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Medical Education Research Forum 2020

5-2020

RIPE Treatment Failure in a Patient with Mycobacterium tuberculosis sepsis

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Recommended Citation

Dabaja, Mohamad and Herc, Erica, "RIPE Treatment Failure in a Patient with Mycobacterium tuberculosis sepsis" (2020). *Case Reports*. 102.

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Learning Objectives

1. Recognize TB sepsis
2. Evaluate for optimization of antimicrobial therapy in the setting of TB sepsis with concern for absorption issues

Case Presentation

A 36-year old Guatemalan male with diabetes mellitus presented with night sweats, productive cough, worsening dyspnea, and chills for the past 3 weeks. The patient had a remote history being incarcerated and moved to the United States from Guatemala 12 years ago, with his last visit being one year prior to current presentation.

At presentation, patient was febrile, hypotensive, tachycardic, tachypneic, and was found to have acute respiratory failure with an elevated lactate. A CT chest was obtained showing bilateral consolidative changes predominantly in the upper lobes and scattered nodule-like opacities with central cavitation. Initial infectious work-up revealed a positive sputum MTB PCR. Rifampin resistance was not detected. In addition, he was found to have co-infection with Influenza B. The patient was started on rifampin, isoniazid, pyrazinamide, ethambutol (RIPE), and oseltamivir.

While on therapy, the patient remained hypotensive, febrile, and hypoxic, requiring multiple transfers to the ICU in which he was placed on a ventilator and vasopressors. Adrenal insufficiency work up was negative. After 24 days of therapy, he continued to be hemodynamically unstable despite a trial of broad spectrum antibiotics and his MTB culture returning pansusceptible to all TB therapy. Repeat Chest CT demonstrated previous findings without significant improvement. Repeat AFB smear after 33 days of treatment still yielded many acid-fast bacteria.

This prompted concern for absorption issues. HIV antigen/antibody combo and RNA were obtained with a negative result. Testing for rifampin and isoniazid blood levels requires a send out lab and takes several days to result. Instead, acetaminophen (APAP) levels were done to get a better idea about absorption. After multiple scheduled doses, testing showed APAP blood levels <10.0 ug/ml, consistent with poor absorption.

Patient's therapy was switched to IV linezolid, IV moxifloxacin, IV rifampin, and oral pyrazinamide, and isoniazid were continued. After 11 days into this treatment the patient no longer required supplemental oxygen, was afebrile for >72hrs, and his blood pressure improved.

Photos

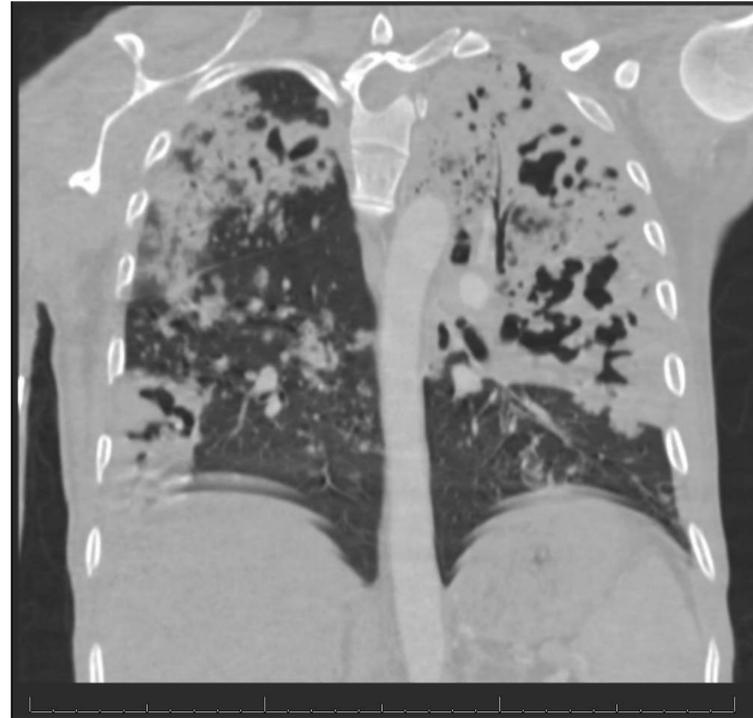


Figure 1. 02/08/2020 (Day of presentation) Multifocal consolidations and cavitary lesions



Figure 2. 3/25/2020 (46 days later) Improvement in the multifocal airspace process and cavitary regions. Note how the left normal lung parenchyma is more visible now.

Discussion

Traditional MTB therapy, RIPE, is the mainstay of treatment and typically results in a high cure rates with high bioavailability (BA) ranging from 89-100%. One consideration in patients who have significant MTB disease burden and do not have clinical improvement despite optimized MTB therapy is oral malabsorption of anti-TB drugs.

Blood levels of isoniazid and rifampin typically take several days to result. A patient with severe disease cannot afford to delay care as it can lead to a poor prognosis with MTB septic shock having an in-hospital mortality of 79.2%(5). Instead, a surrogate using acetaminophen levels (BA 85-98%) after scheduled dosing would be a reasonable alternative. A patient who comes in with a sepsis picture secondary to MTB may need to be converted to intravenous therapy due to decreased gut absorption. The decision to implement this practice early in the treatment algorithm to ensure proper drug blood levels is an important clinical consideration.

Conclusion

Though RIPE therapy is known to be the mainstay of therapy for MTB, it may be less efficacious in a patient with sepsis and gut malabsorption issues. The swift decision to convert from an oral to intravenous anti-TB regimen after assessing absorption with acetaminophen levels is something a clinician should consider in their medical decision making.

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