Sterile Tuberculous Granuloma in a Patient With XDR-TB Treated With Bedaquiline, Pretomanid and Linezolid

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**Introduction**

The Nix-TB study is an open-label trial to assess the safety and efficacy of a 6-month regimen of bedaquiline, pretomanid and linezolid in participants with pulmonary infection with either extensively drug-resistant tuberculosis (XDR-TB) or treatment intolerant/non-responsive multidrug-resistant TB. In a recent report of the first 75 patients to complete the regimen, 89% of the patients had a favourable outcome at primary end-point1.

**Case Description**

A 38 year-old, HIV-1 positive female (CD4: 101 cells/ul) was enrolled with pulmonary XDR-TB. She had no history of seizures and normal neurological findings on examination.

She was started on NNRTI-based regimen two months prior to starting on trial. She changed to abacavir/lamivudine/lopinavir/ritonavir for the trial and was virally suppressed. She sputum culture converted after four weeks of the Nix-TB regimen and completed 26 weeks of treatment with one treatment interruption for asymptomatic pancreatitis.

She developed new-onset seizures one day after completing TB treatment and was hospitalized after a second seizure.

**Investigations**

Neurological examination and lumbar puncture were normal. An outpatient CT brain a month later showed a rim-enhancing lesion in the right temporal lobe suggestive of tuberculosisoma.

Investigations for toxoplasmosis and neurocysticercosis were negative. Lymphoma was also considered. A neurologist assessment and MRI suggested tuberculosisoma (Image 1). An excisional biopsy was done the following month. Histological results confirmed a tuberculosisoma.

**Biopsy Results**

<table>
<thead>
<tr>
<th>GeneXpert</th>
<th>Positive</th>
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<tbody>
<tr>
<td>Culture</td>
<td>Negative at 42 days</td>
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<tr>
<td>Histology</td>
<td>Granulomatous lesion with central necrosis</td>
</tr>
<tr>
<td>Hain MTBDRplus</td>
<td>Rifampicin resistant</td>
</tr>
<tr>
<td>Hain MTBDrsl</td>
<td>Indeterminate</td>
</tr>
</tbody>
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**Image 1: T1 weighted MRI showing rim enhancing lesion in right temporal lobe measuring 11 x 15 x 11mm (AP x ML x CC) with mild perilesional vasogenic oedema**

**Image 2: T2 weighted MRI 6 months post surgery with resolution of granuloma in right temporal lobe**

**Management**

She was started on phenytoin 300mg 3x/day orally after the first seizure. Anticonvulsants were tapered after a MRI six months post-surgery showed no new lesions. She experienced no further seizures. She made a full, uneventful recovery. Two years after completion of treatment, she remained sputum culture negative on her final trial sample.

**Discussion**

Drug-resistant tuberculous meningitis has an almost 100% mortality rate2,3,4. Many TB medicines fail to penetrate the blood-brain-barrier (BBB) resulting in poor outcomes. While it cannot be conclusively stated, this case makes a strong argument that this shortened, all oral regimen, may have sterilized a tuberculoma. Assessing the BBB penetration of new drugs is a priority in this devastating disease. Literature suggests bedaquiline penetrates the BBB poorly5. Pretomanid penetrates well in animal studies (no human studies exist)6. Linezolid is known to have excellent penetration7.

**References**

5. Török K, Knight DA, Price DL, Kiley DP, Inns KR, Lee AT, et al. Pretomanid penetrates well in animal studies (no human studies exist). University of Witwatersrand, Faculty of Health Sciences, Department of Medicine, South Africa. 2010;23(4):858

**Presented in Collaboration With**

Clinical HIV Research Unit

TB Alliance

WITS Health Network

523

- Positive

- MTBDRplus

- Indeterminate

- Rifampicin resistant

- Negative at 42 days

- Granulomatous lesion with central necrosis

- Rifampicin resistant

- Isoniazid resistant

- Indeterminate