TITLE: OROPHARYNGEAL *Encephalitozoon cuniculi* PNEUMONIA

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ABSTRACT

Microsporidia are opportunistic, obligate intracellular, spore-forming fungi belonging to the phylum Microsporidia. Of the more than 1,200 species described, 16 have been identified in intestinal and systemic infections in humans. Although cases of *Encephalitozoon cuniculi* pneumonia are observed in immunocompromised individuals, especially transplant recipients, the airborne route of infection has not been demonstrated. Our objective was to demonstrate the airborne *E. cuniculi* infection as a cause of opportunistic pneumonia. C57BL male or female mice, free of specific pathogens - SPF, at 12 weeks of age, immunosuppressed with cyclophosphamide (Cy), were inoculated with $1x10^7$ spores of *E. cuniculi* oropharyngeal route, constituting the groups: Infected, Cy-Infected, Non -Infected and Cy-Not-Infected. After 15 days, the lungs were collected for histopathological analysis, phenotyping of pulmonary inflammatory cells by flow cytometry and Th1, Th2 and Th17 cytokines in plasma were measured. The infected animals (Cy-Infected and Infected) presented interstitial pneumonia characterized by perialveolar inflammatory infiltrative lesions with a predominance of lymphocytes and plasmacytes. Phenotypic analysis showed a predominance of the $CD8^+$ T lymphocyte population in the lungs. The Cy-Infected group showed an increase in the total macrophage population, in the number and percentage of interstitial macrophages and in the number of alveolar macrophages. Infection by *E. cuniculi* determined a significant increase in IFN-α in the blood of the infected groups, as well as TNF-α, IL-2, IL-4, IL-6, IL-10 were shown to be increased in relation to controls, except for IL -17. The results allowed us to conclude that the oropharyngeal route promoted pulmonary infection by *E. cuniculi* in mice treated or not with cyclophosphamide, establishing itself as a model of interstitial pneumonia.

Keywords: microsporidiosis, opportunistic pathogen, pneumonia, airborne infection, immunosuppressed.

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