Enterovirus antibodies detected in acute flaccid myelitis patients

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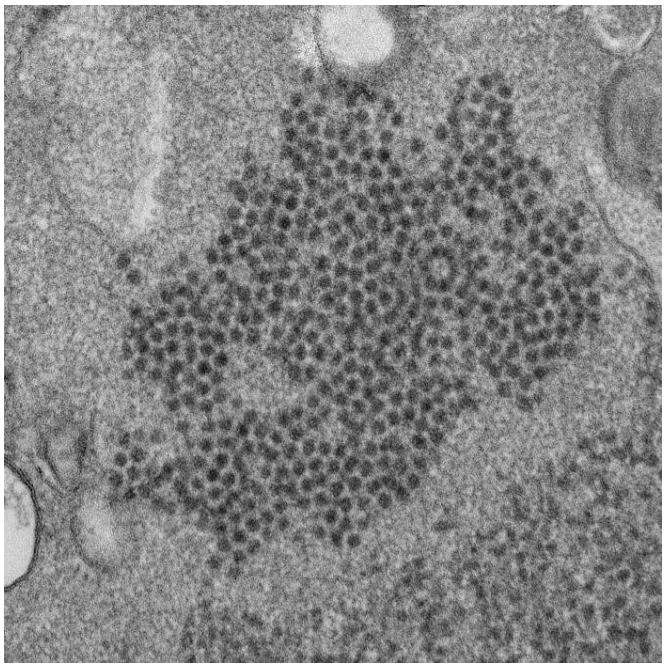

EV-D68. Credit: CDC

A new study analyzing samples from patients with and without acute flaccid myelitis (AFM) provides additional evidence for an association between the rare but often serious condition that causes muscle weakness and paralysis, and infection with non-polio enteroviruses. The National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, funded the research, which was conducted by investigators at Columbia University's Center for Infection and Immunity and investigators from the Centers for Disease Control and Prevention. The findings are reported in the online journal *mBio*.

There have been 570 confirmed cases since CDC began tracking AFM in August 2014. AFM outbreaks were reported to the CDC in 2014, 2016 and 2018. AFM affects the spinal cord and is characterized by the sudden onset of muscle weakness in one or more limbs. Spikes in AFM cases, primarily in children, have coincided in time and location with outbreaks of EV-D68 and a related enterovirus, EV-A71. Both of these viruses typically cause mild respiratory illness from which most people recover fully. Despite the epidemiological link between enterovirus circulation and AFM cases, evidence of direct causality has not been found.

The researchers first looked for direct evidence of enterovirus infection in the cerebrospinal fluid (CSF) of 13 children and one adult diagnosed with AFM in 2018. They also examined five CSF samples taken from people with other central nervous system diseases. The team used a new tool they developed called VirCapSeq-VERT, which can detect any viral genetic material that is at least 60% like that of any known vertebrate virus. They found enteroviral genetic material (EV-A71) in only the one adult AFM case and genetic material from another enterovirus (echovirus 25) in one of the non-AFM cases.

The investigators also sought indirect evidence of enterovirus infection by looking for antibodies to enteroviruses made by the immune system in response to an infection. The team developed a microchip assay, AFM-SeroChip-1, that detects the presence of antibodies generated in response to any human enterovirus (EV-A, EV-B, EV-C or EV-D) infection. Using this assay, the team tested the same 14 CSF samples from the AFM patients. They also tested CSF samples taken from 11 adults with central nervous system conditions, such as multiple sclerosis, and from 10 children with Kawasaki disease, none of whom had AFM.

EV-specific antibodies were detected in the CSF of 79% (11 of 14) of the AFM cases. Of those, six samples were positive for EV-D68, strongly indicating that enterovirus had been in the central nervous system, even though it had not been detected by VirCapSeq-VERT. None of the CSF

samples from children with Kawasaki disease had antibodies that reacted with any enterovirus.

While other etiologies of AFM continue to be investigated, this study provides further evidence that enterovirus infection may be a factor in AFM. In the absence of direct detection of a pathogen, antibody evidence of pathogen exposure within the central nervous system can be an important indicator of the underlying cause of disease, the researchers note.

More information: Nischay Mishra et al, Antibodies to Enteroviruses in Cerebrospinal Fluid of Patients with Acute Flaccid Myelitis, *mBio* (2019). DOI: 10.1128/mBio.01903-19

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