Week 6 Collaboration Café

Diego Aguado-Ramirez, a 56-year-old male with a history of type 2 diabetes and tuberculosis (TB), presents to the clinic for a follow-up on laboratory results obtained three days prior. Approximately six weeks ago, he was diagnosed with TB following exposure to his cousin, who had active TB and was living with him. He was initiated on the standard four-drug intensive regimen comprising isoniazid, rifampin, pyrazinamide, and ethambutol. Three weeks into the treatment, Diego reported experiencing right upper quadrant pain, nausea, vomiting, fatigue, and loss of appetite over the preceding week. Laboratory tests conducted at that time revealed liver function tests (LFTs) elevated to four times the upper normal limit, leading to a diagnosis of hepatitis. Consequently, all four anti-TB medications were discontinued due to concerns of hepatotoxicity. After a three-week cessation of these medications, repeat labs drawn three days ago showed LFTs reduced to less than twice the upper normal limit, and his blood glucose levels were within the normal range. Currently, Diego's physical examination is unremarkable, and the plan is to reinitiate TB treatment, introducing one drug at a time. His current medication regimen includes metformin (Glucophage) 500 mg taken orally twice daily for the management of type 2 diabetes.

According to the "Official American Thoracic Society/Centers for Disease Control and Prevention/Infectious Diseases Society of America Clinical Practice Guidelines: Treatment of Drug-Susceptible Tuberculosis," the standard initial treatment for drug-susceptible TB involves a two-month intensive phase with a four-drug regimen: isoniazid, rifampin, pyrazinamide, and ethambutol. This is followed by a continuation phase of isoniazid and rifampin for an additional four months. However, in cases where hepatotoxicity occurs, as evidenced by significant elevations in LFTs, the guidelines recommend discontinuing the offending agents and reintroducing them sequentially once liver function has improved. The reintroduction process typically starts with the least hepatotoxic drug, gradually adding others while closely monitoring liver function and clinical symptoms. This approach aims to identify the specific agent responsible for hepatotoxicity and to safely continue effective TB treatment.

Given Diego's recent hepatotoxicity likely induced by the anti-TB medications, it is prudent to reintroduce the drugs cautiously. The reintroduction should commence with ethambutol, as it is considered the least hepatotoxic among the first-line TB drugs. Following a period of tolerance, rifampin can be added, given its relatively lower hepatotoxic potential compared to isoniazid and pyrazinamide. Isoniazid would follow, with pyrazinamide reintroduced last, if at all, due to its higher association with hepatotoxicity. Throughout this process, vigilant monitoring of liver function tests and clinical symptoms is essential to promptly identify any recurrence of hepatotoxicity. This stepwise approach allows for the identification of the specific drug responsible for the liver injury while ensuring that effective TB treatment is maintained.

Several considerations are pertinent to Diego's ongoing care:

1. Alcohol Use: Although Diego reports no alcohol consumption, it is important to confirm this, as alcohol use can exacerbate hepatotoxicity.
2. Viral Hepatitis Screening: Assessing for underlying viral hepatitis is crucial, as co- infection can increase the risk of liver injury during TB treatment.