EIA, rapid TP)
  - Detects antibody to Treponemal antigen
  - More sensitive and develop earlier but positive for "life" (85%)  
  - Indicate past or current infection

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**Case**

- 44 year old HIV-infected female, occasionally exchanges sex for money or drugs
- C/o 1 week headache, ringing in right ear with some hearing loss
- RPR 1:16, TPPA reactive

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**ARS Question 5: CSF analysis is necessary**

1. Strongly agree
2. Moderately agree
3. Do not know
4. Disagree
5. Strongly disagree
Indications for CSF Analysis

- Neurological findings
- Ocular abnormalities
- Tertiary disease (dementia, aortic, gumma)
- Treatment failure
  (lack of 4-fold decline at 6, 12 or 24 m)

CDC STD Treatment Guidelines, 2015

ARS Question 6: What is best treatment for neurosyphilis?

1. IV penicillin G 18-24 MU x 14 days
2. IV ceftriaxone 1 gm daily x 10 days
3. Doxycycline 100 mg PO BID x 14 days
4. IV penicillin G 18-24 MU 14 days PLUS penicillin G benzathine 2.4 MU IM on day 14

Syphilis and HIV infection

- Multiple chancre
- May present with overlapping primary and secondary manifestations
- Rarely abnormal serology but slower decline
- Increased risk early neurosyphilis

Zetola and Klausner, Clin Inf Dis 2007
Prevention

- Individual level
  - Reduce exposure
  - Reduce risk of infection after exposure
  - Reduce sequelae of infection

- Population level
  - $R_0$ (reproductive number)
  - Reduce duration of infection

Screening, Treatment and Partner Services

Syphilis increases HIV viral load and decreases CD4 cell counts in HIV-infected patients with new syphilis infections

Kate Bachman, MD, Phoebe Pietr, MD, Melanie Taylor, MD, Peter R. Kerridge, MD, Robert H. Been, MD, Scott D. Holmberg, MD, Anthony D. Blaauw, MD
**CDC Screening Recommendations for Syphilis**

- **Pregnancy**
  - First visit
  - Repeat at 28-32 weeks in high-prevalence areas
- **Men who have sex with men**
  - Every year
  - More frequently (every 3 months) if
    - > 1 partner past 12 months
    - Meet partners online or in sex venues
    - Have sex in conjunction with illicit drug use (especially methamphetamine)
    - Have sex partners who participate in those activities

CDC STD Treatment Guidelines, 2015

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**Increased Testing Associated with Decreased Secondary Syphilis, Australia, 2007-2014**

HIV-infected

HIV-uninfected

Chow et al. Clin Inf Dis 2017
Syphilis Chemoprophylaxis

Molina, Lancet ID, 2018

Doxy 200 mg after sex
73% decline in syphilis

Molina, Lancet ID, 2018

Summary

- Think syphilis
- Screen, Treat, Treat partners, Screen
- Prevention works...if funded
- Doxycycline prophylaxis is highly promising