



A False Sense of Security: Disseminated Tuberculosis Despite a Negative QuantiFERON-TB Gold Test



Maya Marshall¹, Sneha Vaddadi MD², Jacqueline Lee MD², Mithu Molla MD²

¹UC Davis School of Medicine, ²Department of Internal Medicine, University of California, Davis, Sacramento CA

INTRODUCTION

- Over a quarter of the world's population is infected with Tuberculosis (TB)¹ and 5-10% of cases of latent TB infection (LTBI) progress to active TB in an individual's lifetime.^{2,3}
- Though screening tests are widely utilized for diagnosing LTBI, they are far from perfect.
- We describe a case of disseminated TB in a patient treated with aggressive immunosuppression after a false-negative QuantiFERON-TB Gold test.

CASE PRESENTATION

- 29-year-old Filipino gentleman with a history of Crohn's disease presented to emergency department (ED) with two weeks of productive cough and fever.

Past Medical History:

- Patient was born in the Philippines and emigrated to the US in 2015.
- In 2017, the patient had a positive PPD and was prescribed isoniazid for 9 months, but only completed two months of therapy.
- In 2020, he was diagnosed with Crohn's disease and started on an oral steroid taper.
- One month after initiating his steroid taper, his QuantiFERON-TB Gold in-tube (QFT-GIT) test returned negative and he was started on vedolizumab for Crohn's disease.
- Subsequently, he transitioned to infliximab, with his last infusion one month prior to presentation to ED.

Physical Exam:

- On exam, he had normal vital signs with good oxygen saturation at 98% on room air. He appeared thin and chronically ill. His cardiac exam was normal, and he had diminished breath sounds bilaterally. His abdomen was soft and nontender, and his extremities were without cyanosis, clubbing, or edema.

CASE PRESENTATION CONTINUED

Labs/Imaging

- His initial white blood cell count was elevated at 17 K/Cmm.
- Chest X-ray, followed by CT scan, revealed a right middle lobe cavitory lesion and right pleural effusion for which he was placed on empiric antibiotics for community-acquired pneumonia.
- Sputum cultures returned positive for acid fast bacilli and for TB on polymerase chain reaction.
- Antibiotics were discontinued and he was started on rifampin, isoniazid, pyrazinamide, and ethambutol (RIPE) therapy.



Figure 1. Chest x-ray and CT scan showing RML cavitory lesions and right-sided pleural effusion.

- He had an extended hospital course complicated by TB dissemination to the spleen and bone marrow as well as hepatotoxicity from RIPE therapy.
- Eventually, he was discharged on a 3-drug TB regimen (isoniazid, rifampin, ethambutol) with plans for outpatient infectious disease follow-up.

DISCUSSION

- The importance of ruling out mycobacterial diseases prior to starting anti-TNF therapy is universally accepted.⁴
- In recent years, the QFT-GIT test has been recognized and widely applied to the early diagnosis and monitoring of TB.⁵ However, several factors can lead to a false-negative QFT-GIT test, including smoking status, hormone therapy, immunological inhibition, site of infection, and diabetes.⁶
- Our patient likely had a false-negative QFT-GIT test secondary to steroid immunosuppression.
- An individualized approach based on patient factors and epidemiologic risk should be utilized when screening for LTBI.
- Dual-testing with TB skin testing and QFT-GIT prior to starting biologic agents has been proposed to improve sensitivity of screening.⁷

CONCLUSION

- A higher index of suspicion and dual-testing for LTBI can help to avoid a false sense of security when considering aggressive immunosuppression in select patients.

REFERENCES

1. Cohen A, Mathiasen VD, Schön T, Wejse C. The global prevalence of latent tuberculosis: a systematic review and meta-analysis. *Eur Respir J*. 2019;54(3):1900655. Published 2019 Sep 12. doi:10.1183/13993003.00655-2019
2. Diel R et al. Predictive value of interferon-gamma release assays and tuberculin skin testing for progression from latent TB infection to disease state: A meta-analysis. *Chest*. 2012;142:63-75.
3. World Health Organization. Global tuberculosis report 2022. Geneva: World Health Organization; 2022. Accessed November 30, 2022. <https://www.who.int/publications/i/item/9789240061729>.
4. Lichtenstein, Gary R MD, FACC1; Loftus, Edward V MD, FACC2; Isaacs, Kim L MD, PhD, FACC3; Regueiro, Miguel D MD, FACC4; Gerson, Lauren B MD, MSc, MACG (GRADE Methodologist)5,†; Sands, Bruce E MD, MS, FACC6. ACG Clinical Guideline: Management of Crohn's Disease in Adults. *American Journal of Gastroenterology*: April 2018 - Volume 113 - Issue 4 - p 481-517 doi: 10.1038/ajg.2018.27
5. Chen G, et al. Clinical application of QuantiFERON-TB Gold in-tube in the diagnosis and treatment of tuberculosis. *Eur J Clin Microbiol Infect Dis*. 2020;39:607-612.
6. Mari Yamasue et al. Factors associated with false negative interferon-gamma release assay results in patients with tuberculosis: A systematic review with meta-analysis. *Sci Rep*. 2020;10:1607
7. Winthrop KL, Weinblatt ME, Daley CL You can't always get what you want, but if you try sometimes (with two tests—TST and IGRA—for tuberculosis) you get what you need. *Annals of the Rheumatic Diseases* 2012;71:1757-1760.