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In vitro cytokine response to tuberculosis

C Prabha, KSA Khadar *and SD Das
Tuberculosis Research Centre, Chetpet,
Chennai-600 031, India.
*Madras Medical College, Chennai-600 003, India.
e-mail-sulochanadas@rediffmail.com <mailto:e-mail-sulochanadas@rediffmail.com>

ABSTRACT

The outcome of any infectious disease is mainly dependent upon the interplay of the cytokines. These cytokines are grouped into two: Type land Type 2 cytokines secreted by Th1 and Th2 cells that contribute to the pro-inflammatory and anti-inflammatory responses respectively.

INTRODUCTION

Analysis of cytokine pattern in tuberculosis is essential to understand the basic immune response to tuberculosis. Such studies are more important and relevant in our country due to the endemicity of the disease and variation in the Mantoux status of the population. But very few studies based on the cytokine profile in tuberculosis have been reported from India.

OBJECTIVE

The principle of this study was to evaluate the *in vitro* cytokine responses to mycobacterial antigens of the susceptible and the resistant host exposed to infection with *Mycobacterium tuberculosis.*

SUBJECTS AND METHODS

The study population of 75 subjects was grouped as follows 1) Mantoux positive subjects with no disease as control 2) Mantoux positive subjects with newly detected, active pulmonary tuberculosis 3) Mantoux positive subjects with pleural tuberculosis, representing localized extrapulmonary tuberculosis. Each group comprises of 25 subjects and all the diseased subjects were sputum smear positive. Peripheral blood mononuclear cells (PBMCs) were isolated and cultured with 10mg/ml of PPD, culture filtrate (CF) and heat killed of *M. tuberculosis* (MTB). The CF and

heat killed preparations were made from H37Rv strain of *M. tuberculosis.* The culture supernatants were collected after 48 hours. The levels of IFN-**g,** IL-12, TNF-**a** and IL-4 were assessed in the supernatants using ELISA.

RESULTS AND DISCUSSION

PBMCs of the control subjects showed a significant increase in IFN-**g** response to PPD and MTB and TNF-**a** response to PPD. The IL-12 and IL-4 levels did not show any variation. This shows that the healthy infected individuals mounted a better cytokine response, suggestive of Th1, protective type against PPD and MTB antigens than for the secretary antigens (CF) of mycobacteria. The PBMCs of pleural tuberculosis subjects did not show any difference in their cytokine response with respect to *in vitro* antigen stimulation. This could be due to the sequestration of antigen-specific, reactive cells to the site of infection: pleural cavity and hence inaccessible through peripheral blood sampling. This is evident from our previous reports where we have demonstrated the higher CD4+/CD8+ ratio in the pleural fluid and the antigen specific cytokine response of pleural fluid cells 1, 2. Interestingly, PBMCs of active tuberculosis subjects exhibited significant increase of IFN-**g,** TNF-**a** and IL-12 together with the significant decrease in IL-4 levels against PPD, suggesting a definite Th1 response. The antigens CF and MTB had triggered significant IFN-**g** secretion but had negative effect on the secretion of IL-12. The levels of TNF-**a** and IL-4 were significantly decreased in CF but not in MTB stimulated supernatants. The probable cause may be the recruitment of TNF-**a** to the site of granuloma formation and the utilization of IL-12 for the IFN-**g** production. These observations together suggest that the cytokine response in early phase of tuberculosis disease is of Th1 type accompanied by the reduction in Th2 cytokine response. Subsequently, the inability of the host to maintain the Th1 type response and the pathogenic strategies adapted by the tubercle bacilli, together may contribute to the severe outcome of the disease.

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