Many studies have been conducted to understand the neuropathogenesis of viral encephalitis however, no experimental studies so far investigated in detail neuropathological features associated with virus infections of Picornaviridae family of virus isolated from bats in the Amazon region. The Juruaçá virus, one of these agents, has been partially characterized by other as a member of the Picornaviridae family. Although this virus did not cause cytopathic effect (CPE) in primary cultures of CNS cells, it has been associated with brain lesions with reactive gliosis in neonatal mice suggesting that this viral agent may kill neonatal mice by an exacerbated inflammatory response. The aim of this study is therefor to investigate the immune response in the CNS induced by Juruaçá virus in albino BALB/c newborn mice. To that end, we performed immunosorbsent, immunohistochemical and immunofluorescence assays, to study expression of cytokines and microglial morphological changes. Our results demonstrated the presence of viral antigens in different cell types of the CNS, and the presence of reactive microglia distributed throughout the brain and anterior spinal cord. A gradient of microglial morphological changes including frequent amoeboid shapes suggesting an intense inflammatory response was observed mainly in the cerebral cortex, but also in olfactory bulb, anterior olfactory nucleus, midbrain and forebrain near the lateral ventricle. The production of anti-inflammatory cytokine (IL-10) decreased over time, whereas pro-inflammatory cytokine (IL-6, TNF-α and IFN-γ) increased significantly from 8th day post-infection (dpi) onwards. The activation of glial cells, especially microglia, followed by subsequent production of proinflammatory cytokines coincided with the intensification of clinical signs. Taken together the results add a new piece of evidence that Juruaçá virus may kill neonate mice by inducing a fatal exacerbated inflammatory response.

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Fig. 1: Anti-Juruaçá immunolabeled sections from uninfected (A) and infected (B) mice brain on 8th dpi. Anti-IBA1 immunolabeled sections from uninfected (C) (orange arrow, long branches homeostatic microglia), and infected (D) mice at 12th dpi (white arrows, short branches activated microglia; black arrows, amoeboid phagocytic microglia).

Fig. 2: Cytokines production (A) IL-6, (B) TNF-α, (C) IFN-γ and (D) IL-10 in the CNS of albino BALB/c mice, infected with Juruaçá virus after 4th, 8th and 12th dpi. Control: uninfected group; Infected: infected group; 4: 4 dpi; 8: 8 dpi; 12: 12 dpi. Two-way ANOVA, post-test Bonferroni for Multiple Comparison, (***) = p<0.001, (**) = p<0.01 e (*) = p<0.05.