ABSTRACT

Background: The aim of this study was to clarify the pathogenesis of immune reconstitution inflammatory syndrome (IRIS) by examining plasma cytokine and microbial translocation biomarkers.

Methods: A post-hoc analysis of ACTG A5202 was conducted to evaluate cytokine and microbial translocation biomarkers. IRIS cases were defined by A5202 study criteria, and plasma samples were screened for cytokines (IP-10, LPS, TNF, sTNFRII, sCD14, 16s rDNA) and persistent inflammation (CSF IP-10) as part of the study design.

Results: Of 159 subjects with plasma available, 111 (70%) were considered to have experienced IRIS. High baseline levels of IP-10 and LPS were significantly associated with IRIS after adjustment for baseline CD8 count. For plasma cytokines, higher baseline IP-10 and LPS were associated with a greater risk of IRIS with associations explained by non-linear models. For markers of microbial translocation, higher baseline LPS, soluble CD14 and 16s rDNA were all associated with a greater risk of IRIS with associations explained by non-linear models.

Conclusions: Higher baseline plasma IP-10 and LPS should be considered potential biomarkers of IRIS. The results of this study support the use of non-linear models to examine the risk of IRIS in subjects randomized to antiretroviral therapies.

METHODS

1. In three linear models, to improve model generalizability, biomarkers were categorized into tertiles based on the distribution in the entire sample.
2. For each statistical model, univariable Cox models were compared, and a model using tertiles of each cytokine (IP-10, LPS, TNF, sTNFRII, sCD14, 16s rDNA) was selected for each cytokine (IP-10, LPS, TNF, sTNFRII, sCD14, 16s rDNA) in order to examine the association with IRIS after adjusting for baseline CD8 count without adjusting for baseline viral load.
3. The model was then adjusted for baseline CD8 count and viral load.

RESULTS

1. The results of the non-linear models are presented in Table 2. The model using tertiles of each cytokine (IP-10, LPS, TNF, sTNFRII, sCD14, 16s rDNA) was selected for each cytokine in order to examine the association with IRIS after adjusting for baseline CD8 count. The model was then adjusted for baseline CD8 count and viral load.

CONCLUSION

1. Higher baseline plasma IP-10 and LPS should be considered potential biomarkers of IRIS. The results of this study support the use of non-linear models to examine the risk of IRIS in subjects randomized to antiretroviral therapies.

REFERENCES


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