Renal TB Transplant

Lana Yamba, MD, MPH, CCRC

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TB Intensive
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Lana Yamba, MD, MPH, CCRC has the following disclosures to make:

- No conflict of interests
- No relevant financial relationships with any commercial companies pertaining to this educational activity

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Tuberculosis and Hansen's Disease Program/Binational Tuberculosis Program

Texas Department of State Health Services, Region 11

Case Presentation

Case presentation

- 51-year-old Male received a kidney transplant 10/19/ 2023 for ESRD 2/2 DM.
- Living Donor: the wife is the donor.
- He was admitted in Jan 2024 because of fever, night sweat since 11/2023, headache and SOB 12/23 and January 2024. *("Pt was always thinking these s/s were related to his kidney transplant").*
- Renal biopsy done 1/9/2024: Granulomatous inflammation with langhans giant cells and AFB stain but no evidence of rejection.
- Positive culture from a bronchial lavage done 1/12/2024, PCR positive for MTB and no rifampin resistance found. T-Spot: Positive 2/1/2024
- Pan-susceptible to all drugs including moxifloxacin, Molecular testing showed no rifampin resistance.
- PMH: ESRD, T2DM, HIV neg, HTN, recurrent UTI pre-transplant
- Denied prior TB exposure.
- Rifabutin, INH, PZE, EMB started on 1/10/2024 at the hospital.

Source of patient's TB

- Source of patient's TB was unclear but appeared to have manifested clinically within the initial month following transplantation. The donor may be his source as the most likely option.
- Expanded contact investigation: to find the source case for patient's TB. The few people around him had negative TB testing.
- Genotype to help identify a possible source.
- Reactivation: Secondary source was seeded from the lungs. If that was the etiology of renal TB, that meant disseminated disease and other sites, including the CNS, could have been involved.

Imaging & Labs

- CT of chest: 1/10/2024 showing extensive bilateral tree-in-bud and nodular opacities throughout all lobes.
- CXR 1/22/2024: Bilateral miliary nodules most consistent with active TB
- Renal biopsy (1/9/2024) consistent with active TB of the kidney but no evidence of rejection
- Baseline labs: WBC, Hb, AST, ALT wnl, Plt 73, normal total bilirubin; baseline crea: 1.1-1.2 but increasing serum creatinine from 1.10 1/21/2024 to 1.6 on 2/1/2024.
- Early sign rejection:
  - After the diagnosis of TB, anti-rejection medication was held 1/16/2024 and the dose of prednisone decreased to 10 mg daily.
  - Patient with evidence of early rejection on labs from 2/1/2024 with increased creatinine to 1.6
- TB in a transplant patient can be effectively treated even with the immuno-suppression. *Do not stop it!*

Evaluation CNS TB and other TB site

- Extent of disease was unclear.
- H/o of encephalopathy/headaches when hospitalized on 1/2/2024
- MRI with contrast to exclude CNS disease as management will be significantly different, both for the TB therapy and the need for higher doses of steroids.
- MRI Brain with contrast 3/4/2024: Over 20 punctuate foci of enhancement in the cerebral hemispheres and cerebellum. Finding concerning for TB.

Evaluation for Genito-Urinary TB

- Urine AFB results: AFB smear and culture were negative on 3/5/2024.
- UA with micro: Pyuria in the absence of detected bacterial infection could have represented TB infection in the kidney; sterile pyuria was a common finding in renal TB.
- The patient was already on high-dose steroids, which should have lessened the risk of ureteral stricture

Assessment

- Disseminated TB involving the transplanted kidney and bilateral lungs; including CNS and Genito-Urinary TB.

Management

- Patient was placed back on anti-rejection therapy.
- Rifabutin does cause enhanced metabolism/clearance of anti-rejection drugs but much less so than rifampin; these drug interactions are manageable.
- Patient was continuously evaluated for a need of an increased dose of his anti-rejection drugs.
- MRI results showed numerous small punctate lesions scattered throughout the cerebellum consistent with TB.
- Regimen was augmented to:
  - Rifabutin 300 mg daily
  - INH 300 mg daily
  - PZA 2000 mg daily
  - Moxifloxacin 400 mg daily
  - Linezolid 600 mg bid, later was changed to 600mg daily
  - Cellcept, Prograff doses were adjusted, Prednisone 50 mg then taper

Monitor drug levels

- Serum drugs levels:
  - INH (peak 4.0)
  - PZA (peak 51.07)
  - Rifabutin (0.15) were all acceptable and within range.
- Rifabutin peak is at 3 – 4 hours post dose, and the peak level was drawn at 2 hours. It was 0.15. Normal range is usually 0.3-0.9 at 3 – 4 hours post dose.
- We also had a chance to do LNZ through and Peak at one point, it was within range.
- Monitor with serum drug levels to allow adjustment of the anti-rejection regimen if needed.

Wife TB evaluation

- The patient's wife was evaluated for both Pulmonary and Genitourinary TB.
- She was asymptomatic, denied any TB exposure.
- T-Spot negative
- CXR 2/16/24 Negative for TB
- Bacteriology (2/18/24): Sputum AFB smear and culture negative
- Urine AFB smear and culture done 2/18 negative
- Labs were within normal range.
- TB disease/infection was r/o.

Pre-transplant evaluation

CXR pre-transplant

- It is possible he had subclinical TB at time of transplant.
  - 7/14/2023: CXR read as normal.
  - 10/7/2024 -day prior to transplant- CXR-patchy linear stranding of volume loss in the LUL suggestive of post-inflammatory residuum, no change from 7/14/2023.
- CT shows 15 x 13 cm consolidation in the LUL which makes reactivation or progression of subclinical TB in the lungs as a possibility versus the kidney as the site.
- Wife TSPOT was negative
- No documentation whether the patient was screened for TB.

Monitoring complications

Patient has had many hospitalizations for:

- Allograft rejection/worsening of creatinine: post transplant crea never really went below 1
  - 2nd Renal biopsy done 3/6/24 with ACR IA Banff rejection, IF 2+ kappa and trace lambda; pending SPEP, UPEP, IFE and free light chains.
  - Management:
    - Change PZA to three times/week dosing until creatinine improving and < ~ 2.0
    - Drug level of tacrolimus, mycophenalate.
- Recurrent MDR Klebsiella urinary tract infection (was impacting pt recovery)
- Hematologic complications:
  - The decrease in WBC(as low as 1,200): had been on granulocyte stimulating factor.
  - The decrease platelet count
  - Rifabutin was not the cause of his hematological problems nor was the linezolid. These problems were either related to underlying disease issues or other medical problems.

Update on patient's progress

- TB evaluation:
  - Pt is now 6 months into treatment:
    - RBT 300mg daily
    - INH 300mg daily
    - Moxi 400 mg daily
    - PZA 2000mg daily (close monitoring if crea >2.5, GFR<35mg/l, change to renal dosing 3x/week)
  - He remains on maintenance dose of Cyclosporin, Mycophenolate, and Prednisone 5mg daily.
  - Pt is stable, gaining weight, lab now done every 2 weeks
  - CXR:
    - 2 month-CXR in 3/2024 showed slight improvement
    - S/C for a 6month-CXR this month

Update on patient's progress

Labs of 7/03/2024

- CMP: LFTs (AST 36, ALT 39) are improving compared to labs (6/21/24). Crea 2.09, GFR 38
- CBC looks better: WBC at 3.5, low but it's still stable, Plts at 97 and Hb 12.7
- UA: positive nitrites, many bacteria. The methodist will manage that.

. Plan: Continue PZA for at last 6 months then D/C PZA and continue the moxifloxacin, rifabutin and INH to complete the year of treatment . If he continues to do well , we will re-evaluate to determine if moxifloxacin can also be stopped.

Key Take Aways

- Whenever we have miliary TB in a compromised patients they need MRI brain with contrast!
- You need to know the extent of the disease and use a strong bactericidal regimen for the TB.
- TB in a transplant patient can be effectively treated even with the immuno-suppression. Do not stop it!
- Request patients' information pre-transplant - to make sure their TB status pre-transplant is known (TB screening donor and recipient).

Thank you!