A Case of HIV with Multiple Related Infections - Balancing Treatments, Drug Interactions and Side-effects

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Mr K
- HIV
  - 55M diagnosed in 2005
  - HLA B5703 positive
  - Long term slow progressor. Not on ART

- PMH: Essential Hypertension, Malaria, Typhoid fever

- SHx
  - Arrived in 2005 from Cote d'Ivoire
  - Works as a baker and pastry chef
  - Has a wife and 3 children

- Last seen in the Immunology clinic in 2011 with CD4 442, VL 12800 cp/ml
Admission October 2017

- Presented with collapse, fevers and weight loss
- Examination
  - Unwell, thin
  - Temp 38.8 C
  - Chest clear, Abdomen soft, no organomegaly
  - Painful 2cm left supraclavicular lymph node

Investigations

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<tbody>
<tr>
<td>Hb</td>
<td>73</td>
<td>bili</td>
</tr>
<tr>
<td>WCC</td>
<td>5.38</td>
<td>ALT</td>
</tr>
<tr>
<td>Plt</td>
<td>226</td>
<td>ALP</td>
</tr>
<tr>
<td>MCV</td>
<td>76</td>
<td>GGT</td>
</tr>
<tr>
<td>Neut</td>
<td>4.8</td>
<td>alb</td>
</tr>
<tr>
<td>Lymph</td>
<td>0.11</td>
<td></td>
</tr>
<tr>
<td>CRP</td>
<td>280</td>
<td>LDH</td>
</tr>
<tr>
<td>INR</td>
<td>1.2</td>
<td>Hapto</td>
</tr>
<tr>
<td>U&amp;E</td>
<td>NAD</td>
<td>ferritin</td>
</tr>
<tr>
<td></td>
<td></td>
<td>iron</td>
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<td></td>
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<td>transferrin</td>
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<td>T.sat</td>
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Investigations

- Lymph node biopsy: positive for **Acid fast bacilli**
- Blood and urine cultures positive for **Mycobacteria TB**
- Toxoplasma serology: positive IgG
- **CT Abdo/Pelvis**: bilateral supraclavicular lymphadenopathy, enlarged LN around porta hepatis, SMA and para-aortic
- **CT brain and MRI brain**: no evidence of intracranial mass or infection

**Disseminated TB**

Other issues....

- **Advanced HIV**
  - CD4 absolute count 5 (1%), VL 79433

- **Hepatitis B coinfection**
  - Viral load: 2 x10^7 IU/ml, HBeAb & sAg positive, HBeAg neg
  - Treatment naive
  - US abdomen 18 Oct: normal
Other issues....

Moderate to large pericardial effusion
- Secondary to TB. No drainage required
- For repeat ECHO in 2 and 6 weeks prior to initiation of ART to monitor size given risk of IRIS

TB retinitis and HIV retinopathy
- Nil visual symptoms reported
- O/E: subretinal nodules, patchy, poorly defined opacities consistent with TB retinitis.
- For ongoing review

Other issues....

Opportunistic infections/prophylaxis
- Fluconazole 50mg PO for oral candidiasis
- G6PD screening test indicated possible deficiency therefore co-trimoxazole and dapsone avoided - Pentamidine nebulisers for PJP prophylaxis
The challenge

- Disseminated TB
- Advanced HIV
- Hepatitis B
- Pericardial effusion secondary to TB
- TB retinitis/HIV retinopathy
- Oral candidiasis
  - Fluconazole
- PJP prophylaxis
  - Pentamadine

Steroids to prevent TB-IRIS
The challenge

- Disseminated TB
- Advanced HIV
- Hepatitis B
- Pericardial effusion secondary to TB
- TB retinitis/HIV retinopathy
- Oral candidiasis
  - Fluconazole
- PJP prophylaxis
  - Pentamidine

Steroids to prevent TB-IRIS

Needs to be treated prior to initiation of steroids

Treat prior to initiation of antivirals

Treat prior to initiation of steroids

Steroids to prevent TB-IRIS
Treatment

- **Mycobacterium tuberculosis**
  - Commenced Rifampicin, Isoniazid, Pyrazinamide, Ethambutol and pyridoxine (day 0)

- **HIV and Hepatitis B**

Drug Interactions

- **Do Not Coadminister**
  - Elvitegravir/Cobi/FTC/TAF
    - Rifampicin
      - (Genvoya)
  - Elvitegravir/Cobi/FTC/TDF
    - Rifampicin
      - (Stribild)
  - Rilpivirine/FTC/TAF
    - Rifampicin
      - (Odefsey)
  - Emtricitabine/TAF
  - Rifampicin
    - (Descovy)

www.hiv-druginteractions.org
Drug Interactions

**Rifampicin**

![Diagram showing drug interactions between Rifampicin and other drugs](www.hiv-druginteractions.org)

**Clinic Review (day 19)**

- **Mycobacterium tuberculosis**
  - (day 0) Commenced Rifampicin, Isoniazid, Pyrazinamide, Ethambutol and pyridoxine

- **HIV and Hepatitis B**
  - (day 19) Tenofovir disoproxil fumarate/emtricitabine (Truvada)
  - Dolutegravir 50mg BD

- **Preventing TB-associated IRIS affecting pericardium and eye**
  - Planned for Prednisolone 75mg (day 21)
Drug Interactions

<table>
<thead>
<tr>
<th>Drug Interaction</th>
<th>Rifampicin</th>
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<tbody>
<tr>
<td>Prednisolone</td>
<td>• rifampicin increases the plasma clearance of prednisolone by ~50%</td>
</tr>
</tbody>
</table>

Summary

Day 0
Quadruple therapy for treatment of TB

Day 19
TDF/FTC + DTG (Treatment for HIV and Hepatitis B)

Day 21
Prednisolone 75mg (Prevention of IRIS affecting pericardium and eyes)

Day 26
Tolerating ART. Planned to wean prednisolone over 6 weeks. Repeat G6PD screen – not deficient
Admission November 2017
- Day 31 after commencing TB treatment
- Day 12 after commencing ART

- Presented with fever

- O/E:
  - Looked well
  - Supraclavicular and cervical lymphadenopathy
  - Chest clear, Abdominal examination unremarkable
  - Cranial and peripheral nerve examination NAD

- Unable to recall simple details. Apraxia

Axial (T1 post contrast)
T2 flair

October

November
Cerebral toxoplasmosis (unmasking IRIS)

- Sulfadiazine 1g QID
- Pyrimethamine (200mg stat then 75mg OD)
- Ca folinate 15mg OD
- Dexamethasone 8mg QID

Week 6

- Clinically improving but....
Week 6

- Clinically improving but....

![White Cell Count Chart](chart1.png)

![Neutrophils Absolute Chart](chart2.png)

Side-effects

**Hepatotoxicity**
- Hepatitis B IRIS flare?
  - Hepatitis D serology negative
  - Viral load $2 \times 10^6$ IU/mL
    (Initial viral load $2 \times 10^7$ IU/L)

- Drug-induced?
  - Isoniazid
  - Pyrazinamide
  - Rifampicin
  - Sulfadiazine
  - Pyrimethamine
  - Fluconazole

**Bone marrow suppression**
- Pyrimethamine
- Sulfadiazine
- Truvada
- Rifampicin
Week 6

- TB treatment
  - Rifampicin, Isoniazid, Pyrazinamide
  - 1 week later started amikacin, ethambutol and moxifloxacin

- Cerebral toxoplasmosis treatment
  - Sulfadiazine
  - Commenced clindamycin 600mg QID.
  - Pyrimethamine dose reduced to 50mg

Week 10 of TB Treatment
Week 6 of treatment for toxoplasmosis

Before

6 weeks of treatment for cerebral toxoplasmosis

MRI brain T2 flair
Week 10 of TB Treatment
Week 6 of treatment for toxoplasmosis

HIV viral load <40 cp/ml
CD4 count 12

Hepatitis B viral load $8.8 \times 10^5$ IU/ml

Week 10-12

- TB treatment
  - Amikacin, ethambutol, and moxifloxacin
  - Re-introduction of rifampicin followed by isoniazid

- Cerebral toxoplasmosis treatment
  - Clindamycin 600mg QID.
  - Commenced on secondary prevention with sulfadiazine 1g bd and reduced dose pyrimethamine 25mg OD
Week 16

Medications
- Rifampicin
- Isoniazid
- Sulfadiazine
- Pyrimethamine
- Calcium folinate
- Pyridoxine
- TDF/FTC
- Dolutegravir
- Amlodipine

Ceased medications
- Dexamethasone
- Prednisolone
- Moxifloxacin
- Ethambutol
- Clindamycin

Hepatotoxicity (Month 5)
Hepatotoxicity (Month 5)

- TB treatment
  - Rifampicin and isoniazid ceased
  - ALT settled from 965 to 199.
  - Rifampicin and moxifloxacin 400mg OD restarted 2 weeks later
  - ALT continued to fall to 41
  - Isoniazid suspected of causing hepatotoxicity.

- Cerebral toxoplasmosis secondary prevention
  - Sulfadiazine and pyrimethamine switched to Bactrim DS 1 tab bd

Progress

- Month 6
  - Continued leucopenia on Bactrim DS. Changed to atovaquone 750mg tds

- Month 7
  - Ethambutol re-commenced. Continued rifampicin and moxifloxacin

- Month 9
  - Completed TB treatment with rifampicin, moxifloxacin and ethambutol
Progress

- Since rifampicin ceased, WCC improved

- Atovaquone ceased. Bactrim DS re-started

How is Mr K?

- Completed 9 months of TB treatment
- Completed primary treatment for cerebral toxoplasmosis

- Continues treatment for HIV, Hepatitis B (TDF/FTC + DTG)
- Continues secondary prophylaxis (Bactrim)

- CD4 count 128
- HIV viral load <40 cp/ml
- Hepatitis B viral load NOT detected
How is Mr K?

- Back to full time work
- His wife delivered a healthy baby boy!

Plan 27th September 2018

Medications
- Genvoya
- Co-trimoxazole
- Amlodipine

Ceased medications
- Dexamethasone
- Clindamycin
- Prednisolone
- Pyrimethamine
- Sulfadiazine
- Calcium folinate
- Isoniazid
- Pyridoxine
- TDF/FTC
- Dolutegravir
- Rifampicin
- Moxifloxacin
- Ethambutol
- Atovaquone
- Fluconazole
Conclusion

- Case highlights that despite huge advances in treatment, complex cases do still present with the same issues of co-infections, drug interactions and side effects
- Important reminder of starting treatment at the point of diagnosis

Acknowledgements

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Mr K