MULTI-DRUG RESISTANT TUBERCULOSIS (TB)

Christine Bell
Lead TB Nurse, Manchester
Manchester Foundation Trust
• TB is an infectious disease
• Caused by *Mycobacterium tuberculosis*
• Spreads by coughing from a person with disease in the lungs
• Can affect any part of the body (but the most common site is the lungs)
• Following transmission TB can lie dormant for many years before re-activating (latent TB)
• Treatment of latent TB prevents active disease
INDEX CASE

• General Practitioner referral
• 27 year-old female (Roxanne)
• Black African ethnicity
• Born UK
• 4 month history of cough, weight loss and night sweats
• Current use of cocaine and tobacco
• History of mental health issues (on citalopram)
PRESENTING CHEST X-RAY
SOCIAL HISTORY

- Lived with 5 year-old son
- Recent split from child’s father (Russian national) who had been charged with domestic abuse and was on the run from the police
- Not on very good terms with mother
- No work
Initial Investigations

- Weight 42 kg (8 kg loss)
- Bloods
  - Raised inflammatory markers
  - HIV negative
- Sputum for TB examination
  - Alcohol Acid Fast Bacilli (AAFB) on direct smear +++
  - Cepheid GeneXpert positive for Mtb and RIFAMPICIN resistance
  - Hain confirmed not only R resistance but also ISONIAZID resistance
  = MDR-TB
• Negative pressure room
• Within a few days had fallen out with some of the nurses on the ward
• Verbally very abusive, throwing things around the room
• Often leaving to the ward to go to the shops
• PICC line (peripherally inserted central catheter) inserted
• Son looked after by Roxanne’s sister
• Case entered of British Thoracic Society MDR-TB forum
• Public Health England informed
• Clinical psychology referral
TREATMENT

- Amikacin intravenously (IV)
- Pyrazinamide
- Ethambutol
- Moxifloxacin
- Linezolid
- Prothionamide
- Cycloserine
SENSITIVITIES

MICROSCOPY: ***** AFB +++ SEEN *****

CULTURE:
- Mycobacterium tuberculosis

Susceptibility:
- Ethambutol
- Rifampicin
- Isoniazid
- Pyrazinamide
- Rifabutin
- Azithromycin
- Clarithromycin
- Streptomycin

Results:
- Ntx: S
- Oflox: R
- Linezolid
- Prothionamide
- Capreomycin
- Kanamycin

Sample for AFBs: 29.02.16
Received: 01.03.16
Reported: 29.04.16

Final Report: Rob Shorten
• Amikacin IV
• Pyrazinamide
• Ethambutol (resistant)
• Moxifloxacin
• Linezolid
• Prothionamide
• Cycloserine (neuropsychiatric effects)
# Therapeutic Drug Monitoring

## Baseline Tests

<table>
<thead>
<tr>
<th>Blood Tests</th>
<th>Renal function and electrolytes (U&amp;Es), liver function tests (LFTs), bone profile, magnesium (Mg), thyroid function tests (TFTs), uric acid</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Full blood count (FBC), clotting</td>
</tr>
<tr>
<td></td>
<td>HIV, Hepatitis B, Hepatitis C</td>
</tr>
<tr>
<td></td>
<td>66PD deficiency screen</td>
</tr>
<tr>
<td>Other Tests</td>
<td>ECG</td>
</tr>
<tr>
<td></td>
<td>Visual Acuity and Colour Vision</td>
</tr>
<tr>
<td></td>
<td>Audiometry</td>
</tr>
<tr>
<td></td>
<td>Nutritional Assessment</td>
</tr>
</tbody>
</table>
### CONTACT TRACING

<table>
<thead>
<tr>
<th>Family Member</th>
<th>IGRA Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Son</td>
<td>16 mm, +ve IGRA</td>
</tr>
<tr>
<td>Mother</td>
<td>- ve IGRA</td>
</tr>
<tr>
<td>Sister</td>
<td>+ve IGRA</td>
</tr>
<tr>
<td>Niece</td>
<td>10 mm, -ve IGRA</td>
</tr>
<tr>
<td>Friends</td>
<td>IGRA negative</td>
</tr>
<tr>
<td>Social worker</td>
<td>IGRA negative</td>
</tr>
<tr>
<td>Aunt</td>
<td>IGRA negative</td>
</tr>
<tr>
<td>Cousin</td>
<td>17 mm, +ve IGRA</td>
</tr>
<tr>
<td>C’s husband</td>
<td>0 mm, -ve IGRA</td>
</tr>
<tr>
<td>Child 1</td>
<td>19 mm, +ve IGRA</td>
</tr>
<tr>
<td>Child 2</td>
<td>16 mm, +ve IGRA</td>
</tr>
<tr>
<td>Child 3</td>
<td>15 mm, +ve IGRA</td>
</tr>
<tr>
<td>Child 4</td>
<td>18 mm, +ve IGRA</td>
</tr>
<tr>
<td>Child 5</td>
<td>18 mm, +ve IGRA</td>
</tr>
<tr>
<td>Child 6</td>
<td>0 mm, -ve IGRA</td>
</tr>
<tr>
<td>Child 7</td>
<td>0 mm, -ve IGRA</td>
</tr>
</tbody>
</table>

EVERYONE ASYMPTOMATIC

Chest X-rays CLEAR
LAMONT (CHILD 5)

5 year-old boy
Admitted to children’s hospital 2 weeks after Roxanne’s diagnosis with cough and respiratory distress
Diagnosed with presumed MDR-TB
Started Prothionamide, Linezolid, Pyrazinamide, Amikacin (via Hickman line), Ethambutol, Moxifloxacin, (Pyridoxine)
Refused to take oral meds
   gastrostomy
LAMONT PROBLEMS AND SIDE EFFECTS

- Intermittent vomiting
- Bit through Hickman line
- High tone hearing loss (amikacin discontinued)
- Acute line sepsis
- Visual impairment secondary to linezolid
- Linezolid replaced with Clofazimine and Delaminid
- Was already on child protection plan
- Input from school, social services, community paediatric nurses, TB nurses
TREYVON (CHILD 4)

8 year-old boy 
Original screening CXR normal but follow-up raised suspicion and CT showed numerous enlarged intrathoracic lymph nodes 
Diagnosed with presumed MDR-TB 
Started Prothionamide, Linezolid, Amikacin (via Hickman line), Ethambutol, Moxifloxacin, (Pyridoxine)
TREYVON SIDE EFFECTS

- Unable to tolerate Prothionamide (replaced by Cycloserine)
- High tone hearing loss (amikacin discontinued)
- Worsening behaviour secondary to Cycloserine
- Reduced visual acuity secondary to Linezolid – replaced with Clofazimine
- Following discussion with Great Ormond Street Hospital, given Delaminid and IV meropenem (three times a day)
- Community nurses unable to visit 3 times a day
  - Admitted for 6 months
Roxanne said her ex (Sergei) had a longstanding cough
She was unaware of any previous diagnosis of TB
Collected sputum sample
Produced a sample of blood in a syringe
Agreed to ask him to speak on the phone
He wanted treatment without attending hospital
RESULTS FROM SPUTUM

AAFB positive
M tuberculosis
Sensitivities identical to Roxanne (although HAIN showed INH resistance only)
Attended for chest X-ray
Would not agree to be treated by MRI due to concern that we would tell police
Said he would return to Lithuania for treatment
Becoming more agitated and wanted to go home

Often disappeared from cubicle

Sputum smear negative
  • One sample smear and culture negative
  • A further sample smear negative but cultured after 3 weeks

Weight increased, symptoms improved

Tolerating meds

Discharged after 7 weeks of treatment on condition that she would self-isolate

Community IV team for amikacin

TB nursing team for home visits

Social worker contacted

Son returned to her at home after 2 weeks
SLIGHT HICCUP

- IV team unable to contact Roxanne
- She had been admitted to hospital with
  - Fractured calcaneum, acetabulum and pubic ramus
  - She had fallen from a height
  - Went out to a nightclub but unable to find keys on returning home
  - Climbed up a drainpipe to enter an upstairs window but fell
  - Ortho recommended skin traction but Roxanne declined
  - Advised bedrest for 4 weeks – Roxanne hired a wheelchair
FURTHER PROBLEM

- Peripherally inserted central catheter (PICC) line became dislodged 5 months into treatment
- Option 1: continue Amikacin peripherally until Bedaquiline available
- Option 2: insert new PICC line and continue Amikacin for a further 3 months
- Roxanne opted for Bedaquiline
- Also started Clofazimine
- Amikacin stopped
MEANWHILE

- 33 year-old man (Mykolas) from Lithuania presented to North Manchester General Hospital
- Symptoms consistent with tuberculosis
- Abnormal chest X-ray
- Sputum smear positive
- Started standard treatment as out patient initially
- Isoniazid resistant (subsequently identified as resistant to Ethambutol as well)
- Said his friend had been diagnosed with TB and was taking Amikacin, Prothionamide, Pyrazinamide, and Linezolid
- Admitted to hospital and given Rifampicin, Prothionamide, Pyrazinamide and Linezolid
TB NURSES WERE SUSPICIOUS

- Started to investigate the possibility that Mykolas was in fact Sergei
- Further sputum samples cultured M tuberculosis resistant to Rifampicin, Isoniazid and Ethambutol
- Chest radiographs were identical
“Mykolas” defaulted from follow-up after 4 months of treatment
However, he was picked up (as Sergei) by immigration police and returned to hospital
Discussions with Public Health England
Sputum samples obtained
Remained in hospital in police custody
Smear and culture negative after 8 weeks
Deported to Lithuania
Sergei notified Mar/Jul 2016

Roxanne notified March 2016

Z notified Feb 2017

W notified Jun 2017
U notified Jul 2017 in London

X notified Jul 2017

T notified April 2016

Y notified August 2015 in Yorkshire

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ROXANNE OUTCOME

Completed treatment November 2017
LAMONT AND TREYVON
OUTCOME

Both children completed 2 years of treatment
Continue under follow-up at RMCH

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