NeuroAIDS, 2007: Sore Feet & Neurosyphilis

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NeuroAIDS, 2007

Painful feet & twitching calves
Bell’s palsy & a whole lot more
Neurosyphilis with persistently abnormal CSF
Painful Feet & Twitching Calves

44 y/o man admitted for AIDS & neutropenia: “His pain seems like neuropathy, but he has fasciculations… I think.”

History: 10 years ago (5 years after HIV diagnosis), he developed numbness & tingling in the soles of both feet

- CD4 ~200
- Treatment-naïve

Which diagnosis is LEAST likely?

1. Peripheral neuropathy
2. Bilateral radiculopathy
3. Cryptococcal meningitis
   - Cervical spondylosis with myelopathy
Which diagnosis is LEAST likely?

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2. Bilateral radiculopathy
3. Cryptococcal meningitis
4. Cervical spondylosis with myelopathy

More Information

**Interval history:**
Neurologically stable for the next 4-5 years
- ddI-containing regimen for 18 months
- Drug holiday for 3 years
**CD4 80:** HAART started, including d4T 40mg bid
- 1 month later: “walking on balloons,” cramps, minor tingling in fingers
- 4 months later: amitryptiline for worsening pain, new ARVs without d-drug

**Exam:** WDWN man with healing abscesses
- Motor
  - No atrophy, normal strength
  - Occasional calf fasciculations
  - Absent Achilles' reflexes (normal @ knees & in arms), toes down
- Sensory
  - Vibration absent in toes, slightly diminished in fingers
  - Cold decreased to mid-calf, normal in fingers
At this point, I would:

1. Not worry too much about a drug-induced neuropathy.
   • Order an EMG.
   • Schedule a spine MRI.
   • Screen for diabetes and alcoholism, and check a $B_{12}$, RPR & maybe a TSH.
DSP: Diagnoses & Plan

**AIDS (HIV) neuropathy**
- Tx naïve, no other evident cause, CD4 ~200
- Paresthesias > pain, nonprogressive

**Uneventful 18 months of ddI**

**d4T neuropathy**
- Foot pain
- Symptoms & signs to just below knees, also fingers
- Cramps & fasciculations

*No further W/U unless worsens; taper TCA*

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Painful Neuropathy & HIV

**Distal symmetric polyneuropathy**

**Hx:** positive (pain, paresthesias) and negative (numbness) sensory sx

**Exam:** depressed or absent ankle reflexes, distal sensory loss (vibration, temperature, pain)

**Consider:** HIV (especially uncontrolled), d-drugs

**Atypical features**
- prominent weakness hands ≥ feet
- proximal features asymmetry sphincter dysfunction

**If typical features:**

**Med hx:** d-drugs, INH, dapsone, hydroxyurea, metronidazole, vincristine, thalidomide

**Screening:** DM, B₁₂, RPR, TSH
Neuropathy in HIV, 2007

New risk factor: protease inhibitors?

Symptomatic treatment trials:
  Negative: prosaptide
    http://www.plosone.org/article/info:doi/10.1371/journal.pone.0000551
  Positive: cannabis
  Promising?: high-dose capsaicin patch
  Pending: acetyl-L-carnitine for nucleoside neuropathy, pregabalin

Bell’s Palsy & a Whole Lot More

39 y/o man with AIDS (CD4 101, VL >500K) admitted with HA, dysphagia, L hand weakness, unsteady gait & above symptoms

History: off ARVs for a year, HBV/HCV, psoriasis
  Rx for 2° syphilis 3 months ago; unprotected sex since 2 weeks ago: abrupt R facial weakness after 3 weeks of R ear pain, hearing loss, tinnitus; rx valacyclovir & artificial tears

Exam: afebrile, mildly stiff neck
  Alert, conversant with moderate palatal dysarthria
  Mild R V1-3 sensory loss, R hearing loss, severe R LMN facial weakness, R palatal weakness
  ? L hand weakness, ? gait ataxia
Clinically, there is involvement all of the following EXCEPT:

- Meninges
- Cranial nerves
- Cerebral cortex
- Cerebellum or posterior columns
I would:

- Order a CT or MRI.
- Do an LP.
- Get an RPR.
- Consider neuroTB or cryptococcosis.
- All of the above.
Meningitis?

**Head CT, noncontrast:** normal

**CSF**
- Protein 177, glucose 44 (serum 98)
- 3 rbc, 193 wbc (90% lymphocytes)
- Gram stain, CrAg negative

**Rx in ED:** ceftriaxone, vancomycin, ampicillin

**Differential dx:** Listeria, TB, syphilis, VZV, cocci

*IV acyclovir added the next day*

Further Workup

**Treatment failure or reinfection?**

**Rx:** IV PCN G x 14 days

**Followup:**
- Persistent R HL, facial weakness
- Serum RPR 1:128
- Audiogram, repeat LP not done (lost to followup)

**Serum RPR:** 1:1024 (was 1:16)

**CSF VDRL:** 1:32

**Dx:** syphilitic meningitis
Per CDC guidelines, management of neurosyphilis includes all of the following EXCEPT:

1. Benzathine penicillin IM weekly x 3 as sole therapy
2. Repeat CSF exam in 6 months
3. Consideration of desensitization in penicillin-allergic patients
4. Retreatment of CSF has not normalized by 2 years
Neurosyphilis

**Failure of clearance after neuroinvasion:** may be asymptomatic, with increased risk to become symptomatic (the great imitator of neurologic disease)

**Increased risk with syphilitic eye disease**

**Early (weeks to years after 1º infection):** meningeal +/- cranial nerve, stroke (or both)
- Syphilitic meningitis: HA, stiff neck, cranial nerve palsies (hydrocephalus, seizures, myelopathy)
- Meningovascular syphilis: meningitis with ischemic stroke

**Late (years to decades after 1º infection):**
- Parenchymal
  - General paresis (brain)
- Tabes dorsalis (cord & nerve roots)
- Gummatous
  - Cerebral mass lesion
  - Compressive myelopathy
Figure 21. Neurosyphilis cases by case status, San Francisco, 2002-2006.

SF Department of Public Health: STD Annual Summary, July 2007
http://www.sfdph.org/dph/files/reports/default.asp
**Syphilis & HIV: A Bad Combination**

**Major global epidemics**

HIV augments syphilis transmission & vice versa

**In HIV+ patients:**

- Increased risk of neurosyphilis & treatment failure (?)
- Syphilis: ↓CD4 and ↑viral load


**The Great Imitator:**

- Dementia
- Cranial neuropathies
- Meningitis
- Myeloradiculopathy
- Brain/spine mass
- Stroke in a young patient
- Eye/ear disease

HIV-related neurologic disorders are also on the differential of these syndromes.

Serology & CSF

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**Lumbar Puncture**

**Indications:** CDC, 2006

- Syphilis and:
  - Neurologic disease
  - Syphilitic eye disease (otosyphilis?)
- 3° syphilis
- Treatment failure
- HIV+ and:
  - Late latent syphilis
  - Syphilis of unknown duration


**CSF findings:**

- ↑Protein
- ↑Cells (lymphs)
- CSF-VDRL
  - Highly specific in atraumatic CSF
  - 30-70% sensitive
- CSF-FTA
  - Sensitive, not specific
  - Can exclude neurosyphilis
Treatment of Neurosyphilis in Adults

**Aqueous crystalline penicillin G, 18-24 million units/day:** 3-4 million units IV q4h or continuous infusion, 10-14 days

**Alternate:** procaine penicillin G 2.4 million units IM daily with probenecid 500mg PO 4x/day, both for 10-14 days

**Desensitization if penicillin-allergic**

**Jarisch-Herxheimer reaction**

**Benzathine PCN IM weekly x 3 afterwards?**

**F/U:** serial serum serologies & CSF exams


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Neurosyphilis, 2007

**Latest CDC guidelines (August 2006):**
http://www.cdc.gov/std/treatment/

49 MSM (LA, SD, Chicago, NYC) meeting CDC criteria for early neurosyphilis

most also HIV+

1.7% risk for symptomatic neurosyphilis with early syphilis in this group


http://www.cdc.gov/mmwr/preview/mmwrhtml/mm5625a1.htm?s_cid=mm5625a1_e

**Cases continue to increase nationwide, but decrease in SF the past 2 years accompanied by a fall in neurosyphilis.**
HIV+ Man with Neurosyphilis & Persistently Abnormal CSF

48 y/o homeless HIV+ man with prior alcohol withdrawal seizures c/o numbness, pain & weakness in his legs for 3 weeks

- Began after bicycle accident—scalp laceration sutured & left arm cellulitis treated at outside hospital
- ? Bowel/bladder incontinence, minor tingling in his hands, no neck/back pain

Exam: tremulous, disheveled

- Anisocoria (R>L), no nystagmus
- Normal strength, generally hyperreflexic, including AJ, toes down
- Allodynia to thighs, decreased vibration in feet
- No ataxia

Neuropathy & EtOH Withdrawal

Neuropathy due to EtOH +/- HIV

Benzodiazepines, thiamine; antibiotics for UTI
CD4 108, VL 55K, RPR 1:1024

CSF:

- Protein 48, glucose 44 (serum 93)
- #1: 10 rbc, 2 wbc
- #4: 14 rbc, 5 wbc
- VDRL 1:16

Rx: High-dose IV PCN G for 2 weeks
Neurosyphilis

Symptomatic or asymptomatic?

Improving serologies, persistent pleocytosis:

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Sore Feet & Syphilis: Some Perspectives

Neuropathy is the predominant HIV-related neurologic complication in the US.

- New risk factors: ? PIs, age, but not HCV (yet)
- Treatment trial results pending

Neurosyphilis, symptomatic & asymptomatic, remains a challenging clinical problem in HIV+ patients.

- In addition to the usual limits of serologic testing, CSF is difficult to interpret in the setting of HIV.
- Rising incidence of syphilis in the US, particularly among MSM