Isolated and In Labor:
Managing active respiratory tuberculosis in pregnancy and across the U.S.-Mexico border

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Introduction

Scripps Mercy Family Medicine Program is based in a community hospital approximately 9 miles from the U.S.-Mexico border. The program serves a largely Latino underserved community. With such proximity to the border, it is evident to witness the impact that binational movement has on public health, particularly considering TB is endemic in Mexico. Though overall prevalence of TB is improving in both countries, in 2018, the incidence of respiratory TB in San Diego County was 6.8 per 100,000 compared to 57 per 100,000 in Baja California. Tijuana, Mexico has one of the highest rates of TB (approximately 3 times the national average) than other border cities.

Patient Presentation

29 year old G4P2 presented to Maternal Child Health Center for routine prenatal care at 26+6 weeks gestational age. Previous prenatal care was obtained in Mexico.

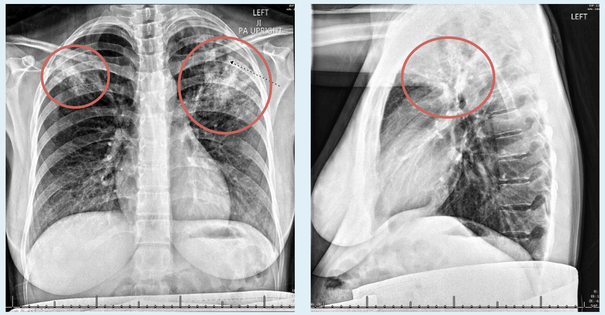
1/29/18
Presented to clinic for her first OB visit. Quantiferon Gold was drawn, which resulted positive.

3/3/18
Was lost to follow up, but returned for routine OB visit. No symptoms reported. Was encouraged to get chest x-ray that day, but left without it getting done.

4/10/18
Returned for OB visit and did not report any current symptoms (but per patient hindsight did report cough 2-3 months ago). Exam was notable for poor weight gain (net +3 lbs.). Chest x-ray done this day showed bilateral upper lobe infiltrates, one of which (left) appeared cavitary. Multiple attempts were made to contact the patient. San Diego Department of Public Health was notified.

4/17/18
Presented for OB visit now at 38+0 weeks gestational age. Was referred immediately to Scripps Hospital Chula Vista emergency room for TB evaluation.

Hospital Course



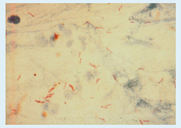
- **Hospital Day 1**
  - Presented to the ED: physical exam was unremarkable—including lungs/chest—but repeat CXR was consistent with prior (pictured above).
  - *M. tuberculosis* PCR resulted positive.
  - Admitted and placed in airborne isolation.
- **Hospital Day 2**
  - First AFB smear resulted positive (4+) without drug resistance to rifampin.
  - ID and Pulmonology services were consulted, and patient was started on rifampin (RIF), isoniazid (INH), ethambutol (EMB), and pyridoxine. Pyrazinamide (PZA) was held off at this time.
- **Hospital Day 3**
  - Perinatology service was consulted, who recommended expectant management of third trimester pregnancy. Induction not indicated given the risk of vertical transmission is low. Intermittent fetal heart rate monitoring.
- **Hospital Days 4-6**
  - Patient remains stable, asymptomatic, and tolerating medications. No symptoms of labor.
- **Hospital Day 7**
  - Patient starts feeling uterine contractions at 02:30. She progressed to complete and delivered a viable male infant weighing 3000 grams via NSVD at 03:11 at 38+6 WGA inside a negative pressure room.
  - Infant was taken immediately to Scripps Chula Vista Level 2 Nursery for evaluation and then transferred to Rady Children's Hospital to start INH and RIF, per Neonatology and Pediatric ID recommendations. Placenta was sent to pathology, which measured 10th %ile in growth.
- **Hospital Day 8-16**
  - PZA was added to antibiotic regimen.
  - Routine postpartum course. Patient remained in isolation and encouraged to breast pump, however patient declined and preferred to formula feed.
  - Repeat AFB smears starting at day 14 still positive (2+).
- **Hospital Day 17**
  - Cleared by San Diego Dept. of Public Health to safely discharge home to Tijuana under these conditions: must live alone, follow up with Mexican Dept. of Public Health in 2 weeks; adhere to RIPE therapy daily, and wear mask in public at all times.

Learning Objectives

- Define the diagnosis of TB and therapeutic management in pregnancy.
- Review RIPE therapy, particularly how these medications affect pregnancy and breastfeeding.
- Identify necessary public health efforts and hospital protocols for successful infectious disease control.

Diagnosis of Pulmonary Tuberculosis

- Chest XR
- Microbiological testing
  - Sputum AFB smear
    - Recommended 3 serial specimens in order to improve sensitivity.
  - Mycobacterial culture (gold standard)
    - Both liquid and solid cultures are recommended.
  - Induced sputum sample is recommended over bronchoscopic sampling.
- Molecular testing: NAAT
  - Include rapid molecular drug susceptibility testing for RIF +/- INH.
- Urine antigen detection in patients with co-morbid HIV infection.



(Top) Ziehl-Neelsen sputum stain.
(Bottom) Fluorochrome sputum stain.

RIPE Treatment and Safety

	Rifampin*	Isoniazid	Pyrazinamide	Ethambutol
Length of Treatment	Daily for 2 months, then daily or twice weekly for 7 months	Daily for 2 months, then daily or twice weekly for 7 month	Daily for 2 months	Daily for 2 months
Pregnancy Category	C Possible risk of dose-dependent teratogenicity based on animal data	C Possible risk of fetal harm at twice the recommended dose	C Controversial evidence regarding theoretical teratogenicity.	B
Breastfeeding Safety	No known risk Drug concentrations in breast milk are not sufficient to treat infants *May cause orange discoloration of milk			
Other Considerations	Consider Vitamin K supplementation	Vitamin B6 supplementation; obtain baseline LFTs +/- at 4 weeks postpartum		May discontinue after 1 month if RIF + INH susceptibilities are in favor

Discussion

1. Pregnancy presents a substantial opportunity to screen, detect, and treat TB.
2. A Quantiferon Gold or PPD should be performed on all pregnant women at high risk of TB.
3. Positive screens should be evaluated with a chest x-ray and microbiological testing if there is high suspicion.
4. Early treatment is key. In general, RIPE therapy is safe in pregnancy, although PZA may be held until postpartum.
5. RIPE medications do not cross the placenta very well and are not found in high concentrations in breast milk, thus proving relatively safe for the fetus and infant. For this reason, infants at risk must be treated individually.
6. Isolation during the antepartum and postpartum phases is recommended for infection control of aerosol transmission.

Public Health Impact

- TB is a reportable communicable disease that prompts quick management to minimize risk of contagion.
- In the immediate postpartum period, mother and infant should be separated and evaluated individually, but need not stay separated during the outpatient treatment phase.
- Patients with active TB are recommended to stay at home as much as possible and wear a (simple face) mask to decrease the risk of airborne transmission during the treatment period.
- Labs (both inpatient and outpatient) are required to report positive *M. tuberculosis* tests to the provider and to the department of public health.
- Departments of public health subsequently notify potential contacts and investigate the effect of infection on the community.
- Departments of public health also have access to screening for contacts as well as resources for treatment adherence for patients.
- A cross-border collaboration of public health agencies is crucial in order to avoid interruption of treatment and ensure public safety from the spread of infection.

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