ANALYSIS OF THE UTILITY OF QUANTIFERON-TB GOLD IN TUBE AND MEASUREMENT OF IFNγ RELEASE BY PERIPHERAL MONONUCLEAR CELLS IN RESPONSE TO DIFFERENT MYCOBACTERIUM ANTIGEN IN THE WORK-UP OF PATIENTS WITH UVEITIS

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BACKGROUND

Mycobacterium tuberculosis infects up to 30 % of the population worldwide (Dye C et al.,1999). Intraocular tuberculosis can be due to direct infection of retinal cells by mycobacterium, but immune response against the infectious agent might also contribute to the development of certain form of tuberculous uveitis (Knox DL.,1994). Intraocular tuberculosis diagnosis remains challenging and is at risk of being misdiagnosed so that immunosuppressive agent may be erroneously given to patients with presumed non-infectious uveitis.
During the past century, the tuberculin skin test (TST) has been the gold standard for the detection of latent and active tuberculosis. Recently Interferon gamma release in vitro assays (QuantiFERON TB-Gold in Tube and T-Spot) has been approved by The Food and Drugs administration as a diagnostic tool for active and latent tuberculosis.

AIM OF THE PROJECT

In this work, we analyzed the utility of interferon gamma release assays in the work-up of patients with uveitis. To achieve this goal we performed QuantiFERON^{TM})-TB Gold in-tube and TST in a series of patients with uveitis. The production of IFN-γ by mononuclear cells in response to purified proteins derivatives (PPD) and other mycobacterium antigen like native heparin-binding hemagglutinin (nHBHA) has been measured by ELISA.

METHODS

In our preliminary previous prospective study, patients with uveitis of unknown origin suspected to be related to tuberculosis or to autoimmune disease were recruited and underwent a standard diagnosis procedure, including TST, chest Xray and a QuantiFERON-Gold. IFN gamma release were also analyzed in response to other mycobacterium antigen (nHBHA).

PRELIMINARY RESULTS

Among the recruited forty six patients, twenty six were TST and QuantiFERON-TB negative. When we analysed the IFN gamma release in response to PPD in the negative group, 88,5% did not respond to PPD as expected. Similarly

the IFN gamma's response to HBHA was negative in 92% of the cases. In 15 patients QuantiFERON-TB Gold and TST were positive. We performed the same analyse in response of purified protein derivative stimulation (PPD) stimulation in the positive group. There was 80% positive results, and only 47% in response to HBHA. Only one patient was negative for both IFN relase in response to PPD and HBHA. Discordant results between QuantiFERON-TB Gold and TST were observed in 5 patients (13%). Among them, only one had a positive QuantiFERON-TB Gold and a negative TST. Thus four patients had a positive TST and a negative QuantiFERON-TB Gold. In this discordant group, no patients exhibited any release of IFN in response to PPD or HBHA, which strongly argue in favor of false positive.

CONCLUSION

Analysis of the IFNγ production in response to PPD and nHBHA seems to add important information in both concordant and discordant group.

The risk of false negative TST is low in nonendemic group. This leads us to suggest the two step strategy. In immuno-competent patients, if the TST is negative, we can consider that the patient has not latent tuberculosis. So we do not need to do the QuantiFERON. On the other hand, if the TST is positive, the results should be confirmed by the QuantiFERON. Concerning immuno-compromised patients, both tests have to be done in order to better evaluate tuberculosis immunity.

When we analyzed the response to HBHA in the positive group, we found two different groups (HBHA positive and HBHA negative).

The aims of our current project are to study if those two groups show some clinical differences in the tuberculosis state or in the ophthalmologic presentation. We also aim to evaluate the role of other cytokines which can take part to this specific immune response against tuberculosis.

A larger sample of patients should be included in order to make definitive conclusions.

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