

中文題目：QuantiFERON-TB testing 在施用 anti-TNF alpha treatment 病人之應用

英文題目：The application of QuantiFERON-TB testing in patients receiving anti-TNF alpha treatment

作者：郭力元<sup>1</sup>、李振豪<sup>1,2</sup>

服務單位：大林慈濟醫院內科部<sup>1</sup>，大林慈濟醫院腎臟內科<sup>2</sup>

## Introduction

Tumor necrosis factor-alpha inhibitors offer an important targeted strategy in a number of inflammatory conditions, including rheumatoid arthritis, the seronegative spondyloarthropathies, psoriasis, and inflammatory bowel disease. However, all TNF-alpha inhibitors increase the risk of tuberculosis (Winthrop, 2020). A prospective study reported the incidence-rate ratio compared with patients who were receiving etanercept was 3.1 (95% CI 1.0-9.5) for infliximab and 4.2 (95% CI 1.4-12.4) for adalimumab (Dixon WG, 2010).

Many of the TB cases associated with TNF-alpha inhibitors likely represent reactivation of latent tuberculosis infection (LTBI), hence the screening for LTBI before initiating therapy has been routinely performed. Also, in areas of low TB prevalence, newly acquired infection contributed with a minority of TNF-alpha inhibitor-associated cases.

The current recommendations of screening include a review of history focused on prior TB exposure, a physical examination, a tuberculin skin test (TST) and/or interferon-gamma release assay (IGRA) (Gerald H. Mazurek, 2010). In Taiwan, because most patients have received Bacille Calmette-Guérin (BCG) vaccine, IGRA is the preferred test.

In this poster, I would like to present a case who was positive in QuantiFERON-TB testing but declined treatment for latent tuberculosis and eventually developed extrapulmonary tuberculosis. The current strategy and reasoning would be reviewed.

## Case presentation

This 59-year-old man was admitted for decreased appetite and abdominal fullness for one month. He had a history of rheumatoid arthritis and CKD stage III.

Regarding his rheumatoid arthritis, it was poorly controlled until he started with

etanercept 4 years ago which significantly eased his discomforts. Before the initiation of treatment, his QuantiFERON-TB testing showed positive but he declined antituberculous agents as he worried about possible side effects such as hepatitis.

On examination, his vitals were stable, but he had positive shifting dullness and dull on percussion of his left lower lung fields. Abdominal sonography showed ascites and pleural effusion in the left chest cavity. His investigation was significant for hypercalcemia and acute kidney injury on chronic kidney disease. He underwent paracentesis and left thoracocentesis. The ascites had a low serum-ascites albumin gradient and the cytology didn't find malignant cells. The pleural effusion was exudative according to Light's criteria, lymphocyte dominant (82%) without malignant cells. The initial AFS was negative in both investigations. However, the sputum culture isolated Mycobacterium. His etanercept treatment was held and he received standard antituberculous agents uneventfully. His renal function, hypercalcemia, ascites and pleural effusion got resolved one month after anti-TB therapy.

### **Discussion**

It has been reported that Many of the TB cases associated with TNF-alpha inhibitors likely represent reactivation of LTBI. In Taiwan, the IGRA has been adapted as a routine investigation before the initiation of TNF-alpha inhibitors. The advantage of the IGRA is that it does not give false-positive results because of prior BCG vaccination and does not require follow-up visit to complete the testing process. However, the interpretation of serial IGRA is complicated by frequent conversions and spontaneous reversions. Also, false-negative results are more likely in immunocompromised individuals.

In general, although in healthy individuals with a low likelihood of M. tuberculosis infection and low likelihood of progression to active TB if infected, a single positive IGRA result should not be taken as reliable evidence, the CDC recommends treatment of LTBI for all patients planning to take a TNF-alpha inhibitor who have a positive IGRA and no evidence of active tuberculosis (Dixon WG, 2010).

The evidence of discontinuation of TNF-alpha inhibitor when initiation of anti-TB therapy was undetermined. The available small phase I trial has shown that in HIV patients it is safe to use etanercept while patient is receiving antituberculous therapy (Wallis RS, 2004). However, these reports involved a different patient population, so further prospective studies are required. It has been reported that discontinuation of a

TNF-alpha inhibitor in the setting of active TB may be associated with a paradoxical worsening of TB, which may be explained by an immune reconstitution inflammatory syndrome. In such cases, the use of glucocorticoids may be beneficial (Hsu DC, 2016).

### **Conclusion**

For patients who are planning to take a TNF-alpha inhibitors, they should receive antituberculous therapy if they have a positive IGRA. The lack of antituberculous therapy could lead to reactivation of latent tuberculosis infection.

### **Bibliography**

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