MANAGEMENT OF PRE-EXTENSIVELY DRUG-RESISTANT TUBERCULOSIS IN A PREGNANT PATIENT: BALANCING PUBLIC HEALTH OBLIGATIONS WITH PATIENT AUTONOMY

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INTRODUCTION

We report on a pregnant patient who declined antenatal treatment for pre-extensively drug-resistant tuberculosis (pre-XDR-TB). We present the management strategies that were implemented by the New York City (NYC) Department of Health and Mental Hygiene (DOHMH) and treating physician in an effort to respect the patient's decision to defer treatment while maintaining the obligation to protect the public.

BACKGROUND

- Management of multidrug-resistant TB (MDR-TB) during pregnancy is complex
  - No standard guidelines exist regarding treatment regimens and their efficacy
  - There is limited data about the safety and use of second- and third-line agents during pregnancy
  - Untreated TB can lead to adverse outcomes such as maternal mortality, congenital TB, neonatal mortality, and transmission
- MDR-TB is a TB strain that is resistant to at least isoniazid and rifampin[1]
  - Pre-XDR-TB is an MDR-TB strain with additional resistance to any fluoroquinolone or second-line injectable aminoglycoside but not both[2]
  - Extensively drug-resistant TB (XDR-TB) is an MDR-TB strain with additional resistance to any fluoroquinolone and at least one of three injectable, second-line drugs[1]

Box 1. Case Management Activities

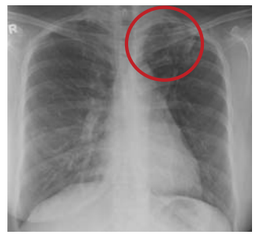
The New York City Department of Health and Mental Hygiene conducts routine case management activities for all tuberculosis patients, which include:

- Patient education and support throughout treatment
- Ensuring adherence to appropriate therapy via directly observed therapy (DOT)
- Provider outreach and collaboration
- Contact investigations

INITIAL PRESENTATION

- 30-year-old gravid patient from India presented to the emergency department with vaginal bleeding at 25 weeks 5 days gestational age
- Self-reported history of TB in 2010
  - Completed 6 months of treatment in India
- Asymptomatic with positive QuantiFERON-TB Gold test, negative acid-fast bacilli (AFB) sputum smear, and negative HIV test
- Chest radiograph: Non-cavitary, consistent with TB (Figure 1)

Figure 1. Chest Radiograph with Left Upper Lobe Infiltrate



METHODS

- The NYC DOHMH and treating physician developed a treatment plan based on phenotypic and rapid molecular drug susceptibility testing (DST) (Table 1)
- Patient declined the recommended antenatal treatment for pre-XDR-TB due to teratogenicity concerns
- Patient's decision to defer treatment was respected and comprehensive public health precautions were taken to prevent public, household, nosocomial, and neonatal transmission (Figure 2)

RESULTS

- To minimize TB transmission, preventative measures were implemented (Figure 2)
- Neonate
  - Postnatally: Asymptomatic, Tuberculin Skin Test negative, chest radiograph normal, 3 gastric aspirates and cerebrospinal fluid AFB and culture-negative
  - Placenta: AFB-negative, no evidence of congenital TB on pathology

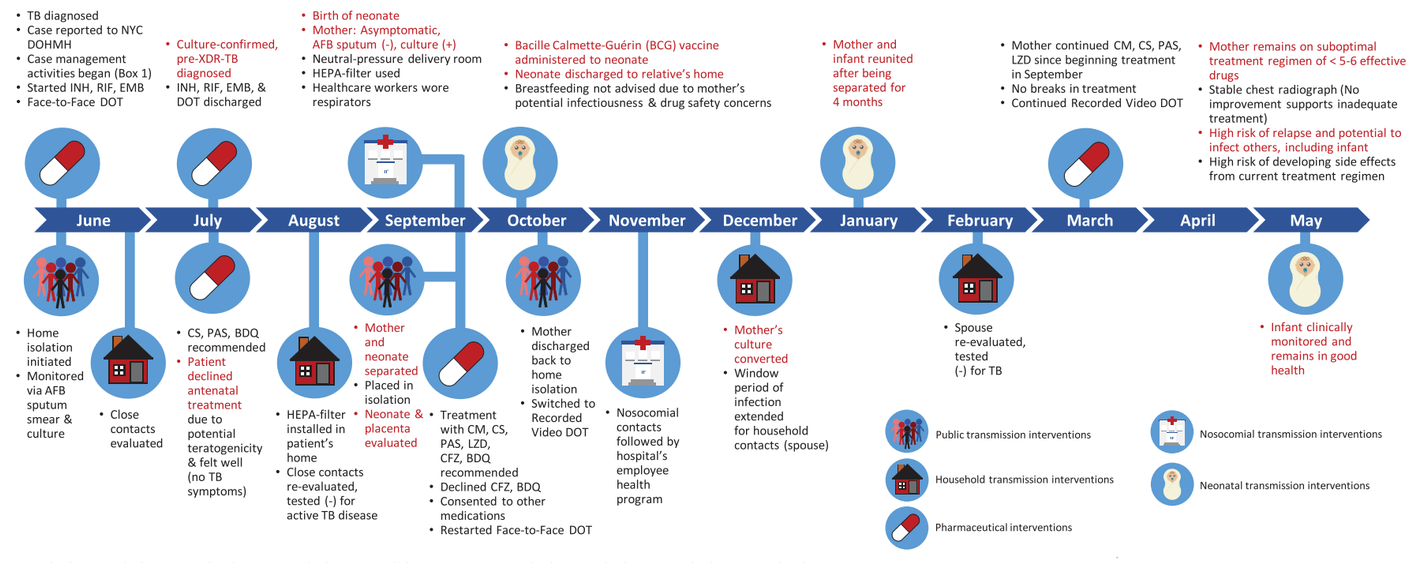
RESULTS

Table 1. Drug Susceptibility Test Results

Drug	Resistant/ Susceptible	Phenotypic DST *	Molecular DST ** (Genes with Mutations)
Isoniazid	RES	✓	✓ (katG)
Rifampin	RES	✓	✓ (rpoB)
Pyrazinamide	RES	✓	✓ (pncA)
Ethambutol	RES	✓	✓ (embB)
Streptomycin	RES	✓	✓ (rpsl)
Rifabutin	RES	✓	
Fluoroquinolones	RES	✓	✓ (gyrA)
Aminoglycosides	SNS		
Cycloserine	RES	✓	
Para-Aminosalicylic Acid	SNS		
Ethionamide	RES	✓	✓ (ethA)
Linezolid	SNS		
Clofazimine	RES	✓	
Bedaquiline	SNS		

*Phenotypic: Conventional, mycobacteria growth indicator tube (MGIT), minimum inhibitory concentration (MIC); **Molecular: Pyrosequencing, whole genome sequencing, Hain GenoType MTBDRsl; ✓ : Confirmation of resistance via specified methodology

Figure 2. Public Health Interventions and Outcomes



Isoniazid (INH), Rifampin (RIF), Ethambutol (EMB), Capreomycin (CM), Cycloserine (CS), Para-aminosalicylic acid (PAS), Linezolid (LZD), Clofazimine (CFZ), Bedaquiline (BDQ)

CONCLUSION

- Whether drug-resistant or drug-susceptible, TB during pregnancy poses unique challenges that can be complicated by treatment declination or deferral
- Management of MDR-TB during pregnancy should be a collaborative partnership between the patient, provider, and health department
- Public health professionals have a responsibility to educate and inform patients about the best treatment options using evidence-based recommendations so that patients can make informed decisions
  - Treatment regimen is tailored to each patient
- Patient decisions regarding medical care should be respected
- Comprehensive efforts to balance public health obligations with patient autonomy are essential

NEXT STEPS

- Clear guidelines for the management of MDR-TB during pregnancy are needed
- More research is needed on the safety and efficacy of second- and third-line drugs during pregnancy and breastfeeding
- More public health professionals need to publish their experiences and anecdotal data

ACKNOWLEDGEMENTS

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