Incompatibility of Tuberculin Skin Test and Interferon Gamma Release Assay; LTBE or not?

Tüberkülın Deri Testi ve İnterferon Gama Salınım Testleri Uyumsuzluğu; LTBE mi Değil mi?

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Question: While the 22-month-old boy was being evaluated because of contact with a patient (grandfather) with bacillary tuberculosis, the TST test was found to be 16 mm. The baby still has no complaints and seems healthy. In the clinical and laboratory evaluation of the baby, active tuberculosis (TB) was not detected and single drug therapy (INH prophylaxis) was recommended for latent tuberculosis infection (LTBI). However, the family later voluntarily had a Quantiferon test done in a private laboratory and the result was reported as negative. Should this child, whose records are found to have a BCG vaccine, be given single-drug therapy (INH prophylaxis) prophylaxis for LTBI?

Answer (Beyhan Bülbül, MD; Mustafa Hacımustafaoğlu, MD)

Introduction and general information: First of all, it will be useful to review some information that can form the basis of the answer. Tuberculosis infection (Latent tuberculosis infection; LTBE) is defined as the development of acquired bacteria-induced immune recognition (T-cell response) in an individual after infected with tuberculous bacteria (Mycobacterium tuberculosis) without clinical or laboratory signs of disease. LTBI is diagnosed in a child who is clinically and radiologically completely normal, with the positivity of tuberculin skin test (TST) or interferon gamma release assays (IGRAs), which indicate that the bacteria has been taken and a cellular response has developed against it. In order for these tests to give positive results, a period of 8-10 weeks (roughly 3 months) should pass from the entry of the M. tuberculosis bacteria into the body.

A child with LTBI appears completely normal and has no clinical or radiological findings. However, they carry the risk of developing clinical TB disease (pulmonary TB or Extrapulmonary TB) in the future. The person with LTBI may develop TB disease later in life; 5-15% in adults, and may be higher if there are additional risk factors. The risk is higher in children (eg 50% in babies <1 year old, 25% between 1-2 years old). About half of them develop TB disease within the first 2 years. In a recent study conducted in the USA and Canada, it was shown that active TB disease developed in 4% of adults (>15 years) within the first 3 months aftercontact of an infectious TB case. Therefore, the possible high risk requires preventive treatment in individuals with LTBI.

Evaluation of TST positivity and positive TST criteria may differ from country to country. In this regard, the criteria of classical scientific sources (mostly American) may be slightly different from the criteria accepted in Turkey. Also, in TST evaluation, positive TST criteria may differ with various factors.
In general, there is no recommendation for routine testing of both tests for the same patient to diagnose LTBI. According to the American Thoracic Society (ATS) and the Infectious Diseases Society of America (IDSA), no testing is indicated if a patient has a low risk of TB infection and a low risk of progression in a developing disease. If a test has been done and if it is positive, it is necessary to repeat it with another test (TST or IGRAs), and if both test results are positive, LTBI should be considered. In Turkey, the recommended test under 5 years of age is TST, and confirmation of the patient with IGRAs is not routinely recommended.

Within the framework of these general approaches, the answer to the question is:

1. First of all, this 22-month-old baby is in the high-risk group both for the development of TB disease (as well as the development of disseminated TB disease) because she is <4 years old, and for being in close contact with an infectious adult.

2. According to the American Academy of Pediatrics (AAP), in children <2 years old, and according to the Turkish Ministry of Health guidelines and ATS/IDSA in children <5 years old, TST is a preferred diagnostic method for LTBI over IGRAs. Therefore, TST is the diagnostic approach to be preferred in this patient. Checking the result with a second test in a risky age group for which TST is recommended is not recommended routinely in the world and in our country. Therefore, IGRAs are not recommended for such a high-risk patient who has undergone TST.

3. Actually, according to classical information; if there is >5 mm TST response in children who have close contact with an infectious adult, and >10 mm in children aged <4 years, even if there is no history of contact (independent of BCG vaccine), it is recommended to consider the diagnosis of LTBI and give prophylactic treatment.

References


