Epidemiological Alert

Acute Flaccid Myelitis associated with enterovirus D68 in the context of Acute Flaccid Paralysis surveillance

1 November 2017

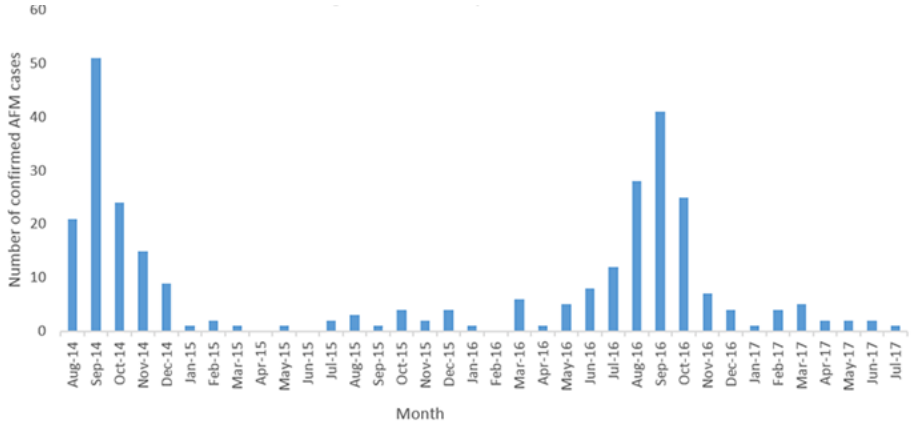
Situation summary in the Americas and other regions

Although enterovirus cases have been reported sporadically since the 1960s, it was not until August 2014 that the first outbreaks were documented in the United States (1).

Between August and December 2014, the United States Centers for Disease Control and Prevention (CDC) reported an increase in acute flaccid myelitis (AFM) associated with an outbreak of respiratory disease caused by enterovirus (EV) D68 (2,3). Among the 120 AFM cases reported in 34 states, the median age was 7.1 years (range: 4.8-12.1 years), 59% were male, and 81% had respiratory disease before the onset of neurological symptoms (4,5). Following this event, voluntary surveillance for AFM was initiated in some states, detecting sporadic cases in 2015 and a new increase in cases in 2016 (**Figure 1**). Cases were also detected in Asia, Canada, and Europe (1).

EV-D68 shares characteristics with rhinoviruses, causing mainly respiratory diseases; however, its role in the pathogenesis of neuroinvasive diseases is not clearly understood.

Figure 1. Acute flaccid myelitis cases in the United States. August 2014 – July 2017.



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In 2016, the European Center for Disease Control and Prevention (ECDC) informed that Denmark, France, the Netherlands, Spain, Sweden, and the United Kingdom reported clusters and isolated cases of severe neurological syndromes in children and adults associated with enterovirus infection among which EV-D68 was detected.[1]

In October 2017, the Argentina International Health Regulations National Focal Point reported a cluster of acute flaccid myelitis (AFM) associated with EV-D68 infection. Between epidemiological week (EW) 13 and EW 21 of 2016, 15 cases of AFM were identified in residents of the provinces of Buenos Aires (13) and Chubut (1 case) and the Autonomous City of Buenos Aires (CABA per acronym in Spanish; 1 case). All cases were in children under 15 years, since the detection occurred in the context of acute flaccid paralysis (AFP) surveillance. This event coincided with the increase in AFP cases in children under 15 years of age observed at the national level between EW 16 and EW 21 of 2016. In 6 of the 15 reported AFM cases, the Regional Poliovirus Reference Laboratory - INEI - ANLIS "Dr. Carlos G. Malbrán" detected the presence of EV-D68. Positive results were obtained in samples of nasopharyngeal aspirate and in one case the same result was also obtained in a cerebrospinal fluid (CSF) sample. In addition, human EV B and human EV C were detected in stool samples of two of the AFM cases; rhinovirus C in one case and coxsackie virus A13 in one case (7).

Considering the context of polio eradication,[2] the switch from trivalent oral polio vaccine (OPV) to the bivalent OPV since April 2016, that AFM is a type of AFP, and the need to increase knowledge about the role of enteroviruses in the epidemiology of neuroinvasive diseases, the Pan American Health Organization / World Health Organization (PAHO / WHO) reminds Member States that enterovirus is part of the differential diagnosis of AFP.

The following is a series of advice to health authorities regarding surveillance, including laboratory detection.

Recommendations for national authorities

Case management

A patient with suspected AFM shall have timely access to health services that manage neurological syndromes. The capacity to make a differential diagnosis is key for defining complementary tests, treatments to follow, guiding rehabilitation and, finally, determining the prognosis.

Surveillance

AFM surveillance associated with enteroviruses is a component of AFP surveillance and, as such, a support for polio eradication efforts. The quality of this surveillance is measured based on the usual performance indicators of AFP surveillance.

[1] European Centre for Disease Prevention and Control. Communicable disease threats report, 13-19 November 2016, week 46. Available at: https://ecdc.europa.eu/en/publications-data/communicable-disease-threats-report-13-19-november-2016-week-46

[2] The last wild poliovirus case in the Americas occurred in 1991.

The following is recommended:

- Investigate all AFP cases in children under 15 or of any age where polio[3] is suspected within 48 hours of notification.[4]
- If there is a strong presumption of AFM, a respiratory sample (necessary for the detection of enterovirus D68) should be obtained and a spinal nuclear magnetic resonance should be considered.
- Investigate any increase or cluster of AFP. In this situation, if cases have clinical characteristic of AFM, a respiratory sample in addition to the stool sample should be obtained.
- Follow up cases, 60 days after the beginning of the paralysis, to determine if they have residual paralysis.

Laboratory

Detection of poliovirus by laboratory is based on virus isolation in cell cultures (L20B and RD), the intratypic differentiation by Reverse Transcription - Polymerase Chain Reaction (RT-PCR) tests and genetic sequencing.

The detection of EV-D68 is performed by molecular techniques (RT-PCR) that can be both conventional or in real time. Per respiratory viruses other than influenza detection protocols, a generic PCR test for enterovirus (respiratory) detection followed by PCR with specific primers for EV-D68 in those samples resulting positives, is recommended.[5]

EV-D68 is a respiratory enterovirus that can be better detected in respiratory specimens. Therefore, in the presence of EV-D68, a nasopharyngeal swab sample should be collected in viral transportation medium or nasopharyngeal aspirate in physiological solution. CSF samples taken (only) by medical prescription may also be used for virus detection. Stool samples that were collected to discard poliovirus[6] may also be used, although it should be taken into account that the possibility of detecting EV-D68 from this type of sample is low.

Collection and shipping of samples

The quality of obtaining, transporting, and storing the obtained samples (whether respiratory or stool) must be guaranteed. For this purpose, it is important that laboratories ensure that the container used to transport the sample is adequate at both the central and subnational levels; the type and quantity (8 grams for feces) of the sample is sufficient; the appropriate cold chain is maintained and the sample is correctly packed and identified.

For the collection and transport of respiratory samples, it is recommended to follow the PAHO/WHO Operational Guidelines for Sentinel Severe Acute Respiratory Infection (SARI) Surveillance, 2014 (8).

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[3] Use the case definition in the PAHO/WHO scientific and technical publication No. 607 - "Poliomyelitis Eradication Field Guide". Available at: http://www.paho.org/hq/index.php?option=com_docman&task=doc_download&gid=3052&Itemid=270

[4] All AFP cases should be reported within 14 days of the onset of paralysis.

[5] For molecular detection, the implementation of the CDC protocols "Enterovirus D68 (EV-D68) 2014 outbreak strain-specific real-time reverse transcription / Polymerase chain reaction (rRT-PCR) assay instructions-Version 10/14/2014" is recommended. Available at: https://stacks.cdc.gov/view/cdc/25698

[6] The stool sample should be obtained within 14 days of the onset of paralysis.

References

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3. Aliabadi N, Messacar K, Pastula DM, *et al*. Enterovirus D68 Infection in Children with Acute Flaccid Myelitis, Colorado, USA, 2014. Emerging Infectious Diseases. 2016;22(8):1387-1394. doi:10.3201/eid2208.151949

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8. PAHO/WHO. Operational Guidelines for Sentinel Severe Acute Respiratory Infection (SARI) Surveillance, 2014. Available at: http://www.paho.org/revelac-i/wp-content/uploads/2015/10/2015-cha-operational-guidelines-sentinel-sari.pdf

9. PAHO/WHO. Scientific and technical publication No. 607 - "Poliomyelitis Eradication Field Guide". Available at: http://www.paho.org/hq/index.php?option=com_docman&task=doc_download&gid=3052&Itemid=270

Related Links

- PAHO/WHO - Poliomyelitis: http://www.paho.org/hq/index.php?option=com_content&view=article&id=7069&Itemid=1712&lang=en

- PAHO/WHO. Practical Guide: Inactivated Poliovirus Vaccine (IPV) Introduction. Washington, DC: PAHO, 2014. Available at: http://www.paho.org/hq/index.php?option=com_docman&task=doc_download&gid=27707&Itemid=270&lang=en