Mycobacterial Infections and HIV

Complex cases from Imperial College Healthcare NHS Trust, St. Mary’s Hospital, London, UK
Presented by Gareth Tudor-Williams,
with thanks to my colleagues and patients in the Family Clinic

Please email referrals to caroline.foster@imperial.nhs.uk
Case 1  Background

- Boy, born in SSA in 2011
  - 2 x antenatal HIV test- one negative, one positive
  - Father negative: parents chose to believe mother’s negative HIV test
  - SVD at 40/40
  - BCG given at 5 days
  - Immunisations given according to national policy
  - Breast fed until 1 ½ yrs
  - Hospitalised with malaria, aged 20 months: 3 day admission during which he developed oral thrush, but apparently not tested for HIV
- Moved to UK February 2013
- Poor appetite and faltering growth during 2013
- Developmental concerns
Initial presentation

• November 2013
  • Presented to General Practitioner – 5/7 cough, Rx amoxicillin p.o.
  • Admitted to District General NHS Hospital
    • Bilateral pneumonia with acute respiratory failure
    • IV cefuroxime and clarithromycin
    • Intubated and ventilated

• Transferred to PICU at Tertiary Referral NHS Hospital
  • ETT secretions: PCP PCR positive
  • HIV-1 antibody positive, HIV VL 18,000,000 c/ml, CD4 250 (23%)
  • CMV viraemia 16,000 c/ml
  • Quantiferon gamma: indeterminate, no AFBs on ETT secretions
  • No growth on blood cultures
  • TP antibody reactive (RPR, TPPA, VDRL negative), Hep A ab positive, Hep B sAg negative, HCV ab negative
Transferred to specialist HIV centre, St Mary’s Hospital, Imperial College NHS Trust, London

Treatment:
- Extubated within 72 hours
- Oxygen requirement resolved over about 10 days
- 3/52 iv co-trimoxazole and subsequently dapsone p.o.
- 2/52 iv ganciclovir

Further investigations:
- HIV subtype CRF02_AG
- HLA-B*5701 negative
- Baseline resistance: wild type
Antiretroviral therapy:

- 30 Nov 2013
  - Abacavir
  - Lamivudine
  - Zidovudine
  - Nevirapine
- 12 Dec 2013
  - Nevirapine stopped (elevated LFTs)
  - Raltegravir started

**Ten days later**
- New onset fevers
- Not feeding
- BCG site inflamed, axillary adenopathy and sub-clavicular mass
- Hepatosplenomegaly with persistent transaminitis
No prizes for guessing the diagnosis!

- BCG IRIS
- Blood cultures positive for *M. bovis*

What treatment would you advise?
No prizes for guessing the diagnosis!

• **BCG IRIS**
  • Blood cultures positive for *M. bovis*

• What treatment would you advise?

• We started:
  • Isoniazid
  • Rifabutin
  • Ethambutol
  • Moxifloxacin
  • Steroids – prednisolone at 2mg/kg, weaned off over 3 weeks
Case 1  Progress

- 9 Jan 2014
  - Still in hospital
  - VL increased
  - Resistance testing and Therapeutic Drug Monitoring requested

- 12 Feb 2014
  - TDM for raltegravir revealed sub-therapeutic levels
  - RTG dose increased by 25% (no integrase resistance)
  - Nevirapine restarted

- Persistent neutropenia
  - Many potential culprits amongst the drugs he was receiving
  - Stopped dapsone (unconvinced he had clinical PCP)
ART

- Paediatric Virtual Clinic (20.3.14)
- Viral load plateau’d: 100-200 c/ml
  - Stop Raltegravir
  - Start BD Kaletra liquid with TDM for Lopinavir and nevirapine.
  - Continue triple nucleoside – consider switching AZT for TDF granules if neutropenia persists

- PVC (17.4.14)
  - KAL, NVP, AZT, 3TC, ABC,
  - Adequate TDM – NVP and LPV
  - Low level viraemia, disseminated BCG
  - No resistance mutations including integrase
  - Plan: Stop NVP, continue KAL AZT 3TC ABC and repeat KAL TDM at 2 weeks
IRIS continued to cause problems

- Fevers daily after steroids weaned, extensive bilateral axillary and cervical adenopathy, chest wall abscesses requiring surgical drainage, BCG site remained inflamed despite 4 drug anti-mycobacterial regimen

- What would you do?
IRIS continued to cause problems

• Fevers daily after steroids weaned, extensive bilateral axillary and cervical adenopathy, chest wall abscesses, BCG site remained inflamed despite 4 drug anti-mycobacterial regimen

• What would you do?

• We gave a trial of thalidomide 5mg/kg/day for 2 weeks
  • No improvement

• Restarted Prednisolone late March 2014
  • Weaned slowly and stopped Nov 2014
Over the next two years…

• Continued problems with suppurative chest wall lesions
• Multiple surgical drainage attempts
• Auramine stains / 16-sRNA / cultures NEGATIVE

• Viral load eventually reached undetectable, and nevirapine was dropped from regimen

• CD4 counts uniformly between 2,000 – 3,000
As of May 2016

- **ART**
  - Zidovudine 120mg bd
  - Lamivudine 75mg bd
  - Abacavir 120mg bd
  - Kaletra 2.4ml bd
- **Anti-mycobacterial**
  - Rifabutin 170mg MWF
  - Isoniazid 150mg od
  - Moxifloxacin 200mg od
  - Ethambutol 300mg od
- **Other**
  - Abidec, pyridoxine
  - **MONTELUKAST COMMENCED** – made no clinical difference to IRIS
• GTW d/w Mark Cotton: since all growth –ve ? Stop anti TB treatment
Insights from Stellenbosch

• Fistulation seen in some patients over more than 2 years
• Surgical interventions don’t really solve the problem
• Would consider stopping antimycobacterials, but had only gone down this route for localised disease
• Prof Schaaf quoted by Helena Rabie: efficacy of ‘medieval poultices’ of INH and PAS applied topically for scrofula

• We were not brave enough to stop anti-mycobacterials

• Arranged interferon gamma/IL12 pathway assays and other cytokine profiling.
Hot off the press:

Assays show that he has impaired release of interferon-gamma and no evidence of receptor

Started a therapeutic trial of IFN-gamma, 20 July 2017

Please invite me back next year to let you know the outcome!