Another New HIV Diagnosis

P. Young, RPAC
Shelley A Gilroy, MD
Albany Medical College
June 3, 2014

The Patient

- 21-year-old male college student with rash x 1 month, beginning on his face
  - Non-tender & non-pruritic
  - Spread to extremities and genitalia within two weeks.
- Seen at college infirmary – no diagnosis.
- Denied F/C/N/V/D; denied CP/SOB; denied penile dc; denied HA; denied previous skin condition.
- Lesions continued to spread and worsen.
Additional History

- Patient returned to infirmary, with no diagnosis
  - Requested HIV testing at Infirmary
- HIV rapid test positive
- Transfer to AMCH ED within one hour of positive test

Systems Review

- ROS: Subjective fever in December, attributed to viral illness
  - Subjective fever 1 day prior to ED evaluation
  - Mild URI symptoms x 3 days
**Past History**

- PMH: Tib-fibula fracture/repair; no prior STI; immunizations current
- ? PCN allergy in childhood
- Meds: None
- SH: Occasional marijuana; social ETOH; negative IVDA/meth/etc.
  - Unprotected sex – men>women;
  - Receptive/insertive, with 3 partners within 3 months; 4-5 partners in six months, most recently ~3 months ago.
- FH – Non-contributory

**Physical Exam**

- PE: T 99.9 F orally, BP 136/64, P 106, R 18, 98%
- General: A & O x3, NAD
- HEENT: NC/AT; PERRL; no intraoral lesions
- Cardiovascular: RRR; no murmurs
- Respiratory: Clear
- Musculoskeletal: Negative
- Abdomen: Nontender; no masses; negative
- Skin: Many erythematous, well-demarcated, annular lesions
  - Non-blanching, indurated, and rubbery
  - Non-fluctuant and non-tender, with mild excoriation
  - Face/torso/forearms/genitalia/? soles/palms
  - Non-dermatomal, and non-vesicular
Labs

- CBC 4.48>12.0<265,000
  - CMP unremarkable
  - CXR negative
  - Urine negative
  - **Rapid HIV screening test** +
  - **RPR** nonreactive

Differential Diagnosis

- HIV-related rash
  - i.e. Kaposi’s, eosinophilic folliculitis, bacillary angiomatosis
- Secondary syphilis
- Disseminated GC
- Referred to HIV Practice for care
Office Visit- Next Morning

- T 97.8 F, P 90, BP 110/78, R 17, Pulse ox. 98% on RA. No pain.
- Not ill-appearing
- Oropharynx clear
- Palpable, posterior cervical and inguinal nodes, < 1 cm
- Lungs clear
- Heart and abdomen benign
- Skin showed multiple, nodular, erythematous, somewhat violaceous lesions, 1-3 cm in diameter
  - Across forehead, chest, back, abdomen, genitals, arms and legs
  - A couple of small macules on the palm of one hand and his feet
- Neurological exam and remainder of exam were unremarkable.
Next...

- Called the lab and asked for special testing....

- Meanwhile, proceeded with the skin biopsy

Skin Biopsy

- VACUOLAR INTERFACE and PERIFOLLICULAR LYMPHOCYTIC DERMATITIS
  - D-PAS stain is negative for yeast, hyphae and bacteria.
  - IMMUNOPEROXIDASE RESULTS: Antibodies to spirochetes, Treponema and Borrelia, are negative.

- Differential diagnosis of erythema multiforme, drug eruption or viral exanthem
Lab Called Back - Same Day

- Repeat RPR after dilution 1:512
- Given doxycycline for 3 weeks, and called patient back to receive oral azithromycin 2 gms times one dose
  - He is clarifying PCN allergy with his mother
- Warned about possible Jarisch-Herxheimer reaction

Additional Lab Data

- CD4 450 cells/cmm (19%)
  - CD8 1700 cells/cmm
  - CD4/CD8 ratio of 0.25
- HIV RNA 212,000 c/mL
- Hepatitis A IgG positive
- Hepatitis C Ab negative
- HSV Type II IgG positive
STI Screening

- Urine NAAT positive for GC
- Throat NAAT positive for GC and chlamydia
- Rectal NAAT positive for chlamydia
- Blood cultures negative
- Serum Bartonella PCR negative

Prozone Effect

- False negative response resulting from high antibody titer which interferes with formation of antigen-antibody lattice necessary to visualize a positive flocculation test.

Specimen Handling

- All test specimens producing any degree of roughness or reactivity with the RPR card test antigen in the qualitative test should be retested by using the quantitative procedure.

- In addition, a specimen should be tested for the prozone phenomenon when the clinician suspects syphilis, but the qualitative RPR is nonreactive.

CDC: RAPID PLASMA REAGIN 18-MM CIRCLE CARD TEST; NHANES 2001-2002

Syphilis Outbreak in NYS

February 2014
To: Hospitals, Emergency Rooms, Family Medicine, Infectious Disease, OB/GYN, Community Health Centers, College Health Centers, Local Health Departments, Internal Medicine and Primary Care Providers.

From: New York State Department of Health Bureau of STD Prevention And Epidemiology (BSTDPE)

HEALTH ADVISORY: SYPHILIS ALERT
Early infectious syphilis cases increased 30 percent in New York (excluding New York City) in 2013 (N=490) compared to 2012 (N=375). Increases have been noted in nearly every region of the State with cases reported in both urban and rural parts of the State. Men accounted for 92% of cases with 72% of male cases documented to occur among men who have sex with men (MSM)...

If you suspect syphilis infection or syphilis exposure, treat presumptively at the time of initial assessment...
Syphilis is a human infectious disease caused by the bacterium *Treponema pallidum* spirochete. 
- Transmitted by direct contact with lesion during primary or secondary stage, in utero by the transplacental route, or during delivery through an infected canal 
- Any organ can be involved - infinite number of clinical presentations

The Centers for Disease Control and Prevention define the stages of syphilis as follows:
- 1. Infectious syphilis includes the stages of cutaneous primary, secondary, and early latent syphilis of less than 1-year’s duration.
- 2. Latent infections (i.e., those lacking clinical manifestations) are detected by serologic testing. 
  - Early latent disease < 1-year 
  - Late latent disease > 1-year 
- Tertiary syphilis with cardiovascular, neurological, ocular or deep cutaneous presentation
Primary Syphilis

- Cutaneous ulcer of mucous membranes 10 - 90 days (avg 21) after exposure, at site of initial contact
  - Papule undergoes ischemic necrosis and erodes.
  - Painless to tender, hard, & indurated.
  - Painless, hard, discrete regional lymphadenopathy appears within 1-2 weeks.

- Healing with scarring in 2-3 weeks.
- Untreated ~25% → second stage, ~75% → latent
Secondary Syphilis

- 6 weeks (2 weeks to 6 months) after chancre
  - Duration 2-10 weeks
- Mucocutaneous lesions (chancre), flu-like syndrome, and generalized adenopathy.
- Distribution/morphology varied, and can be confused with other diseases.
- Usually bilaterally symmetric, typical of systemic cutaneous d/o

Secondary Syphilis (cont’d)

- Diffuse, symmetric macular/papular eruption -- entire trunk and extremities, palms/soles**.
- Discrete red, red-brown
- Scaly, smooth, & occasionally, but rarely, pustular
Macular Lesions of Secondary Syphilis

- Large, raised, gray to white lesions of warm, moist areas
  - Mucous membranes in mouth and perineum → condyloma lata, proximate to primary chancre
- Systemic symptoms - fever, headache, malaise, anorexia, sore throat, myalgias, and weight loss.

Secondary Syphilis (cont’d)
Testing for Neurosyphilis

- Risk factors for neurosyphilis:
  - Serum RPR titer 1:32 or higher
  - HIV infection, CD4 cell count 350/mm³ or less
  - Among HIV+ patients, ocular disease more common
- CSF white blood cell (WBC) count >20/mm³
- Positive CSF VDRL

Outcome

- Treated for syphilis with doxycycline for 21 days, due to PCN allergy
- Treated with azithromycin 2 gms
- Started on HAART
- Test of cure for GC/Chlamydia - all sites negative
- RPR now 1:32
- Viral load 135 copies/mL; CD4 595/33%
**Syphilis serologic screening algorithms**

### Traditional
- Quantitative RPR
  - RPR+ or other treponemal test
    - TP-PA+ or other treponemal test
      - TP-PA+ Syphilis (past or present)
      - TP-PA+ Syphilis unclear
    - TP-PA- or other treponemal test
  - RPR- or other treponemal test

### Reverse sequence
- Quantitative EIA
  - EIA+ or OIA
    - TP-PA+ or other treponemal test
      - TP-PA+ Syphilis (past or present)
      - TP-PA+ Syphilis unclear
    - TP-PA- or other treponemal test
  - EIA- or OIA

---

**Which algorithm?**

- **Traditional algorithm**
  - Detects active infection
  - High rate of biologic false positives
    - Confirmation with treponemal test
      - Use of both tests results in a high positive predictive value
  - Can miss early primary and treated infection

- **Reverse sequence algorithm**
  - Detects early primary and treated infection that might be missed with traditional screening
  - Nontreponemal test needed to detect active infection
  - Ideally, EIA and CIA should have perfect specificity
    - EIA and CIA are nonspecific
    - High rate of false positive results
    - Varies by risk of population

---

MMWR 2011; Vol 60(5)
Take-Home Points

- 1) Must call your lab if you suspect syphilis, and RPR is non-reactive.
- 2) Diagnosis would have been easier if reverse syphilis algorithm, used by some labs, had been done.
- 3) Syphilis and HIV remain the “Great Masqueraders!”

Questions?