

New Study Identifies Likely Culprit of Mysterious AFM

By Anna DeNelsky

Enterovirus (EV) infection is likely the culprit in acute flaccid myelitis (AFM), a rare, yet serious disease responsible for partially paralyzing more than 500 children in the United States since 2014, according to a recent study (*mBio* (<https://mbio.asm.org/content/10/4/e01903-19>) 2019 10 (4): e01903-19. doi: 10.1128/mBio.01903-19).

Affecting the nervous system, specifically the gray matter of the spinal cord, AFM causes muscle and reflex weakness. In some cases, AFM can lead to partial or complete paralysis, according to Nancy Messonnier, MD (CAPT, USPHS, RET), the director of the National Center for Immunization and Respiratory Diseases at the CDC, in a press conference earlier this year, but the exact cause has alluded researchers.

Scientists at the Center for Infection and Immunity (CII) of Columbia University Mailman School of Public Health; the CDC; and the University of California, San Diego reexamined the cerebrospinal fluid (CSF) of patients with AFM for signs of EV using two methods.

First, the CSF of 14 patients with AFM and five non-AFM patients was analyzed using a tool developed by the team called VirCapSeq-VERT, which can detect any viral genetic material that is at least 60% similar to any known vertebrate virus, according to a press release from the National Institutes of Health. Enterovirus RNA was found in only one adult AFM case and one non-AFM case.

Next, CSF samples and blood serum were tested to detect antibodies to any EV (EV-A, EV-B, EV-C or EV-D) using a microchip assay, AFM-SeroChip-1, also created by the research team. Enterovirus-specific antibodies were found in the CSF of 79% (11/14) of the AFM cases. Six

of the samples were EV-D68-positive, revealing that the virus was in the central nervous system, even though it had not been detected by VirCapSeq-VERT, which can be an important indicator of the underlying cause of the disease.

“Further work is needed with larger prospective studies; nonetheless, these results take us one step closer to understanding the cause of AFM, and one step closer to developing diagnostic tools and treatments,” said co-lead investigator Nischay Mishra, PhD, an assistant professor of epidemiology at Columbia’s CII, in New York City.

Spikes in AFM cases have coincided in time and location with outbreaks of EV-D68, yet evidence of direct causality has not been found. The single-stranded, positive-sense RNA virus typically clusters in children younger than 5 years and causes mild respiratory illness with peak activity in late summer and early fall, according to Brian Currie, MD, MPH, who wrote a review article on the disease in *Infectious Disease Special Edition*.

A CDC analysis launched in response to the 2014 outbreak of EV-D68 documented 120 AFM cases from 34 states. Of the patient respiratory samples, 20% were EV-D68-positive; samples sent less than seven days before the onset of symptoms were 47% positive. However, Dr. Currie explained, the respiratory infection could not be definitively identified as a cause of AFM due to an inability to detect EV in the patients’ CSF.

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