Editorial: Tuberculosis in Post-Liver Transplant Recipients—A Road Less Traveled!

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In the last decade, despite improvement in survival after liver transplantation (LT), the scourge of infections remains troublesome with significant associated mortality (7-88%).¹ Post-LT patients are immunosuppressed and are predisposed to flares of latent or incident infections.¹ Post-LT patients in India, a high burden country for tuberculosis (TB)² and liver disease-related immune dysfunction, are predisposed to acquire tuberculous infections.³ While treatment of evident infection through sputum testing, chest radiogram, or molecular testing in a symptomatic patient is clear, a controversy exists regarding the latent TB infections in India.⁴,⁵ Although guidelines recommend testing, with interferon-gamma release assays (IGRAs), the adherence to such guidance remains suboptimal (up to 30%) worldwide.⁴,⁵ There are several reasons for nonadherence—lack of data on the rate of pre-transplant latent infections, presumed low prevalence of reactivation of latent infections post-LT,² unclear interpretation of tuberculin test, cost of IGRA assays, potential hepatotoxicity, and risk of resistance due to isoniazid use in pre-LT patients, and lack of data to show a reduced incidence of TB infections with latent TB treatment.⁶ Nonetheless, radiological evidence of past TB, definite contact with the smear-positive patient, proof of active/past TB in the donor, and recognition of tubercular granulomas in explant liver histopathology are expert recommendations for the treatment of latent/active TB in post-LT patients.⁵

In this issue of Journal of Gastrointestinal Infections (JGI), TRS et al⁹ reported a series of patients with tubercular ascites (n = 6, 75% of all patients with ascites) after 2 to 4 months post-LT, with a low-serum-ascites albumin gradient (SAAG; n = 6), high-protein (n = 6), lymphocytic ascites (n = 6) with high adenosine deaminase (>40U/L, n = 2), Gene-Xpert or polymerase chain reaction positivity (n = 4), and response to medical treatment in the absence of vascular obstruction or other confounding factors. A high prevalence of TB in post-LT patients with ascites is quite alarming, although not entirely unexpected. Although it correlates with infections as the commonest cause of post-transplant ascites,⁷ the likelihood of persistent ascites (beyond 4 weeks of LT) rather than recent-onset ascites suggests reactivation of latent TB. Interestingly, all patients with tubercular ascites had the refractory ascites (RA) in the pre-transplant period. Patients with RA (high SAAG) have markedly deranged portal hemodynamics that is likely to persist for a few months after transplant.⁸ Therefore, it is pertinent to demonstrate the resolution of ascites and drop in SAAG after transplant to establish TB as the sole cause of ascites. Moreover, one should also exclude mixed tubercular and cirrhotic ascites in a pre-transplant setting.

Active TB should be treated as an immunocompetent person in post-LT recipients.⁴ Due to their superior sterilizing activity, rifamycin-based regimens are recommended to treat TB in the post-transplant setting by American Society of Transplantation guidelines. Rifamycins are cytochrome-P450 isoenzyme inducers and reduce plasma concentrations of tacrolimus, sirolimus, everolimus, and cyclosporine. Thus, frequent immunosuppressant dose optimization and concentration monitoring are required while patients are on treatment. If costs and drug interactions are a significant concern, levofloxacin-based therapies may also be used.

Unfortunately, the mortality of TB-infected post-LT patients remains high (30-100%).⁵ There is an unmet need to explore the prevalence, risk factors, and outcomes of TB in the post-LT recipients.

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