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TEACHING FILES (GRAND ROUNDS)

NEGATIVE QUANTIFERON TB GOLD TEST IN A LADY WITH POSITIVE TUBERCULIN SKIN TEST – HOW TO INTERPRET?

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Clinical Problem:
A 27-year-old married female presented in 2025 with history of scanty menses, anxiousness towards conceiving and past contact history of tuberculosis (TB). She was nulliparous and has been trying to conceive for 1 year. Seven years ago, patient's sister was treated for cervical lymph node tuberculosis (TB) with anti-tubercular therapy (ATT) for 6 months. Subsequently, the patient had cough and was suspected to have pulmonary TB radiologically (reports not available) and took ATT for 3 months in 2018. On presentation to us in 2025, examination findings were normal. Her tuberculin skin test was positive 3 cm. Chest X-ray was normal. USG abdomen and pelvis showed a right ovarian dermoid cyst and left terminal hydrosalpinx. QuantiFERON TB Interferon-gamma release assay (IGRA) test was negative.

How to interpret QuantiFERON TB Gold (QFT) test in this patient? Should this lady be treated for latent TB?

Discussion:

TB infection occurs when you breathe in TB bacteria while you are exposed to someone who has active TB in their lungs. Usually, the body's defences control the infection, but the bacteria can remain in the body for years in an inactive or 'latent' state. Previous vaccination with the Bacillus Calmette-Guerin (BCG) vaccine, has been linked to a false positive tuberculin skin test (TST) due to antigens causing cross-reactivity.[1] When BCG is administered during infancy, its impact on the TST is generally minimal, particularly a decade or more after vaccination. However, BCG given after infancy tends to result in more frequent, longer-lasting, and stronger TST responses[2] These findings highlight the importance of considering a history of BCG vaccination when evaluating TST results, regardless of how much time has passed since the vaccine was given.[2] TST cannot differentiate between *Mycobacterium Tuberculosis* (MTB) infection and other Nontuberculous mycobacterial (NTM) infections caused by different mycobacterial strains.[3] Common NTM infections are caused by *Mycobacterium marinum* and *fortuitum* with *M. marinum* more likely to cause skin infections while aquatic environments are a potential source of contact with *M. marinum* and *fortuitum*.[3] The QFT is a blood test that measures the body's immune response to TB bacteria. An interferon gamma release assay (IGRA) has higher specificity and uses antigens not present in BCG, hence fewer chances of cross-reactivity, which may be used instead of the TST in determining whether to treat or not to treat. It detects the release of interferon-gamma (IFN-γ) by T-cells when exposed to TB antigens. If the IFN- γ response to mitogen minus the response to nil antigen is $\leq$1.5 IU/mL, the test is interpreted as indeterminate. If $\geq$1.5 with tuberculin response between 15% and 30%, MTB infection is likely if risk is identified but unlikely for low risk. With $\geq$30%, MTB infection is likely.[4] Some non-tuberculous mycobacteria (NTM) species, such as *Mycobacterium kansasii, Mycobacterium marinum, and Mycobacterium szulgai*, contain genes encoding early secretory antigenic target-6 (ESAT-6), culture filtrate protein-10 (CFP-10) and TB7.[5] These TB-specific genes can be detected by the QFT. As a result, individuals infected with these NTM species may also yield positive IGRA results.[5] However, clinical observations suggest that positive IGRA findings in M. kansasii infections are relatively uncommon.[5] In patients with positive MT and negative IGRA, active TB is not suspected and the positive MT could be due to either previous BCG vaccine or past NTM infection. A chest radiograph is also essential in excluding diagnosis of TB. Additionally, if tested too early after being exposed to TB bacteria, the test might not detect the infection, leading to a false negative.[6] Therefore, waiting at least 6 to 8 weeks after potential exposure before getting tested ensures more reliable results.[6] Patients with positive MT and positive IGRA should be medically evaluated for TB disease. More tests, such as a chest radiograph, are needed to rule out TB disease. Negative MT and positive IGRA can occur either due to an error in preparing the purified protein derivative (PPD), improper administration of the intradermal injection, or incorrect interpretation of results.[7] Immunosuppressed individuals may also yield false-negative results.[7] Thus, in our patient, the negative QFT is suggestive that the patient does not have latent TB and the positive TST in the patient could be due to exposure to NTM or previous BCG vaccination. The patient was not treated for latent TB and just advised a close follow up.

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References:

1. Montane Jaime LK, Akspaka PE, Vuma S, Justiz-Vaillant AA. A healthy patient with positive mantoux test but negative quantiferon Gold assay and no evidence of risk factors - to treat or not to treat? IDCases. 2019 Oct 15;18:e00658.
2. Farhat M, Greenaway C, Pai M, Menzies D. False-positive tuberculin skin tests: what is the absolute effect of BCG and non-tuberculous mycobacteria? Int J Tuberc Lung Dis. 2006 Nov;10(11):1192-1204.
3. Nontuberculous Mycobacterium (NTM) Infection in Aquatic Workers with Purified Protein Derivative (PPD) and Gold QuantiFERON Tests. Available at URL: https://digitalcommons.unmc.edu/cgi/viewcontent.cgi?article=1136&context=gmerj. Last updated in December 2020.
4. Guidelines for Using the QuantiFERON®-TB Test for Diagnosing Latent Mycobacterium tuberculosis Infection. Available at URL: https://www.cdc.gov/mmwr/preview/mmwrhtml/rr5202a2.htm. Accessed on 24 June 2025.
5. Sato R, Nagai H, Matsui H, Kawabe Y, Takeda K, Kawashima M, et. al. Interferon-gamma release assays in patients with Mycobacterium kansasii pulmonary infection: A retrospective survey. J Infect. 2016 Jun;72(6):706-712.
6. IGRA TB TEST. Available at URL: https://www.testing.com/tests/igra-tb-test/#:~:text=Are%20test%20results%20accurate?,after%20the%20exposure%20to%20TB. Last updated on 19 December 2023.
7. Chao CC, Lin CJ, Chen HS, Lee TL. Negative Mantoux test in a patient with definite pulmonary and ocular tuberculosis. Taiwan J Ophthalmol. 2015 Oct-Dec;5(4):182-186.