QuantiFERON TB Gold Test: the new standard for screening of latent tuberculosis in patients with rheumatoid arthritis?

Petros Efthimiou, Sunita Sood

Ann Rheum Dis 2007;**66**:276. doi: 10.1136/ard.2006.061184

We read with interest the report by Ponce de Leon *et al.*¹ where the authors argued that tuberculin skin testing (TST) may not be an optimal test for the diagnosis of latent tuberculosis infection (LTBI) in patients with rheumatoid arthritis. We would like to contribute to these findings, based on our clinical experience with a new screening tool called the QuantiFERON TB-Gold (QFT-G) Test.

Although screening policies vary considerably between countries, it is generally recommended that all patients with rheumatoid arthritis should undergo screening for *Mycobacterium tuberculosis* latent infection before the initiation of treatment with biological agents, especially tumour necrosis factor (TNF) α inhibitors.² Patients with rheumatoid arthritis may not be able to produce an adequate delayed-type hypersensitivity reaction to tuberculin because of their deficient cell-mediated immunity.³⁻⁵

QFT-G is a whole-blood, antigen-specific test that uses synthetic peptides representing two *M. tuberculosis* proteins, early secretory antigenic target-6 and culture filtrate protein-10. After incubation for 16–24 h, the amount of interferon γ secreted by monocytes in response to these antigens is measured.^{6,7} T-SPOT.TB, not yet available in the US, is another antigen-specific blood test that uses the enzyme-linked immunospot assay technique.

These new tests may be applicable to patients with rheumatoid arthritis, where false-negative TST can have adverse consequences in patients treated with TNF inhibitors. We have identified two patients in our rheumatology clinic (Division of Allergy, Immunology and Rheumatology, New Jersey Medical School, Newark, New Jersey, USA) who were TST negative but were subsequently diagnosed with LTBI by the QFT-G Test.

Patient 1 is a 73-year-old black woman who presented with symmetric bilateral synovitis of the metacarpophalangeal joints, was seropositive for rheumatoid factor and antinuclear antibodies, with radiographic evidence of inflammatory erosive arthropathy. She was diagnosed with rheumatoid arthritis and had a negative TST. She was an incomplete responder to methotrexate and corticosteroids, and the decision was made to initiate anti-TNF treatment. Repeat TST was again negative 2 months after the first testing. However, she tested positive for QTB-G and is currently completing a 9-month isoniazid/vitamin B₆ course for LTBI. A confirmatory chest radiography showed apical pleural thickening and upper lobe fibrosis, consistent with a history of primary tuberculosis.

Patient 2 is a 61-year-old black man with severe erosive rheumatoid arthritis, who screened negative by TST before immunosuppressive treatment. A preoperative chest radiograph showed mild interstitial scarring, without any pleural abnormality. He responded partially to methotrexate and became a

candidate for anti-TNF treatment. Positive QTB-G testing prompted the initiation of a 9-month isoniazid/vitamin B₆ course.

In summary, QTB-G may be a more sensitive screening tool for LTBI in patients with rheumatoid arthritis with impaired delayed-type hypersensitivity response to tuberculin. Additional benefits include the following: a single patient visit to draw the blood sample, results can be available within 24 h, it is not subject to reader bias and, most importantly, it is not affected by prior BCG (bacille Calmette–Guérin) vaccination.⁷ However, the test is not widely available yet, and careful studies comparing it to the TST are needed to validate our findings in the population with rheumatoid arthritis.

Authors' affiliations

Petros Efthimiou, Division of Allergy, Immunology, and Rheumatology, Department of Medicine, New Jersey Medical School, UMDNJ, Newark, New Jersey, USA

Sunita Sood, Department of Medicine, New Jersey Medical School, UMDNJ, Newark, New Jersey, USA

Competing interests: None.

Correspondence to: Dr Petros Efthimiou, Division of Allergy, Immunology and Rheumatology, Department of Medicine, New Jersey Medical School, UMDNJ, 90 Bergen Street, DOC#4700, Newark, NJ 07103, USA; efthimpv@umdnj.edu

Accepted 2 November 2006

Published Online First 24 November 2006

REFERENCES

- 1 Ponce de Leon D, Acevedo-Vasquez E, Sanchez-Torres A, Cucho M, Alfaro J, Perich R, *et al.* Attenuated response to purified protein derivative in patients with rheumatoid arthritis: study in a population with a high prevalence of tuberculosis. *Ann Rheum Dis* 2005;**64**:1360–1.
- 2 Wolfe F, Michaud K, Anderson J, Urbansky K. Tuberculosis infection in patients with rheumatoid arthritis and the effect of infliximab therapy. *Arthritis Rheum* 2004;**50**:372–9.
- 3 Nizam S, Emery P. Attenuated response to purified protein derivative in patients with rheumatoid arthritis. *Ann Rheum Dis* 2006;**65**:980.
- 4 Emery P, Panayi G, Symmons D, Brown G. Mechanisms of depressed delayed-type hypersensitivity in rheumatoid arthritis: the role of protein energy malnutrition. *Ann Rheum Dis* 1984;**43**:430–4.
- 5 Emery P, Panayi GS, Nouri AM. Interleukin-2 reverses deficient cell-mediated immune responses in rheumatoid arthritis. *Clin Exp Immunol* 1984;**57**:123–9.
- 6 Mori T, Sakatani M, Yamagishi F, Takashima T, Kawabe Y, Nagao K, *et al.* Specific detection of tuberculosis infection: an interferon-gamma-based assay using new antigens. *Am J Respir Crit Care Med* 2004;**170**:59–64.
- 7 Centre for Disease Control and Prevention. TB Elimination-QuantiFERON-TB Gold Test, 2006. www.cdc.gov/tb.

Abbreviations: LTBI, latent tuberculosis infection; QFT-G, QuantiFERON TB-Gold; TNF, tumour necrosis factor; TST, tuberculin skin testing