Top Ten Things Rheumatologists Should (And Might Not) Know About Tuberculosis

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In our tuberculosis (TB) clinic we see large numbers of patients referred by rheumatologists. These referrals are mostly for those being considered for immunosuppression with anti-tumour necrosis factor (TNF) alpha inhibitor therapy or other agents. To a lesser extent, we see patients with active TB involving bones and joints. The following is a list of the top ten issues we feel important to share with our rheumatology colleagues that have been gleaned from our experience over the past decade.

1. Tuberculin Skin Test

The Tuberculin Skin Test (TST) is a highly sensitive test in immunocompetent individuals and is our preferred test for the diagnosis of latent TB infection in such patients. However, it must be planted, read, and recorded correctly as false positive and negative results can have serious consequences. A threshold of ≥ 5 mm induration is considered positive for latent TB infection among patients being considered for, or taking anti-TNF alpha inhibitors. In RA patients taking traditional non-steroidal disease-modifying antirheumatic drugs (DMARDs), such as methotrexate, the threshold is 10 mm.

2. Interferon Gamma Release Assays

TST specificity can be reduced in individuals who have received Bacillus Calmette–Guérin (BCG) vaccination, especially if received after five years of age. Interferon Gamma Release Assays (IGRAs) may be used for such individuals, as they are more specific than the TST.

3. Positive TSTs

BCG vaccination within the first year of life is generally not responsible for positive TSTs in adulthood. Given that the vast majority of countries give this vaccine just after birth, prior vaccination only occasionally enters into our interpretation of a positive TST.

4. Test Sensitivity

Sensitivity of the TST is reduced in immunocompromised individuals. The T-SPOT.TB (IGRA) test is more sensitive than the TST but may not available in many areas. Like the TST, sensitivity of the Quantiferon Gold (IGRA) test is suboptimal in immunosuppressed patients.

5. Latent TB Infection

There is no gold standard test to diagnose latent TB infection. Discordant results between the TST and IGRAs must be interpreted in the context of epidemiological and clinical risk-factors for TB.

6. Risk Factors

The 5 mm TST cutoff to diagnose latent TB infection in patients being considered for anti-TNF alpha therapy may be problematic: many patients being tested will have no TB risk factors, but nonetheless may be required to be tested prior to receiving anti-TNF alpha therapy. Testing patients with no risk factors is generally discouraged because the positive predictive value is extremely low (*i.e.*, the vast majority of positive TSTs would not represent latent TB infection). A recent decision analysis supports this approach, although we recognize that there are medical-legal issues that drive testing in this population.

7. Corticosteroids

Corticosteroids also pose an increased risk of TB reactivation. A dose equivalent to 15 mg of prednisone for more than one month should be considered a risk for TB reactivation. Where possible, such patients should be tested for latent TB infection before starting immunosuppressive therapy.

8. Initiating Treatment for Latent TB Infection

Isoniazid (5mg/kg up to a maximum of 300 mg per day) for nine months or rifampin (10mg/kg up to a maximum of

600 mg per day) for four months are appropriate treatments for latent TB infection. Both require regular monitoring of liver function tests, especially in patients who are concurrently receiving hepatotoxic medications. It is critically important to first rule out active TB before initiating treatment for latent TB infection.

9. Therapeutic Concerns

As a potent inducer of cytochrome P450, rifampin therapy will significantly increase corticosteroid metabolism and could induce an Addisonian crisis in some patients on long-term corticosteroids.

10. Accurate Diagnosis

Consider TB as a cause of chronic progressive monoarticular arthritis in the appropriate setting (*e.g.*, in a foreign-born patient from a TB-endemic country). Sending fluid and/or tissue for mycobacterial culture can be very helpful to establish the diagnosis.

Suggested Readings

1. Canadian Thoracic Society and the Public Health Agency of Canada. Canadian Tuberculosis Standards, 7th Edition. Available at: *http://www.respiratoryguidelines.ca/tb-standards-2013.*
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3. Diel R, Goletti D, Ferrara G, et al. Interferon-γ release assays for the diagnosis of latent Mycobacterium tuberculosis infection: a systematic review and meta-analysis. Eur Respir J 2011; 37(1):88-99.
4. Hazlewood GS, Naimark D, Gardam M, et al. Prophylaxis for latent tuberculosis infection prior to anti-TNF therapy in low-risk elderly patients with rheumatoid arthritis: A decision analysis. Arthritis Care Res (Hoboken) 2013; 65(11):1722-31.

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