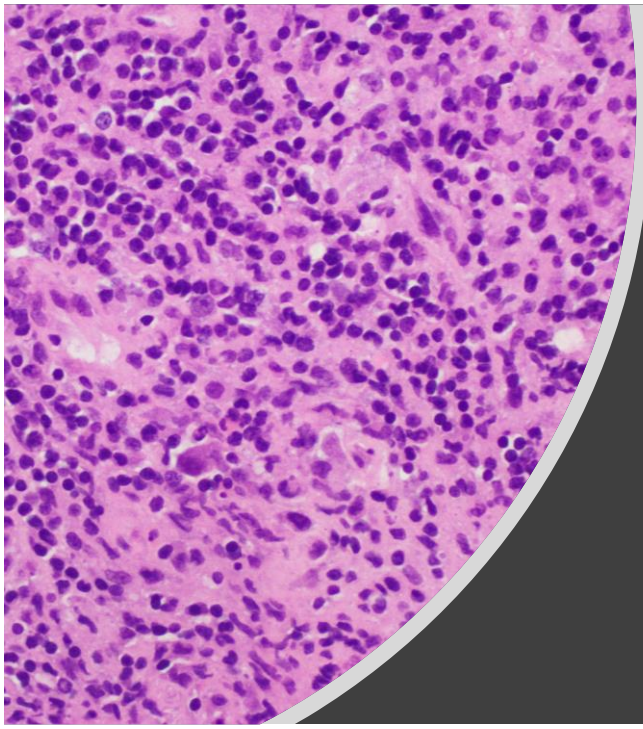


The Imitation Game

Early Spinal Syphilitic Gumma in HIV-infected patient

Dr Anne Hoey

HIV&AIDS: Case Presentation Breakfast

Sep 25, 2018

Our Case- Mr XY

36 year old male marketing officer with R leg weakness, R facial numbness and bowel and bladder symptoms on the background of well controlled HIV infection

<u>Background</u>

Lives with parents (unaware of HIV diagnosis)

Social smoker and drinker

MSM with no current partner

No IV drug use, previous occasional cocaine binge and methamphetamine use

Background

Medical History

HIV; Dx in 2012

- HLAB5701 negative
- Subtype B fully susceptible virus
- Commenced treatment: 2015 *Stribild* elvitegravir/cobicistat/emtricitabine/ tenofovir disoproxil fumarate
- *Genvoya* since August 2016 elvitegravir/cobicistat/emtricitabine/ tenofovir alafenamide
- Nadir CD4 count 580/µL most recent 1080/µL
- No complications, compliant

TB screening negative

- Mantoux and CXR 2015

Sexually Transmitted Infections

- Secondary Syphilis April 2015
- Rectal Chlamydia and Gonorrhoea Dec 2016
- Last STI screen negative in September 2017

Lumbar back pain Dec-Jan 2017

- CT Lumbar Spine 29/1/18 showed moderate canal stenosis at L4/L5
- Tx steroid injection

History of presenting complaint

R tongue loss of sensation followed by facial numbness

- MRI B: Expanded thickened appearance of the R trigeminal nerve
- CT Cervical Spine : Mild L disc bulge of C5/6 level with no canal stenosis

Rapidly progressing R leg weakness 3 weeks later

- Initially difficulty dorsiflexion of ankle, progressed to weakness of whole leg within days
- Difficulty getting an erection, initiating urination and constipation
- Seen by a neurologist who noted profound weakness of all muscle groups of the R leg and reduced muscle tone on PR

On examination in ED

Normal observations

Afebrile, PR 87, BP 124/93, sats 97%

Cardiac, respiratory and abdominal examination unremarkable

Neurological examination

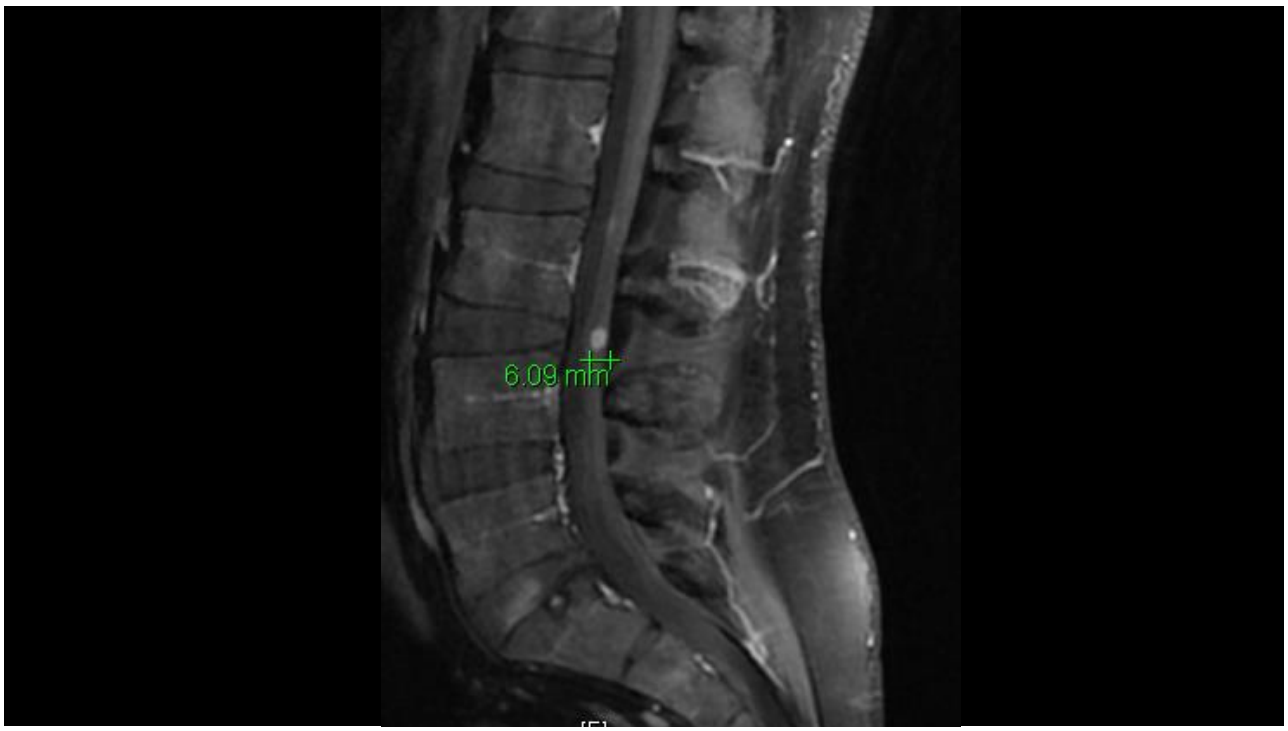
Cranial nerves: Trigeminal – V1 and V2 absent pin prick and light touch;
Muscles of mastication intact (V3)
L leg normal tone and power intact on left. L patella 2+ L plantar absent
R leg normal tone; absent patella and plantar reflex. Hip and knee 2/5 flexion and extension, ankle 0/5 flexion and extension
Patchy sensory loss bilaterally from T10 level
Urinary retention: Post-void bladder scan 350ml

Investigations on admission

Bloods

WCC 6.6 Neut 3.9 Lymph 2.2 Hb 141 Plt 253
INR 1. APTT 28
LDH 162 CRP 24
Bili 9 Total Protein 82 Alb 40 GGT 94.
Normal AST/ALT/ALP eGFR > 90


20.29 mm
[H]
[F]


6.09 mm

Progress…

Lumbar puncture

- Protein 2.54g/L, glucose 1.7mmol/L, LDH 35
- Cell count: 2 RBC, 6 PMNs, 301 mononuclear cells

CT CAP

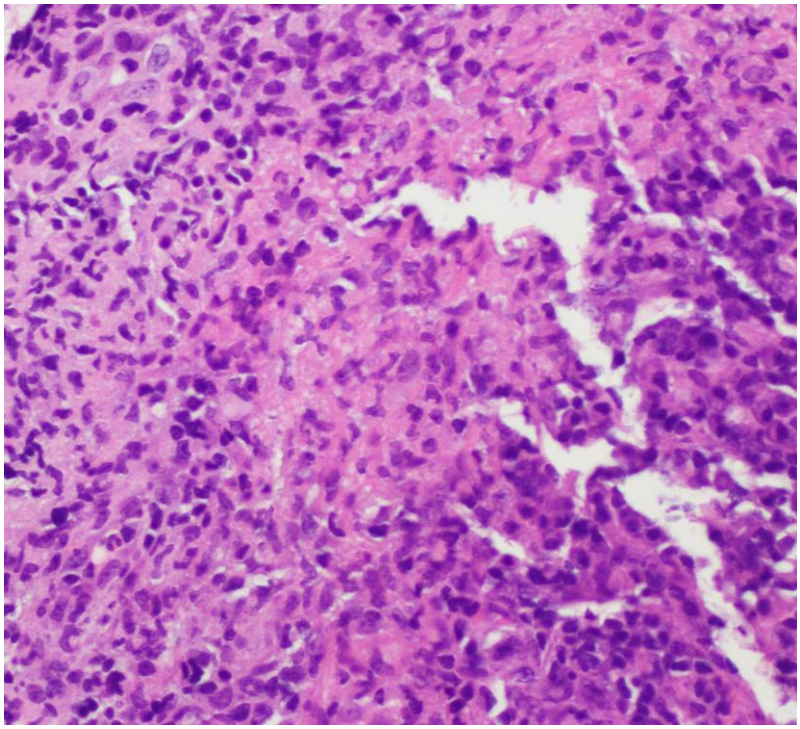
- No lymphadenopathy or signs of malignancy

Thoracic laminectomy and biopsy (limited) of T10 intradural lesion and commenced on dexamethasone

Histopathology

Biopsy T10:

- MCS no growth; AFB negative
- A few Reed-Sternberg cells seen on histopathology on a polyclonal lymphoplasmacytic background
- Tissue toxoplasma/CMV DNA negative
- Special stains for fungi and acid fast bacilli negative
- The overall appearances are those of an atypical lymphoid proliferation suspicious of a lymphoproliferative disorder with some features suspicious of Hodgkin lymphoma



Progress…

- Early presumptive diagnosis lymphoma
- Plans made for sperm banking, Intrathecal methotrexate, and systemic Chemotherapy with view to autologous stem cell transplant
- Plans made to change anti-retrovirals to non-boosted regimen
- at MDT decision made to deliver urgent radiotherapy to T10 lesion

Further Investigations

Urgent PET scan

The lesions in the right trigeminal nerve root and T10 thoracic spinal cord demonstrate increased FDG activity. No uptake at L3/L4
Diffuse bone marrow uptake may represent involvement by a similar process or reactive activity
No FDG avid lymphadenopathy or splenic disease.

Further CSF results:

MCS: no growth
EBV DNA positive (509 copies/mL)
Negative CMV/VZV/HSV/Enterovirus/Meningococcus/Toxoplasma
No malignant cells on cytology or abnormal B cell populations on CSF flow cytometry

Additional Results

CD4 count 1090/µL. Suppressed HIV viral load

ACE 24
EPG: No paraprotein. K:L ratio of 0.93
Cryptococcus Ag < 2
Brucella Ab < 8
Serum EBV IgM negative
HCV negative
Bone marrow
- Normocellular marrow with very mild dyserythropoietic changes
- No abnormal B cell populations on flow cytometry

Progress...

New LFT derangement (GGT 646 from 94; ALT 849 from 21)

Serology results
- *T. pallidum* Ab reactive 23.95
- *T.pallidum* particle agglutination titre (TPPA) – reactive >320
- Rapid plasma regain (RPR) reactive 1:64

Commenced Benzylpenicillin 1.8g Q4h

Dexamethasone continued to prevent Jarisch-Herxheimer reaction

Progress…

Further CSF testing

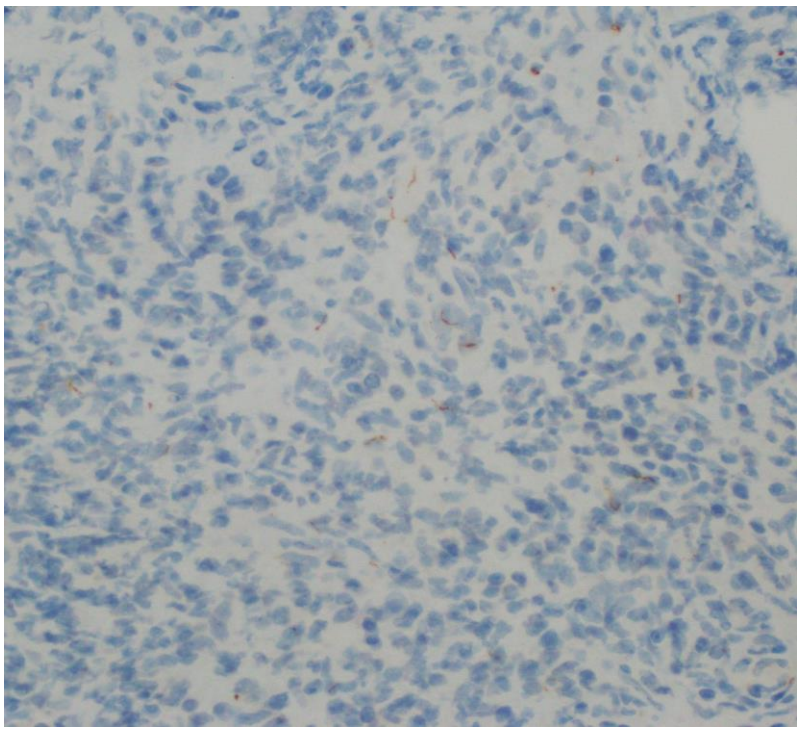
- VDRL reactive 32
- *T. pallidum* FTA reactive
- TPPA titre >80
- *T. pallidum* PCR negative

No uveitis/retinitis on opthalmology review

Spirochetes

Add on immunoperoxidase staining for spirochetes

Immunoperoxidase staining for spirochetes shows scattered spirochete organisms amongst the granulation tissue in keeping with syphilis infection. The atypical lymphoid infiltrate is thus **most likely related to the syphilis infection** and a lymphoproliferative disorder is unlikely. Correlation with CSF PCR and syphilis serology is recommended.



Discharge

Successful trial of void

Improvement in R leg weakness and was walking with crutch

Discharged with an infuser for total 15 days Benzylpenicillin 1.8g Q4h

Spontaneous erections and return of bowel continence soon after discharge

3 month review

Residual weakness only R toe dorsiflexion

Paraesthesia trigeminal nerve lesion, anaesthesia lower R groin

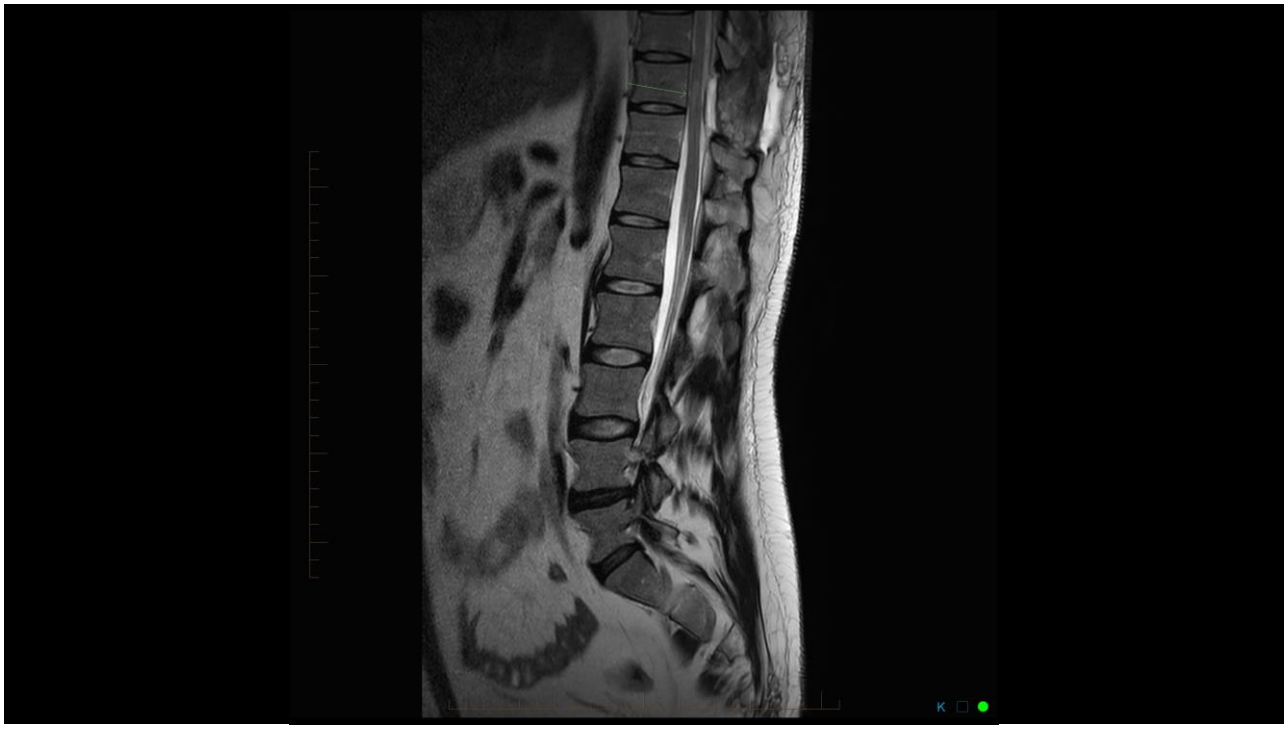
RPR 1:8 (from 1:64)

MRI spine 6 weeks

- resolution of T10 lesion, L4/5 lesion and minimal residual cord oedema at T10 only

MRI brain 8 weeks

- Significant improvement trigeminal nerve, no longer thickened, but persistent changes compatible with neuritis



Case comments and questions

1. CNS Syphilitic gumma uncommon presentation neurosyphilis
2. Commonly misdiagnosed as malignancy
3. Very rapid progression to disease from previously unreactive RPR
4. Reactivation vs reinfection with rapid progression ?

Cerebral syphilitic gumma

- Syphilitic gumma well described but rare manifestation of meningeal neurosyphilis
- Fargen et al 2009;
  - 156 cases
  - CSF Syphilis serology positive in 64%
  - 37% cases complete resolution signs and symptoms, 37% partial
  - 46% complete resolution on imaging, 46% partial
  - 11 cases were in HIV positive patients

Table 1. Clinical Features and Prognosis of Intraspinal Gummas

Study	Language	Age (years)/Sex	Onset Symptoms	Duration	Treatment	Follow-Up	Outcome	
							Symptoms	Lesion on Imaging
Dhasmana et al., 2013[4]	English	40/M	Headache, nausea, photophobia, lower backache, paraplegia	3 months	Biopsy + prednisolone (40 mg/day for 3 days) + benzylpenicillin (24 million U/day for 17 days)	6 months	Significant improvement	Disappeared
Zhou et al., 2014[5]	English	49/F	Paraplegia, sensory disturbance	10 years	Methylprednisolone + aqueous penicillin G (0.2 million U/kg/day for 15 days), followed by benzathine penicillin (2.4 million U/week for 3 weeks) + complete lesionectomy	4 years	Complete recovery	N/A
Molina-Olier et al., 2012[6]	Spanish	47/F	Shoulder pain, paraplegia, sphincteric disturbance	2 days	Lesionectomy + ceftriaxone sodium (2 g/day for 14 days)	6 months	No improvement	N/A
El Quessar et al., 2000[7]	French	25/F	Brown-Séquard syndrome	2 years	Lesionectomy + penicillin G (dosage N/A)	10 months	Partial improvement	Stable*
Colli et al., 1979[8]	Portuguese	48/F	Backache, paraplegia, sensory and sphincteric disturbances	2 months	Lesionectomy	18 months	Partial improvement	N/A
Wu et al., 2009[9]	Chinese	51/M	Lumbar and back pain, right leg weakness	2 months	N/A	N/A	N/A	N/A
Zhang and Tian, 2013[10]	Chinese	51/M	Chest and back pain, paraplegia, sensory disturbance	10 days	Lesionectomy	N/A	N/A	N/A
Present case	English	65/F	Neck, shoulder, and back pain, tetraplegia, sensory disturbance	2 months	Complete lesionectomy + prednisone (20 mg/day) + aqueous penicillin G (24 million U/day for 14 days)	29 months	Partial improvement	Stable

M, male; F, female; N/A, not available.
*Stable indicates no recurrence or radiologic progression was observed.

Yang et al 2016

8 reported cases of spinal syphilitic gumma

Only 5 of 8 tested for HIV, all negative

DIAGNOSTIC DILEMMA
Thomas J. Marrie, MD, Section Editor

THE AMERICAN JOURNAL of MEDICINE

Commonly misdiagnosed as malignancy

Misdirected by a Mass: Syphilis

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SECONDARY SYPHILIS PRESENTING AS CUTANEOUS T-CELL LYMPHOMA IN AN HIV-POSITIVE PATIENT
A. Laungani, J. McDonnell, W. Bergfeld and K. Sellheyer
Department of Dermatology, The Cleveland Clinic Foundation, Cleveland, OH, USA
J Cutan Pathol 2005: 32: 67–70
Blackwell Munksgaard. Printed in Denmark

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Secondary Syphilis with Tonsillar and Cervical Lymphadenopathy and a Pulmonary Lesion Mimicking Malignant Lymphoma

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Rectal Syphilis Mimicking Histiocytic Lymphoma

Mary Rachel Faris, M.D., James J. Perry, M.D., Thomas G. Westermeier, M.D., John Redmond, III, M.D.

American Journal of Clinical Pathology, Volume 80, Issue 5, 1 November 1983, Pages 719–721, https://doi.org/10.1093/ajcp/80.5.719

Possible reactivation?

Further History

TPA negative Feb 2015

Anal ulcer March 2015, secondary syphilis April 2015 rash to scrotum and penis

RPR 1:128

Treated with with benzathine penicillin 1.8g IMI stat and Doxycycline 100mg bd for 10 days

1:1 23/10/15 NR 19/2/16

NR RPR since, (checked every clinic visit)

Sexual exposure early September, NR RPR 29/9/17

Reactivation cont.

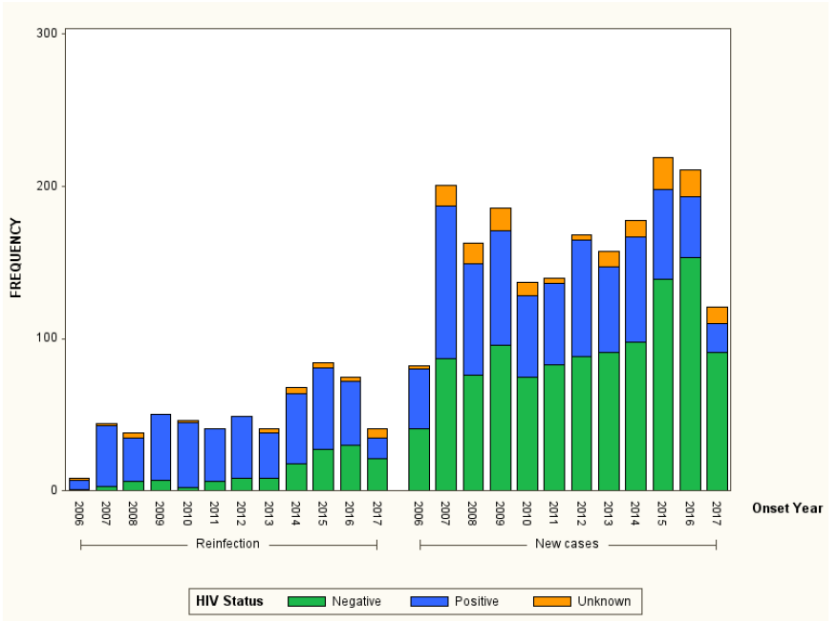
- Previous reports of neurosyphilis (symptomatic and asymptomatic) occurring in HIV+ patients after standard treatment

- Zhou et al (2012)

  Case study of 17 HIV- patients with secondary syphilis that developed neurosyphilis (symptomatic or asymptomatic) after standard treatment, with fourfold decrease in RPR

  NONE of these patients had non-reactive RPR

Figure 5: HIV status of new syphilis cases and reinfections April 2006 – June 2017 (study period)



HIV and syphilis co-infection

Rapid progression

Author	year	Age	HIV	Symptoms	Lesion	Past syphilis	Diagnosis	Outcome
Fargen	2009	59					etes opsy	No further Tx; resolution symptoms and VDRL 3/12
Tsuboi	2016	21	CD4 456	fatigue, head & neck discomfort 1/52	lobe	neg 5/12	serology	14/7 benpen; no signs/symptoms 2/12 Improv MRI
Kodama	2018	36	Neg	R facial pain & palsy, sensorineural hearing loss 2/52	L temporal lobe, VII and VIII nerve	RPR TPHA neg 5/12, TPHA 1:145 3/12 prior	CSF and serology	14/7 ceftriaxone; Resolution MRI 2/52, improved Sx

Impression: Re-infection more likely based on non-reactive RPR, sexual exposure, current incidence and previous reports of similar cases

Summary and conclusions

- Unusual case of spinal cord syphilitic gumma in well controlled HIV patient with negative RPR 4 months prior to symptom onset
- This case most likely re-infection with rapid progression
- Information is limited but most cases demonstrate response to treatment
- Syphilis is on the rise, re-infection common in HIV patients
- Remains the great imitator; expect the unexpected

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Diagnosis Neurosyphilis

- Diagnosis requires positive syphilis serology and lumbar puncture
- CSF VDRL preferred test; highly specific but sensitivity 30-70%
- CSF FTA-ABS sensitive but not specific; rule out test if both negative
- HIV- patients with negative CSF-VDRL; CSF lymphocytes >5/µL or protein >25mg/dL may considered diagnostic
- HIV+ patients with negative CSF-VDRL; diagnosis difficult as HIV may cause pleocytosis
- PCR sensitivity only 42%

Further progress…

- Repeat RPR early September 1:64 (tested in parallel)
- CSF 6/9
  Protein 0.37 g/L glucose 3.5mmol/L
  Red cells <1, PMN <1, mononuclear cells 4
  VDRL 8 (previously 32)
  TPPA reactive 80 (previously >80)
  FTA reactive
  T. pallidum PCR negative

- Further sexual exposures; treated for reinfection