TITLE: IMPLICATIONS OF THE IL-17 AND IL-23 RESPONSE IN THE AGGRAVATION OF CELL LESION CAUSED BY THE YELLOW FEVER VIRUS IN THE PARENCHYMA HEPATIC IN HUMAN FATAL CASES

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ABSTRACT:

Yellow fever (YF), caused by the Yellow Fever Virus (YFV), has historically been considered one of the most dangerous infectious diseases. Reemergence events have been observed in non-endemic areas and in endemic areas with historically low YFV activity. IL-17 is the cytokine identity of the Th17 profile and it is involved in secretion of cytokines and chemokines, which will have a chemotactic effect on neutrophils, inducing recruitment, activation and migration at the site of infection. IL-23 acts by stabilizing the differentiation of Th17 cells, in addition to leading to their maturation. Several studies in human material have shown that disease progression is related to the pattern of *in situ* immune response in the liver of patients who died of severe forms of the disease but did not show the implications of the IL-17 and IL-23 in the response to aggravation of the cell damage caused by the YFV in the hepatic parenchyma in fatal cases of YF. Twenty-one human liver samples diagnosed as positive for YFV were used and others five were used as negative controls for *Flavivirus* that died from other causes and preserved the liver parenchyma. Expression of IL-17 and IL-23 *in situ* was based on the Labeled StreptAvidin Biotin Method. Statistical analysis was performed on *GraphPad Prism* 5.0 using one-way ANOVA, Tukey and Pearson's correlation, significance level of 5% ($p \leq 0.05$). Quantitative analysis of IL-17 and IL-23 in situ revealed that immunostaining was predominant in the midzonal zone of the hepatic parenchyma in fatal cases of YF compared to the control. This is the first study to highlight the implications of the IL-17 and IL-23 response on aggravation in the cell damage in the liver parenchyma in human fatal cases by the YFV. Therefore, it is worth highlighting that both cytokines can mediate the activation of M1 macrophages and consequently promote the generation of ROS that are responsible for causing cell injury and trigger the phenomenon of cell death by apoptosis and midzonal necrosis that are characteristic of the pathogenesis of the infection by YFV in humans.

Keywords: Yellow Fever, physiopathology, IL-17, IL-23.

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