Title: The performance of flow cytometry in the diagnosis of latent tuberculosis infection in patients under treatment with anti-TNFα and other biological agents

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Body: Introduction: Detection of IFN-γ synthesis in the cytoplasm of activated CD4+ T cells by flow cytometry [intracellular cytokine flow cytometry (ICCFC)] is a new method to diagnose tuberculosis (TB) infection. The aim of this study is to investigate the performance of Mantoux, Quantiferon Gold In-tube (QFN-G-IT) and ICCFC in patients with collagen vascular diseases who are on treatment with biological agents, including anti-TNFα. Methods: Mantoux, QFN-G-IT and ICCFC were performed in 54 medically immunosuppressed patients and in a cohort of immunocompetent individuals consisting of a group of 39 close contacts with an index case of TB. Results: In patients under anti-TNFα treatment, 28/54 (52%) were ICCFC ESAT-6 (+), compared with QFN-G-IT (+) who were 3.7% (p<0.0001), and Mantoux positive who were 15% (p<0.0001). Additionally, 35/54 (65%) were ICCFC PPD (+) (p<0.0001 in comparison with QFN-G-IT (+) and p<0.0001 in comparison with Mantoux positive). In close contacts, 27 were ICCFC ESAT (+) (69%) in comparison with QFN-G-IT (+) who were 41% (p <0.02). 29 were ICCFC PPD (+) (74%) (p=0.0047 vs QFN-G-IT (+)). However, there was no statistical difference between ICCFC and Mantoux. ICCFC indeterminate results were observed in the immunosuppressed (5/54) and in 5 out of 39 immunocompetent patients (p=ns). Conclusion: The performance of ICCFC for the diagnosis of TB infection is better than QFN-G-IT and Mantoux in patients under immunosuppressive treatment and in immunocompetent close contacts. The robustness of ICCFC test is not substantially affected by the administration of immunosuppressive treatment.