"Rapid progression to gummatous tertiary syphilis in an HIV patient"

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Infectious Diseases Basic Trainee

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Case

25 yo M ATSI

- April 2017 "under schedule" psychiatry inpatient at peripheral hospital
- *Admitted following attempt to strangle family dog*- psychosis and depression
  - PHx September 2016 - admitted with suicidal ideation
  - Hx of amphetamine use and drug induced psychosis
  - Several ED presentations for over 18 months
- **HIV and syphilis serology (+ve)** during admission
  - Patient not surprised, HIV +ve in 2012

Social history

- ATSI : mother Torres Strait Islander, father Italian
- Lives with mother and sister, *unaware of HIV diagnosis*
- Employed in public hospital system (in administration)
- Very anxious about HIV disclosure
- Family history of bipolar disorder and depression
- History of domestic violence with previous partner
- MSM multiple partners last 7 years, variable protection
- Amphetamine, marijuana
- Denies IDU - needle phobia!

HIV chronology

- May 2012 - HIV diagnosed (by GP in Jannali). Never commenced ART.
- April 2015 – June 2016 treated for syphilis, incompletely, by 3 GPs on 3 occasions, HIV status unknown to GPs:
  - April 2015: penile chancre swabbed – syphilis PCR +ve, no serology (!). Commenced 10 days IM procaine – only attended 5 times (GP Kirawee)
  - July 2015: persistent chancre declined IM benzathine penicillin (GP Menai). 14 days PO doxycycline 100mg BD (unsure of compliance).
  - June 2016: 14 days PO doxycycline 100mg BD & agreed to outpatient IM benzathine, not attended. (Another GP Menai)

Progress in peripheral hospital

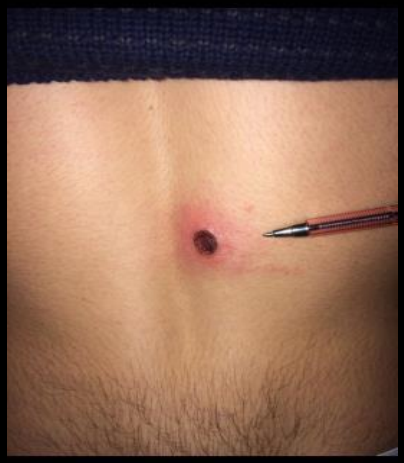
Examination late April

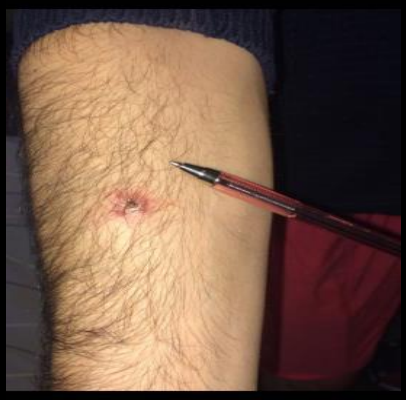
- Psychosis settled, demeanor agreeable
- 2 ulcerated skin lesions: back & forearm (? 2 weeks)
- Other examination unremarkable

Further results

- HIV VL 46,916 copies/ml , 4.67$\log_{10}$
- CD4 210
- RPR 64
- TPPA >320
- Other STI screen clear

Lesions: late April





Progress during admission

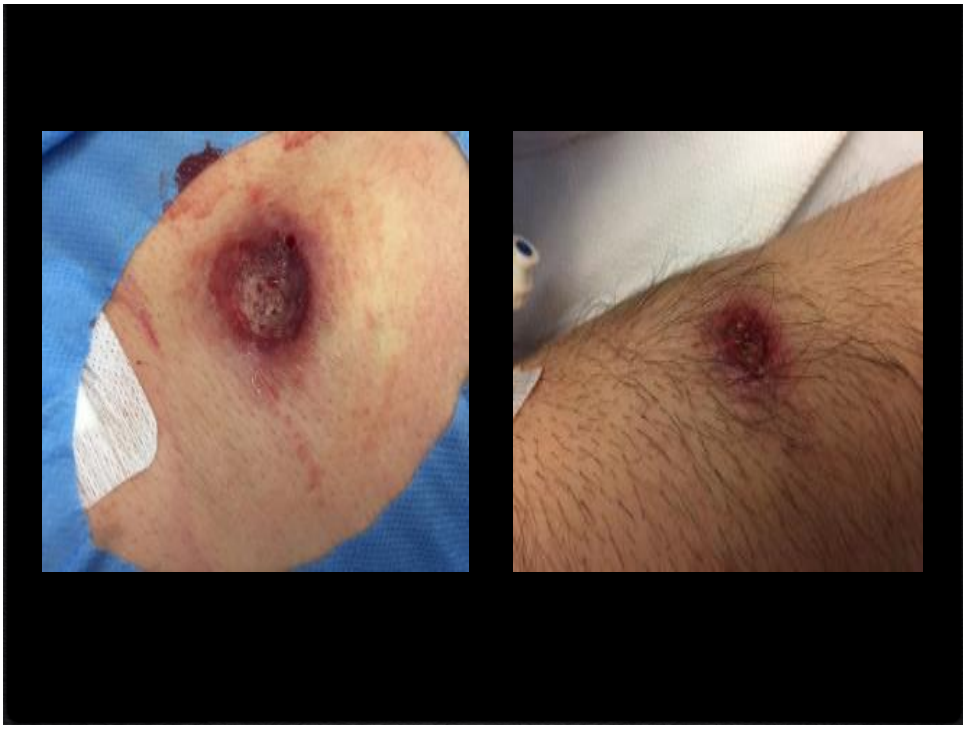
- Untreated HIV 5 years
- Needs transfer to tertiary hospital for MRI brain, LP and management
- Schedule lifted, to allow him to go home to get belongings…
- Absconded prior to transfer
- Uncontactable for 10 days
- During this time went interstate, with vague history of activities there

Transfer to SGH 23rd May

- Brought in by police to SGH from home
- Scheduled under supervision of psychiatry team

Examination

- Calm agreeable affect
- Nil systemic symptoms
- Nil neurological signs, nil ocular signs
- CV examination unremarkable
- anogenital examination 2cm penile scar
- 2 x painful ulcerated skin lesions
  - 2cm x 1.5cm lesion on back
  - 1cm x 1cm circular lesion on right forearm
  - biopsy performed



Initial investigations SGH

Bloods Late May

- RPR 128 *(Increased from 2nd May RPR 64)*
- HIV VL 122, 762 copies/ml , $\log_{10}$ 7.09
- CD4 count : 200 mm^3 (19%)
- Neg serology: Toxo, HSV, HBV, HCV; Neg crypto Ag

CSF

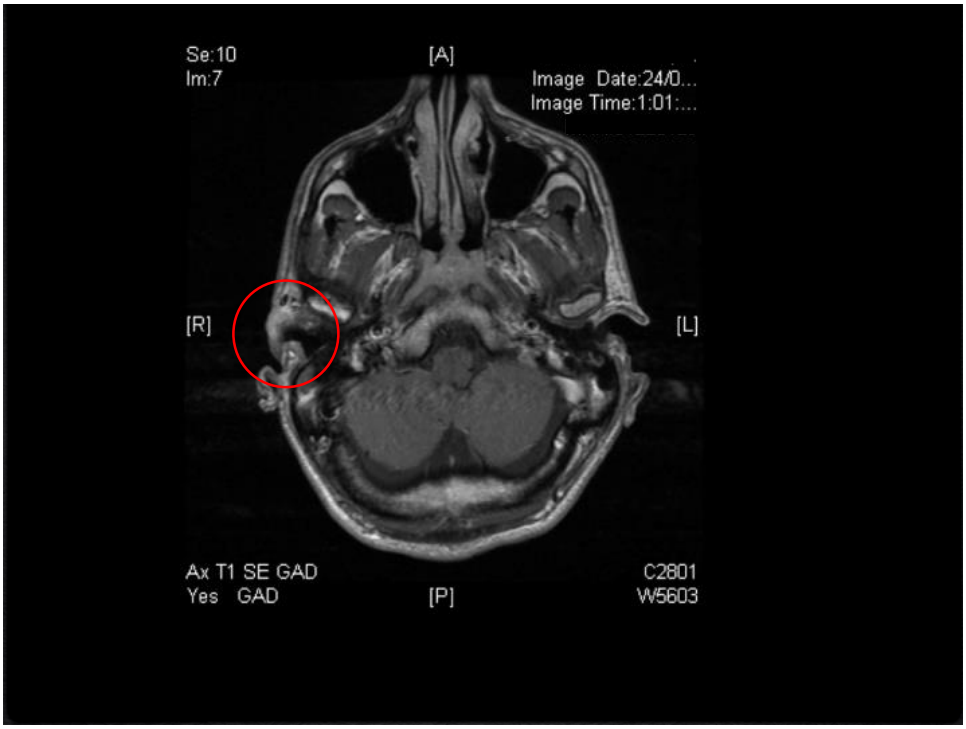
- HIV VL 14, 780 copies/ml, $\log_{10}$4.17
- Opening pressure 17cm, protein 0.26, glucose 3.0
- Gram stain: no organisms , <1 PM , < 1 MN

Urine drug screen

- Positive for cannabinoids and amphetamines

Ulcer Swab

- + ve GBS



Progress

Day 1 Commenced IV benzyl penicillin 1.8g IV 6 hrly, empirically for neurosyphilis

- *Triumeq* commenced (HLAB57 –ve)

Day 2 Schedule lifted, commenced on olanzapine

- Mother & daughter creating conflict on the ward
- High risk of absconding

Leading to management dilemma:

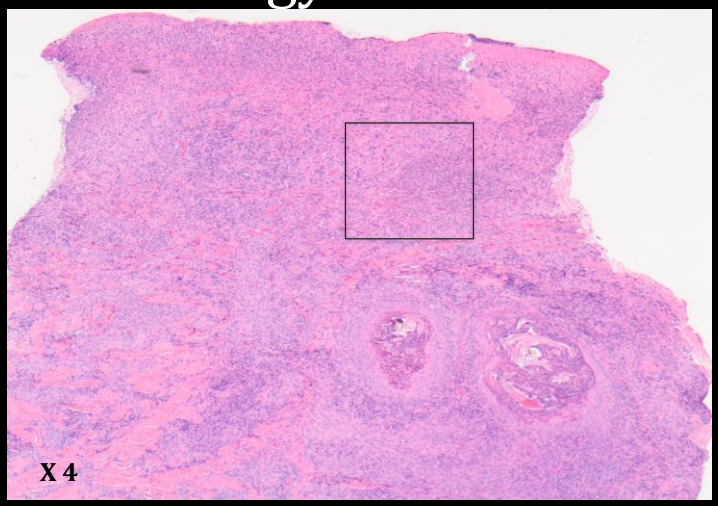
- Change to IM benzathine penicillin?
  OR push on with IV Rx given preliminary CSF results??

- *CSF: PCR, VDRL and FTA pending*

Treatment

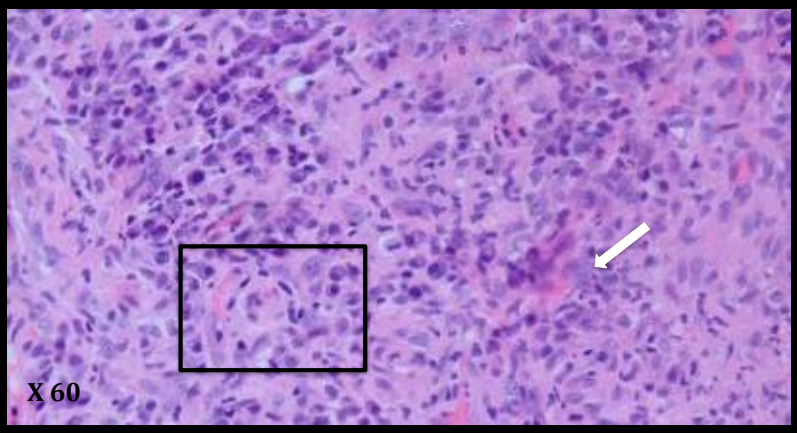
- **Day 2 :** changed IV benzylpenicillin to IM 2.4g benzathine
- **Day 3:** CSF VDRL non-reactive
  CSF TPPA 1:160 (CSF Adenovirus IgG -ve)
  normal TTE, ophthalmology review normal
- **Day 7:** Reactive CSF FTA-ABS, awaiting syphilis PCR
  Skin biopsy : ulcer granulomas c/w gummas
  +ve Warthin Starry

Histology –skin ulcer



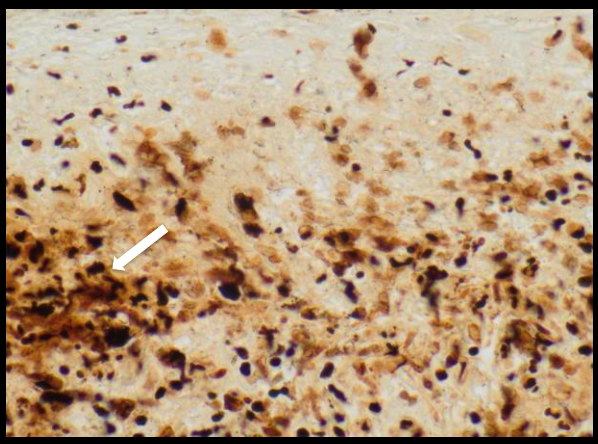
Abundant neutrophilic inflammatory debris

Histology



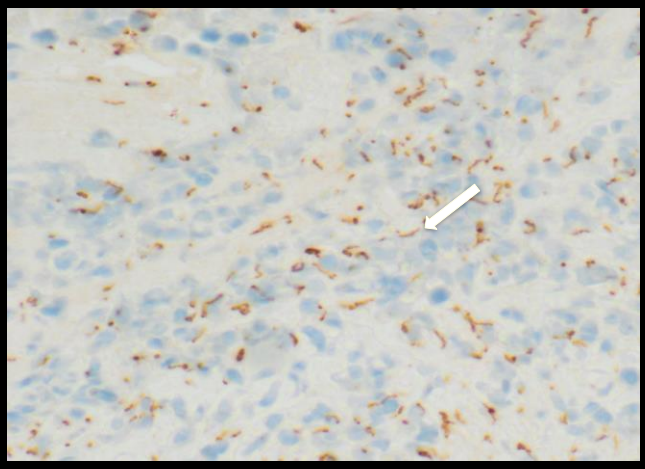
Prominent periadnexal and perivascular inflammatory infiltrate
Prominence of plasma cells
Biopsy base of ulcer showed granuloma

Day 7 biopsy results



Warthin Starry stain initially negative,
repeat staining strongly positive

IPX from biopsy



Note arrow showing *Treponema pallidum* staining
Treponema pallidum DNA detected on PCR

Treatment

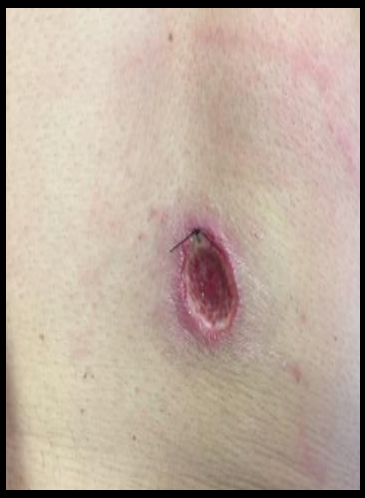
Day 7:

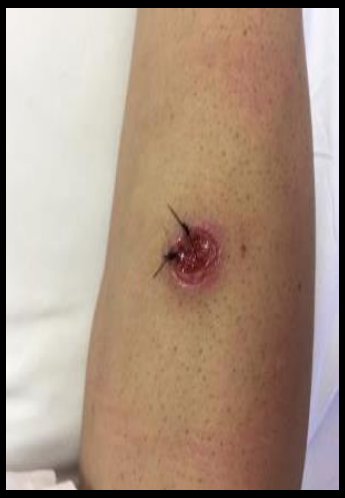
- Recommenced on IV benzylpenicillin
- Continued on Triumeq, olanzepine

Day 17 : self-discharged with PICC line

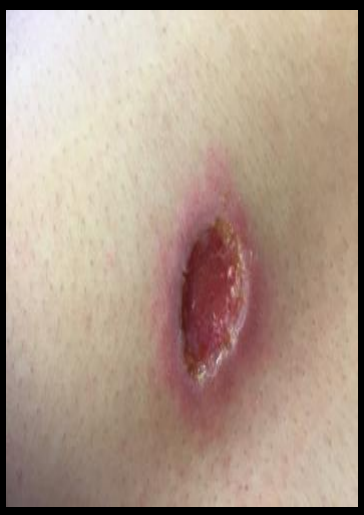
4 weeks later PICC removed in ED, nil further contact

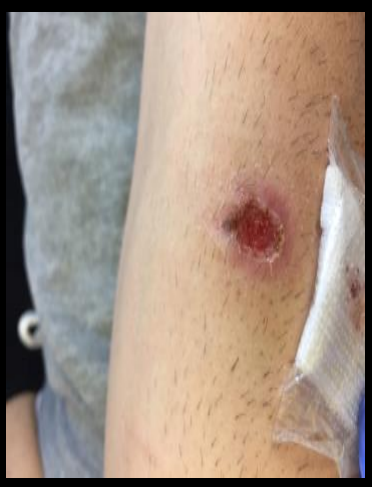
Day 5 penicillin





Day 10 IV penicillin





Case summary

- Rapidly progressing skin lesions consistent with gummas
- Tertiary Syphilis:
  - skin, bone (?), neurosyphilis (?)
- HIV untreated 5 years, asymptomatic, immunosuppressed
- Mental health illness
- Disclosure anxiety
- Cultural background
- Needle phobia
- Financial stressors
- Contact tracing

Syphilis

- **Primary** 2-6 weeks
  - Chancre: 2 -3 weeks after sexual contact. 0.5-2cm painless papule that ulcerates. Regional non tender lymphadenopathy.
  - Usually solitary but multiple chancres have been described in HIV pts [1, 2]
- **Secondary** 6-12 weeks
  - Haematogenous dissemination: 3-6 weeks symptoms occur after resolution of primary stage → Rash, mucosal lesions, condylomata lata [2]
- **Tertiary** 1-30 years

1) Gummatous syphilis
2) Cardiovascular syphilis
3) Neurosyphilis

Gummas

- The gumma is a granulomatous inflammatory response to a small number of spirochetes
- Rare, more common in patients with untreated HIV
- Potential to form in any organ but commonly occurs in skeleton, spinal and mucosal areas
- 4-10 years post infection, however in HIV patients *may occur after a few months only* [1]

HIV & Syphilis

- HIV patients rapidly progress from early syphilis to gummatous or neurosyphilis [2]
- In a study of 117 HIV infected patients with neurosyphilis 33% were asymptomatic [3]
- Risk of increased HIV VL
- Rapid decline in CD4 counts , leading to earlier CD4 nadir
- HIV patients 3-4 fold increase [5,6,7] of developing neurosyphilis if:
  - CD4 count < 350 cells/µµL
  - RPR titer > 1:128 [4]

Neurosyphilis

CSF Diagnosis in HIV patients:

CSF VDRL reactive: almost diagnostic

- CSF leukocyte count (usually elevated in HIV > 5 WBCs/mm3)
  - If >20 likely neurosyphilis
  - If 6-20, check CD4 count <200, serum HIV RNA , and HIV treatment status
  - Then assess CSF FTA and PCR, if reactive/ +ve then treat [8,9]

Our patients CSF*:*

- *No organisms on Gram stain*
- *<1 polymorph*
- *<1 mononuclears*
- *Serum CD4 count 200*
- *VL 7 log copies in serum*
- *CSF FTA POS, TPPA 1:160, VDRL NEG*

Test validity

- CSF VDRL
  - +ve considered diagnostic
  - Very specific, lacks sensitivity
- *Depending on definition of neurosyphilis, sensitivity for VDRL reported as low as 50% [6]*
- *Negative CSF VDRL does not exclude syphilis*

- CSF FTA-abs
  - less specific, but highly sensitive for neurosyphilis.
  - Neurosyphilis is highly unlikely with a –ve CSF FTA
  - *less specific, even more so in patients with acellular CSF [10]*

- CSF TPPA
- sensitivity ≈ FTA
- specificity high if >1:320 and ≈ VDRL if titre>1:640[5]

Treatment guidelines

- **Australian Therapeutic Guidelines**
  - *IV benzylpenicillin 1.8g Q6hrly 14 days for:*
    - Tertiary syphilis with gummas
    - Neurosyphilis
    - Cardiovascular disease
- **IDSA, CDC and British (BASHH) guidelines**
  - *IV benzylpenicillin 1.8g Q4hrly 14 days for:*
    - Neurosyphilis (alternate IM or PO regimens available)
  - *IM benzathine 2.4MU weekly x 3 sufficient:*
    - Gummatous lesions
    - Cardiovascular disease

Issues

- Diagnosis of neurosyphilis (FTA vs VDRL)?
  - FTA, TPPA reported to be more sensitive,
  - FTA negative excludes neurosyphilis in asymptomatic patients
  - VDRL lack sensitivity, higher specificity
- Optimal modality & duration of syphilis treatment (IV v IM)
- Ongoing syphilis monitoring (RPR, eyes, heart, LP etc)
  - Repeat LP and progress MRIB?
  - Is the mastoiditis a gumma?
- HIV management
- Mental health management
- Self harm & public health risk?

Acknowledgements

- Verbal consent from patient for case report and pictures
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