Disseminated Pre-XDR TB

NAR 2023 - Challenging Case Session - Feb 24, 2023

William Connors MD FRCPC
Infectious Diseases / Tuberculosis Medicine
St. Paul’s Hospital / Vancouver General Hospital / BC-CDC
Clinical Assistant Professor – University of British Columbia
20 yo female from India ‘previously healthy’

Cough x months, recent ‘steroids’ via GP
Fever for weeks, worse dyspnea = ER

Hypoxia → respiratory failure = ICU

Collateral:
- In Canada x 6 months = student
- Contact with TB (uncle) 8 month prior
- TB screening (pre-arrival) = ”clear”

HIV/HBV/HCV negative, non-diabetic
**Admit**

June 2022

Wt ~45kg

**TB DIAGNOSIS**

Sputum AFB +
Xpert + & rpoB mutation
Empiric RIPE + MOXI
ARDS Steroids

**Pre-XDR / TBM**

MDDR = RMP/INH/FQ/PZA mutations
CSF = AFB+
Added Dexamethasone/ASA
Regimen Intensified

**ARDS / QUERY MILIARY TB**

Hypoxemic Resp. Failure = ICU

**Wk 1**

**Wk 2-4**

**NEUTROPENIA (<0.5)/PNEUMOTHORACES**

LZD dose reduced
MERO/CLAV stopped
G-CSF
Bilateral Chest Tubes

**Wk 2-4**

**Mth 2-3**

ICU → ward
Wt 43kg

**Drug Susceptibilities (@~wk 6)**

Geno/Phenotypic **RESISTANT**

- Rifampin
- Isoniazid (high level)
- Fluoroquinolone
- Ethambutol
- Pyrazinamide

**Phenotypic SUSCEPTIBLE**

- Aminoglycosides
- Linezolid
- PAS

**Pre-XDR vs XDR**

<table>
<thead>
<tr>
<th>Month</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>RMP/INH</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PZA/EMB</td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MOXIFLOXACIN</td>
<td>400mg</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MERO- CLAVULIN</td>
<td></td>
<td>2g TID</td>
<td></td>
</tr>
<tr>
<td>LINEZOLID</td>
<td></td>
<td>1200 mg</td>
<td>600mg (TDM ok)</td>
</tr>
<tr>
<td>AMIKACIN</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CYCLOSERINE</td>
<td></td>
<td>500mg BID</td>
<td>500 AM / 250 PM</td>
</tr>
<tr>
<td>CLOFAZIMINE</td>
<td></td>
<td>100mg OD</td>
<td></td>
</tr>
<tr>
<td>BEDAQUILINE</td>
<td></td>
<td>400 mg OD</td>
<td>200mg TIW</td>
</tr>
<tr>
<td>DELAMANID</td>
<td></td>
<td>100mg BID</td>
<td></td>
</tr>
</tbody>
</table>
Treatment of pre-XDR TBM…

What drugs?
What doses?
What duration?
What evidence?
OUTCOME & PLAN

Discharged from hospital after 5 months (culture conversion @ ~3mth)

- Clinically well, good drug tolerance (BDQ/CYCLO-B6/PTM/LZD/CLOF)
- Plan 18+ months from CNS conversion (~21mth) of 5-drug regimen

<table>
<thead>
<tr>
<th>Month</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>RMP/INH</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PZA/EMB</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MOXIFLOXACIN</td>
<td></td>
<td>400mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MERO- CLAVULIN</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LINEZOLID</td>
<td></td>
<td>1200 mg</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AMIKACIN</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CYCLOSERINE</td>
<td></td>
<td>500mg BID</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CLOFAZIMINE</td>
<td></td>
<td>100mg OD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BEDAQUILINE</td>
<td></td>
<td>400 mg OD</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DELAMANID</td>
<td></td>
<td>100mg BID</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

It takes a village = Surrey Memorial Hospital ID Team (Denise Werry), BCCDC/NML Mycobacteriology Teams (Inna Sekirov), BCCDC TB Program, Lisa Chen (UCSF Center for TB) and our patient.