

Tuberculosis: Public Health Aspects

Dear Editor,

Re: Tuberculosis Post-Liver Transplantation: A Rare but Complicated Disease

This interesting case of post-liver transplantation tuberculosis (TB) was published in the March 2005 issue of the *Annals*.¹ Despite the difficult situation, the authors were able to institute TB treatment and achieve a successful outcome.

The authors have, however, made some statements which could lead to public health misconceptions:

(1) The term “standard 6-month anti-TB therapy” should not be loosely used. Standard 6-month anti-TB therapy refers specifically to regimens which include rifampicin, isoniazid and pyrazinamide in the first 2 months (initial intensive phase) of treatment, followed by rifampicin and isoniazid in the next 4 months (continuation phase). This distinction has to be made because this standard 6-month (short-course) chemotherapy regimen has been shown in British Medical Research Council (BMRC) trials to achieve the best outcomes in terms of cure and relapse prevention² and is the recommended first-line regimen in developed countries.^{3,4} In special circumstances where drug toxicity (as in this case) or drug resistance are genuine concerns, TB regimens have to be tailored for individual patients, but these regimens should not be called “standard” regimens. The readership should not be misled into believing that 2 months of rifampicin, isoniazid, ethambutol and ofloxacin followed by 4 months of ethambutol and isoniazid is a “standard 6-month” regimen.

(2) It was stated in the paper that “Screening for latent TB is generally performed by tuberculin skin testing or screening chest X-ray”. Over the last 100 years, the tuberculin skin test (TST) has been the only practical means to diagnose latent TB infection (LTBI) (more recently, new gamma-interferon assays for detecting latent TB infection have been introduced, and they may replace the TST in future). The chest x-ray is not used to screen for LTBI, its use in this situation being to exclude active pulmonary TB in a person with a positive TST in whom treatment of LTBI is considered.

(3) It was also stated, “However, tuberculin testing for latent TB infection is not applicable in our local population as it lacks sensitivity to distinguish between BCG-vaccinated and TB infected populations.” The basis upon which this statement was made is unclear. Firstly, we believe the authors may have mistyped “sensitivity” instead of “specificity”, i.e., the TST is not specific enough to

distinguish between BCG and TB. More serious is their assertion that the TST “is not applicable in our local population”. In Singapore, we have found that, although BCG vaccination/re-vaccination can interfere with the interpretation of the TST, it does not render the test useless. Indeed, in schoolchildren, we found that meaningful thresholds of TST which indicate higher risk of breakdown to active disease could be determined.⁴ In addition, in close contacts, we were able to utilise the TST meaningfully despite our BCG-vaccinated population.⁵ In fact, using the TST to identify candidates for treatment of LTBI among close contacts of infectious TB cases has been a key TB control strategy in Singapore’s TB control programme since 1998, and this initiative, we believe, played a vital role in reducing our once stagnant TB rate from 57 per 100,000 population in 1998 to 39 per 100,000 in 2004.

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Dear Editor,

Re: Authors' Reply

We welcome the constructive comments regarding our article on tuberculosis post-liver transplant.¹

We agree that "standard therapy" usually consists of 2 months of rifampicin, isoniazid and pyrazinamide, followed by 4 months of rifampicin and isoniazid. The initial therapy was 4 drugs in our patients and had to be modified subsequently owing to toxicity. Our therapy is thus not standard in a general sense but standard initial therapy for someone with a compromised liver status.

We also agree that screening for latent TB infection (LTBI) generally consists of a TB skin test and a chest x-ray (CXR), not a CXR alone. However, historically, CXR has been used and there are little data on the evidence for TB skin tests in highly immunocompromised patients, especially immediately post transplant.² In fact, 1 recent study conducted in 547 liver transplant recipients in Spain suggested that radiological features of prior TB infection on CXR was more accurate than the tuberculin skin test (TST) in diagnosing LTBI.³

Lastly, we feel that the utility of the TST in countries where BCG vaccination is highly prevalent is still a controversial subject. The quoted Singapore study showed that a positive TST may be a risk factor for future tuberculosis

reactivation; yet even with a 16-mm threshold, sensitivity was only 55%.

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