ORT_08 - Analysis of coxsackievirus B5 infections in the central nervous system in Brazil: insights into molecular epidemiology and genetic diversity

Raiana Scerni Machado[1]; Francisco Gomes Neto[2]; Maria de Lourdes Aguiar Oliveira[2]; Fernanda Marcicano Burlandy[2]; Fernando Neto Tavares[3]; Edson Elias da Silva[2]; Ivanildo Pedro de Sousa Junior[2].
[1]Fundação Oswaldo Cruz (Fiocruz);
[2]Instituto Oswaldo Cruz/Fiocruz;
[3]Instituto Evandro Chagas.

Introduction: Human enteroviruses (EV) are small, non-enveloped RNA viruses belonging to the *picornaviridae* family. Although most EV infections may be asymptomatic, these viruses are associated with a wide spectrum of clinical presentations, including severe central nervous system (CNS) syndromes. Coxsackievirus B5 (CVB5) is one of the most prevalent EV-types in humans and epidemics caused by these viruses are reported annually worldwide.

Objective: The aim of the present study was to describe the molecular and epidemiological aspects of CVB5 obtained from cerebrospinal fluid and stool samples of patients with aseptic meningitis or acute flaccid paralysis and to explore the viral genetic diversity.

Methodology: Viral isolation was performed in cell lines (Hep2C and RD). Then, viral RNA was extracted from infected cells, followed by cDNA synthesis and PCR for total amplification of the gene that encodes the main viral capsid protein (VP1). Finally, the nucleotide sequencing reaction was performed based on the Sanger method. The evolutionary characteristics and geographic history of these viruses were evaluated through phylogenetic analysis.

Results: From 2005 to 2018, 57 isolates of CVB5 were identified in the scope of the Brazilian Poliomyelitis Surveillance Program. Phylogenetic analyses of VP1 sequences revealed the circulation of two CVB5 genogroups, with genogroup B circulating until 2017, further replaced by genogroup A. Network analysis based on deduced amino acid sequences showed important substitutions in residues known to play critical roles in viral host tropism, cell entry, and viral antigenicity. Amino acid substitutions were investigated using the Protein Variation Effect Analyzer (PROVEAN) tool, which revealed two deleterious substitutions: T130N and T130A. To the best of our knowledge, this is the first report to use *in silico* approaches to determine the putative impact of amino acid substitutions on the CVB5 capsid structure.

Conclusion: This work provides valuable information on CVB5 diversity associated with CNS infections, highlighting the importance to evaluate the biological impact of certain amino acids substitutions associated with epidemiological and structural analyses.

Keywords: Enterovirus; Coxsackievirus B5; Central nervous system