

New evidence points to viral culprit in AFM child paralysis

August 13 2019

Scientists at the Center for Infection and Immunity (CII) at Columbia University Mailman School of Public Health, the U.S. Centers for Disease Control and Prevention (CDC), and the University of California San Diego report antibody evidence in cerebrospinal fluid (CSF) that points to enterovirus (EV) infection as a cause for acute flaccid myelitis (AFM), a disease responsible for partially paralyzing more than 560 children in the United States since 2014. Results of the study appear in the journal *mBio*.

AFM patients, upwards of 90 percent of whom are children, present with severe weakness in one or more limbs, usually within a month of a respiratory or gastrointestinal illness, leading clinicians and scientists to posit that a pathogen is behind AFM. A preliminary CDC analysis found that more than 40 percent of children with AFM had evidence of EV RNA in respiratory or fecal samples. Yet in CSF, they found EV in only 4 of 567 total confirmed cases.

In the new study, researchers reexamined the CSF of AFM patients for signs of EV using two methods. First, they analyzed CSF from 14 AFM and 5 non-AFM patients with central nervous system diseases using a specialized high throughput sequencing technology developed by CII called VirCapSeq-VERT. They found EV RNA in only one adult AFM case and one non-AFM case. Next, CSF samples and [blood serum](#) from cases and controls were tested for antibodies to EVs using high density peptide microarrays that represent the capsid proteins of all species of human EV (EV-A, EV-B, EV-C, and EV-D). Researchers found

antibodies to EV peptides in 11 of 14 AFM patients (79 percent), significantly higher than non-AFM controls (1 patient, 20 percent). Six of 14 CSF (43 percent) and 8 of 11 blood sera (73 percent) from AFM patients were immunoreactive to an EV-D68-specific peptide, whereas no controls were immunoreactive in either CSF or sera. The researchers also tested CSF from the 14 individuals with AFM and six controls for evidence of tick-borne diseases (TBD) using the TBD Serochip, a test developed by CII to simultaneously detect antibodies to eight tick-borne pathogens. They found no evidence of TBD pathogens.

"Physicians and scientists have long suspected that enteroviruses, a family of viruses responsible for polio, another paralyzing disease, are behind AFM, but there has been little evidence to support this idea," says co-lead investigator Nischay Mishra, Ph.D., assistant professor of epidemiology at CII. "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."

"Pathogen discovery has historically focused on direct detection of infectious agents. The introduction of new methods that allow us to also test for footprints of exposure will lead to new insights into infectious diseases," says co-senior author Ian Lipkin, MD, director of CII.

Provided by Columbia University's Mailman School of Public Health

Citation: New evidence points to viral culprit in AFM child paralysis (2019, August 13) retrieved 5 May 2024 from

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