Acute Flaccid Myelitis (AFM): Evolution of the Case Definition and Public Health Surveillance, United States

Last updated March 7, 2019
Objectives

- Provide a history of the evolution of the case definition for AFM
- Describe the information needed to report cases suspected of having AFM to public health for case classification
Slide 2 notes

This presentation provides a history of the evolution of the case definition for AFM that is used for surveillance in the United States. Slides will also emphasize the importance of identifying and reporting cases of AFM and the information needed when reporting cases suspected of having AFM.
Investigation of AFM in the US, 2014

- On September 12, 2014 CDC was notified of 9 children in Colorado with:
  - Focal extremity weakness, cranial nerve dysfunction or both
  - MRI: multi-level gray matter lesions of the spinal cord, brainstem, or ventral nerve roots

- A large outbreak of respiratory illness due to enterovirus D-68 (EV-D68) occurred at the same time in Colorado; although a temporal association was noted, laboratory testing of cerebrospinal fluid did not provide conclusive evidence of a single pathogen as a cause

- In response to these cases, CDC launched a surveillance system to capture AFM cases nationwide
The national investigation of AFM began when CDC was notified on September 12, 2014 of 9 children in Colorado presenting with:

- Focal extremity weakness, cranial nerve dysfunction or both AND
- An MRI with gray matter lesions involving multiple segments of the spinal cord, brainstem, or ventral nerve roots

A large number of cases of respiratory illness due to enterovirus D-68, or EV-D68 were happening at the same time in Colorado. Although a temporal association was noted, laboratory testing of cerebrospinal fluid did not provide conclusive evidence of a single pathogen as a cause.

In response to these cases, CDC launched a surveillance system to capture AFM cases nationwide.
Confirmed case of AFM
• Onset of acute limb weakness, AND
• Magnetic resonance image (MRI) showing a spinal cord lesion largely restricted to gray matter, AND
• In a patient ≤21 years of age

Sept 12, 2014- CDC notified of 9 cases in CO
Sept 26, 2014 HAN to call for national reporting
To determine the extent of the problem, CDC released an official Health Advisory through the Health Alert Network on September 26, 2014 requesting that states with patients meeting the case definition for AFM report them to CDC.

The case definition proposed for national reporting included the following: A patient with acute onset of focal limb weakness AND predominant gray matter lesions on spinal MRI, in a person 21 years of age or younger, occurring on or after August 1, 2014
Evolution of the surveillance case definition for AFM

**Confirmed case** of AFM
- Onset of acute limb weakness, AND
- Magnetic resonance image (MRI) showing a spinal cord lesion largely restricted to gray matter, AND
- *In a patient ≤21 years of age*

**Probable case** of AFM
- Acute onset of focal limb weakness, AND
- Cerebrospinal fluid (CSF) with pleocytosis (white blood cell count >5 cells/mm³)

- **Sept 12, 2014**
  - CDC notified of 9 cases in CO

- **Sept 26, 2014**
  - HAN to call for national reporting

- **June 2015**
  - CSTE adopted standardized case definition

- **2014**
- **2015**
- **2016**
- **2017**
In 2015, the case definition was opened to persons of all ages to cast a wider net for cases. In addition, a probable case definition was added to include cases without MRI findings but with CSF pleocytosis. We know that MRI images can be normal in the first 72hrs after limb weakness, so this probable definition allowed us to capture cases who never got a repeat MRI. Case counts were low in 2015 despite heightened awareness after the spike in 2014.
Evolution of the surveillance case definition for AFM

**Confirmed case of AFM**
- Onset of acute limb weakness, AND
- Magnetic resonance image (MRI) showing a spinal cord lesion largely restricted to gray matter, AND
- In a patient ≤21 years of age

**Probable case of AFM**
- Acute onset of focal limb weakness, AND
- Cerebrospinal fluid (CSF) with pleocytosis (white blood cell count >5 cells/mm³)

**Changed “focal” to “flaccid” and added “for consistency, review and final case classification will be done by experts in national AFM surveillance, similar to the review required for final classification of paralytic polio cases”.

- Sept 12, 2014 CDC notified of 9 cases in CO
- Sept 26, 2014 HAN to call for national reporting
- June 2015 - CSTE adopted standardized case definition
- June 2017 - CSTE adopted revisions to case definition
After a resurgence in cases in 2016, we modified the confirmed case definition in 2017 to change “focal” to “flaccid” to specify the type of weakness. We also added that the final case classification is to be done by a national panel of experts in AFM, similar to what is done for paralytic polio cases.
Reporting of cases of suspected AFM

Clinician suspects AFM and:
- performs MRI
- obtains specimens
- completes patient summary form
When a clinician suspects a patient has AFM, an MRI should be performed and specimens collected. Clinicians should contact their state or local health department to report the suspected case of AFM as soon as possible. Specimen collection includes CSF, serum, stool and nasopharyngeal (NP) swabs which are used for both patient-specific diagnostic testing as well as to inform the overall national investigation into the etiology of AFM. Although certain tests can be performed at the local hospital or lab, all specimen types should still be sent to CDC as well for additional testing including enterovirus typing, pathogen discovery, and immune markers.
State and local health departments:
• Reviews information from suspect case
• Collects medical data*
• Coordinates specimen transport

Clinician suspects AFM and:
• performs MRI
• obtains specimens
• completes patient summary form

* Medical data includes: hospital notes, neurology and infectious disease consult notes, MRI reports and images, laboratory test results, vaccination history, and discharge summary when available.
The health department then reviews the information, works to collect the medical data, which includes hospital notes, neurology and infectious disease consult notes, MRI reports and images, laboratory test results, vaccination history, and discharge summary when available, and coordinates with CDC to send the information and samples. These data are used to classify cases and investigate potential etiologies and risk factors for AFM.
State and local health departments:
- Reviews information from suspect case
- Collects medical data*
- Coordinates specimen transport

Clinician suspects AFM and:
- Performs MRI
- Obtains specimens
- Completes patient summary form

Case determination made by expert panel
- Patient form and medical data
- MRI reports and images

* Medical data includes: hospital notes, neurology and infectious disease consult notes, MRI reports and images, laboratory test results, vaccination history, and discharge summary when available
CDC will then forward the information to the expert neurology panel which is comprised of both CDC and external experts. The panel classifies cases as either Confirmed, Probable or Not a Case. Beginning in 2017, two neurologists are assigned to review each case. If their determinations are discordant, a third is brought in for adjudication.
State and local health departments:
• Reviews information from suspect case
• Collects medical data*
• Coordinates specimen transport

Clinician suspects AFM and:
• performs MRI
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Case determination made by expert panel
• Patient form and medical data
• MRI reports and images

Case determination sent to clinician by State/Local Health Department

Case determination sent to State/Local Health Department by CDC

* Medical data includes: hospital notes, neurology and infectious disease consult notes, MRI reports and images, laboratory test results, vaccination history, and discharge summary when available
The case classification report is then forwarded to the health department, who then communicates the information to the clinician. It is important to point out that this case classification DOES NOT take the place of the medical diagnosis for the patient. It is used for public health surveillance purposes, including measuring disease burden and evaluating trends. It is NOT meant to supersede the physician’s final diagnosis for their patient.
Specimens to collect and send to CDC for testing of cases of suspected AFM

<table>
<thead>
<tr>
<th>SAMPLE</th>
<th>AMOUNT</th>
<th>TUBE TYPE</th>
<th>PROCESSING</th>
<th>STORAGE</th>
<th>SHIPPING</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSF</td>
<td>1mL (collect at same time or within 24hrs of serum)</td>
<td>Cryovial</td>
<td>Spun and CSF removed to cryovial</td>
<td>Freeze at -20°C</td>
<td>Ship on dry ice</td>
</tr>
<tr>
<td>Serum</td>
<td>≥0.4mL (collect at same time or within 24 hours of CSF)</td>
<td>Tiger/red top</td>
<td>Spun and serum removed to tiger/red top.</td>
<td>Freeze at -20°C</td>
<td>Ship on dry ice</td>
</tr>
<tr>
<td>Stool</td>
<td>≥1 gram (2 samples collected 24hrs apart)</td>
<td>Sterile container</td>
<td>n/a</td>
<td>Freeze at -20°C</td>
<td>Ship on dry ice. Rectal swabs should not be sent in place of stool.</td>
</tr>
<tr>
<td>Respiratory (NP)/</td>
<td>1ml (minimum amount)</td>
<td>n/a</td>
<td>Store in viral transport medium</td>
<td>Freeze at -20°C</td>
<td>Ship on dry ice</td>
</tr>
<tr>
<td>Oropharyngeal (OP)</td>
<td></td>
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<tr>
<td>swab</td>
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</table>
This table illustrates which samples to collect and send to CDC for AFM testing.

CSF, respiratory, and stool specimens are now all being tested for enteroviruses and results are provided within 7-10 days of receipt at CDC. Stool specimens are also tested for poliovirus and those results are also communicated within 14 days.

Remaining CSF and serum specimens will be used to inform the overall pathogenesis and potential etiologies of AFM through pathogen discovery and evaluation of immune-mediated mechanisms. Since these tests are not intended to provide patient-specific diagnoses and are not CLIA-certified, results will not be provided to the submitter. Information learned from surveillance testing will be disseminated rapidly to health departments, providers, and the general public when available.
Summary

• Clinician awareness is critical to understanding more about this rare illness
  - We need all clinicians to be vigilant for AFM
    - Urgent care/emergency room physicians, general pediatricians, family physicians, nurse practitioners, infectious disease specialists, neurologists, radiologists, infection control practitioners, etc.

• Suspected cases of AFM should be reported to the health department and specimens should be collected as soon as possible
  - Sharing of information leads to improved understanding of AFM and its pathogenesis to help inform treatment and prevention strategies
In summary, clinician awareness is critical to helping us better understand this rare illness.

That is why we need all clinicians to remain vigilant for AFM, including urgent care and emergency room physicians, general pediatricians, family physicians, nurse practitioners, infectious disease specialists, neurologists, radiologists, infection control practitioners, and others.

Suspected cases of AFM should be reported to the health department and samples should be collected as soon as possible.

Sharing of information will lead to improved understanding of AFM and its pathogenesis which will help inform treatment and prevention strategies for your patients.
For additional information visit: www.cdc.gov/afm
Contact CDC at: AFMinfo@cdc.gov