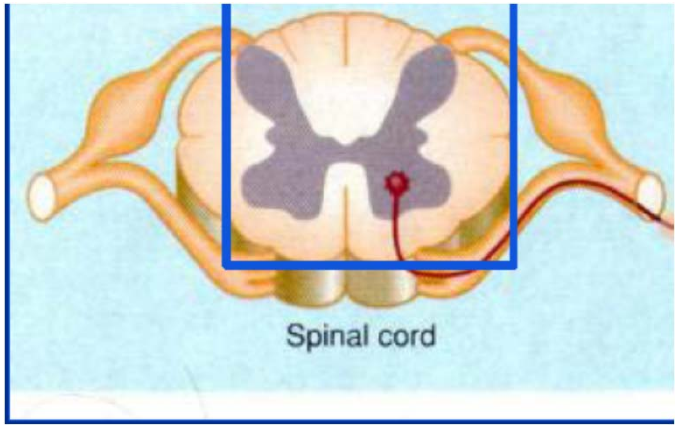
A MYSTERY DISEASE: ACUTE FLACCID MYELITIS

Fatma Levent, MD

OBJECTIVES

- Clinical presentation
- Initial evaluation
- Treatment considerations
- Reporting patients to public health

ACUTE FLACCID MYELITIS (AFM)



The term “Acute Flaccid Myelitis (AFM)” was first used in fall 2014 to describe patients with sudden onset of limb weakness but no known cause

Identical in clinical presentation to poliomyelitis and affects gray matter (neurons) of the spinal cord

AFM may be caused by other viral pathogens:

- non-polio enteroviruses
- flaviviruses (West Nile virus, Japanese encephalitis virus)
- herpesviruses
- adenoviruses

CLINICAL PRESENTATION

Most patients describe preceding illness 1-2 weeks before weakness onset

- Symptoms include fever, rhinorrhea, cough, vomiting or diarrhea

Onset of weakness is rapid, within hours to a few days

Weakness is in one or more limbs and may be accompanied by stiff neck, headache, or pain in the affected limb(s)

Cranial nerve abnormalities may be present

- Facial or eyelid droop
- Difficulty swallowing or speaking
- Hoarse or weak cry

WHAT TO DO?

- Hospitalization is recommended when AFM is suspected
- Rapidly manage patients that deteriorate and develop respiratory compromise
- Obtain specimens early to optimize yield for detecting a pathogen
- Perform appropriate MR imaging
- Consult with neurology and infectious diseases experts to guide treatment and clinical management decisions

INITIAL EVALUATION

History – Important to collect information on any illness in the past 2-3 weeks

- Note respiratory and gastrointestinal symptoms, with or without fever
- Ask about hand-foot-mouth lesions

Other symptoms that may be indicative of AFM include:

- Decreased appetite or difficulty swallowing
- Increased sleepiness or inactivity
- Neck, shoulder or back pain, or headache
- Pain in extremities
- Bowel or bladder change

NEUROLOGIC EXAMINATION

- Note tone and reflexes in each extremity and look for asymmetry in muscle strength and in gait
- Conduct a thorough cranial nerve assessment looking for facial, palatal and shoulder asymmetry as well as hoarseness or hypophonia
- Sensory exam is often normal in patients with AFM
- Assess the ability to protect airway, and respiratory sufficiency (with negative inspiratory force, if able)

SPECIMEN TESTING PROTOCOLS PER CDC

- To support the updated testing protocols, CDC will prioritize testing of cerebrospinal fluid (CSF) and serum to optimize yield of an etiologic agent or possible mechanism for AFM.
- CDC will conduct routine testing and typing of CSF, respiratory specimens and stool for enterovirus/rhinovirus, and poliovirus testing of stool specimens to rule out the presence of poliovirus.
- Additional testing protocols are being developed to look for AFM biomarkers and studies to identify possible mechanisms for AFM are underway.
- **Pathogen-specific testing should continue at hospital or state public health laboratories and may include CSF, sera or whole blood, stool, and respiratory specimens.**

LABORATORY SPECIMEN COLLECTION

- Collect specimens rapidly to increase the chance of pathogen detection
- Testing at the hospital*:
  - Nasopharyngeal and oropharyngeal swabs for respiratory multiplex testing and enterovirus (EV) PCR
  - Rectal swab for EV PCR
  - Cerebrospinal fluid (CSF) cell count with differential, protein and glucose; oligoclonal bands; PCR for EV, HZV, VZV (or a meningitis/encephalitis panel)
  - Serum: EV PCR, anti-MOG (Myelin Oligodendrocyte Glycoprotein) and anti-aquaporin antibodies
  - NP (or OP), serum, CSF, and stool specimens should be routed through state health departments to CDC for further testing

*Hopkins SE,E Irick MJ, Messacar K. Acute Flaccid Myelitis Keys to Diagnosis, Questions About Treatment, and Future Directions. JAMA Pediatrics 2018 Nov 30. doi: 10.1001/jamapediatrics.2018.4896

MRI IMAGING

Imaging should be guided by clinical presentation

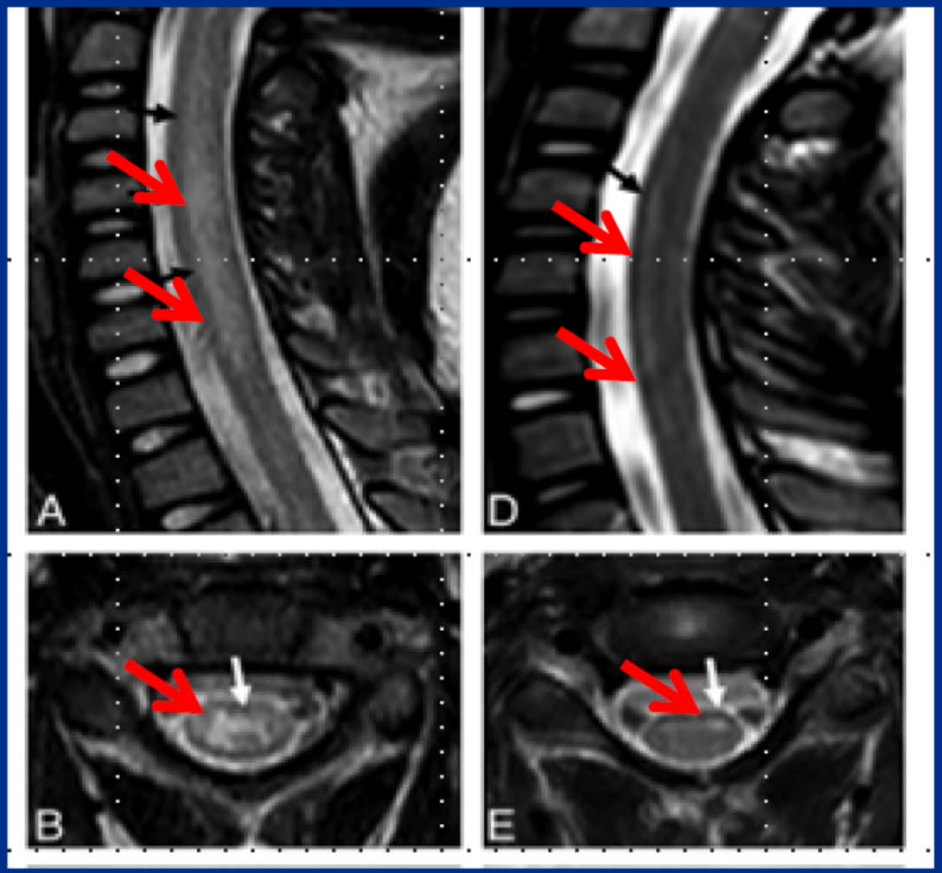
Use a 3 Tesla magnet where possible

- Imaging within the first 72 hours of limb weakness may be normal, and should be repeated if clinically indicated
- Axial and sagittal images are most helpful in identifying lesions
- Multiple levels of the spinal cord are often involved, consider imaging entire spinal cord
- In patients with cranial nerve deficits, high cuts of brain stem or total brain MRI should be considered
- Although lesions are predominantly gray matter, some patients with AFM may have white matter involvement

Characteristic MRI findings of AFM

A, B. Sagittal and axial images demonstrating hyperintensity of the entire central gray matter of the thoracic spinal cord; on axial imaging, demonstrating characteristic 'H' shape pattern.

D, E. Sagittal and axial images demonstrating T2 hyperintensity confined to the left anterior horn cells (best demonstrated in E) .



*From Maloney JA et al. Am J Neuroradiol 2015;36(2):245-50

DIFFERENTIAL DIAGNOSIS

AFM may resemble:

- Synovitis
- Neuritis
- Limb injury
- Guillain-Barre syndrome (GBS)
- Transverse myelitis
- Stroke, including spinal stroke
- Tumor
- Acute cord compression
- Conversion disorder

Careful examination and laboratory testing can help guide diagnosis • AFM must be high on differential diagnosis in late summer or early fall, especially in patients with preceding viral symptom

INTERIM CLINICAL CONSIDERATIONS

Developed in November 2014 with input from experts in infectious diseases, neurology, critical care, virology and public health epidemiology §

In 2018, information was formally updated

- Review of the peer-reviewed published literature
- Consultation with clinical experts in the management of AFM
- Update to the Interim Clinical Considerations is available on the CDC AFM website at: https://www.cdc.gov/acuteflaccid-myelitis/index.html

TREATMENT

For three main treatments, **intravenous immunoglobulin (IVIG), corticosteroids**, and **plasmapheresis**, there is not enough human evidence to indicate a preference or an avoidance for their use at this time

Treatment decisions should be made in conjunction with neurology and infectious diseases experts

Potential benefits of using corticosteroids for spinal cord edema or white matter involvement must be balanced by potential harm due to immunosuppression in the setting of a possible viral infection

There is no indication for the use of other immunosuppressive agents in the management of AF

OTHER TREATMENTS

Fluoxetine is a selective serotonin reuptake inhibitor that demonstrates activity against enteroviruses

- Both in a mouse model and retrospective case comparison of AFM patients, neither showed improvement of neurologic outcomes
- There is no indication that fluoxetine should be used for the treatment of AFM

For other anti-viral medications or **interferon**, there are currently no data to indicate benefit

REPORTING TO PUBLIC HEALTH

CDC conducts national surveillance for AFM under a standardized case definition

Clinicians are encouraged to report all patients meeting the clinical criteria for AFM to their state or local heath department

- Clinical criteria for AFM: acute flaccid limb weakness

Reporting should be done as soon as flaccid limb weakness is recognized to increase the chances of obtaining early specimens for etiologic testing

- No laboratory results, or MRI results are needed to report the patient to the health department

For more information on reporting, see CDC's webpage for clinicians and health departments: • https://www.cdc.gov/acute-flaccid-myelitis/hcp/

Job Aid for Clinicians

How to send information to the health department about a patient under investigation (PUI) for AFM

1 **Identify PUI for AFM: patient with onset of acute flaccid limb weakness**

2 **Contact your health department when you identify a PUI for AFM. For health department contact information, call the CDC Emergency Operations Center at 770-488-7100.**

SPECIMEN COLLECTION

Collect specimens as close to onset of limb weakness as possible and store as directed (see table on reverse side)

Work with your health department to coordinate submission of specimens for testing at CDC.

- Specimens should be shipped overnight to arrive at CDC Tuesday through Friday.
- Specimen submission form (DASH) should be completed for each specimen submitted.

AND

INFORMATION SHARING

Send copies of the following to your health department for sharing with CDC:

- admission and discharge notes
- neurology and infectious disease consult notes
- MRI report
- MRI images
- vaccination history
- laboratory test results

SEND TO

HEALTH DEPARTMENT

3 **Health department completes AFM Patient Summary Form, compiles medical records, and sends information to CDC. Patient will be classified by national AFM experts.**

4 **After expert review, patient classification is given back to health department and relayed to clinician by health department.**

REPORTING

Recognize AFM early

Be alert for onset of acute flaccid limb weakness and consider AFM on your differential diagnosis

Collect specimens & then get MRI

Collect cerebrospinal fluid (CSF), serum, stool, and nasopharyngeal (NP) swab as soon as possible, and handle and store specimens properly

Rapidly report to health department

If the MRI shows a spinal lesion with some gray matter involvement, alert the health department and send specimens and medical records

Diagnosis & medical management

Refer to specialists, monitor for signs of worsening symptoms, hospitalize if indicated, and begin treatment and rehabilitation

Putting Together the Pieces of AFM

WHO
570 AFM cases, mostly children, since 2014

WHEN
AFM outbreaks have occurred every two years starting in 2014, in late summer and early fall

WHERE
48 states and D.C. have had AFM cases since 2014

WHAT
CDC believes viruses, including enteroviruses, play a role in AFM

SURVEILLANCE FOR AFM

Biennial U.S. outbreaks of acute flaccid myelitis (AFM) have been recognized since 2014. Most cases occur in children during late summer and early fall.

During 2018, 233 confirmed AFM cases were reported, the largest number since surveillance began in 2014.

Upper limb involvement only was more prevalent in confirmed cases (42%), as was report of respiratory symptoms or fever (92%) within 4 weeks preceding limb weakness onset.

Median intervals from onset of limb weakness to hospitalization, magnetic resonance imaging, and reporting to CDC were 1, 2, and 18 days, respectively.

Vital Signs: Surveillance for Acute Flaccid Myelitis — United States, 2018

MMWR Weekly / July 12, 2019 / 68(27);608–614

SURVEILLANCE FOR AFM

From January through December 2018, among 374 reported cases of **AFM**, 233 (62%) (from 41 states) were classified as confirmed, 26 (7%) as **probable**, and 115 (31%) as **non-AFM** cases.

Median ages of patients with confirmed, probable, and non-AFM cases were 5.3, 2.9, and 8.8 years, respectively.

Laboratory testing identified multiple Enterovirus/Rhinovirus (EV/RV) types, primarily in respiratory and stool specimens, in 44% of confirmed cases.

Among confirmed cases, the interval from onset of limb weakness until specimen collection ranged from 2 to 7 days, depending on specimen type.

Interval from onset of limb weakness until reporting to CDC during 2018 ranged from 18 to 36 days, with confirmed and probable cases reported earlier than non-AFM cases.

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TESTING

- Among all 233 patients with confirmed AFM, CSF, respiratory specimens, and stool specimens were tested from 74 (32%), 123 (53%), and 100 (43%) patients, respectively
- The highest positive yield (44%) was from respiratory specimens, of which **EV-D68** was most commonly detected; only two (3%) CSF specimens tested positive (one each for **EV-D68** and **EV-A71**).
- Testing of specimens from probable and non-AFM cases also identified multiple EV/RV types.
- Stool specimens from all patients with available specimens tested negative for poliovirus.
- Among specimens sent from 31 patients (17 confirmed, three probable, and 11 non-cases) for arboviral testing, all were negative.

MEDIA RELEASE
July 9, 2019

- **Dr. Robert Redfield, CDC Director**
- "CDC continues to pursue the definitive cause and mechanisms that define this disease and we sincerely appreciate the important contributions of the AFM Task Force in helping us get closer to critical answers," said CDC Director Robert Redfield, M.D. "I urge physicians to look for symptoms and report suspected cases so that we can accelerate efforts to address this serious illness."

PROGNOSIS

Recovery varies among individuals with AFM. Most do not recover fully, but patients do regain strength and motor function over time to varying degrees.

The most affected muscle may be the least likely to recover.

Physical and occupational therapy are also believed to be critical for recovery in AFM.

FUTURE DIRECTIONS

The Acute Flaccid Myelitis Task Force

A workgroup of the Board of Scientific Counselors, Office of Infectious Diseases

The Acute Flaccid Myelitis Task Force is a nationwide group of physicians, scientists, and public health experts from a variety of disciplines and institutions. The Task Force is committed to moving the AFM research agenda forward to better understand the causes of AFM, and review and update clinical guidance on the management of patients with AFM.

SUMMARY

- Most patients have a preceding illness 1-2 weeks before limb weakness and may be febrile at the time of presentation
- Clinicians should consider AFM on the differential diagnosis of patients who present with acute flaccid limb weakness
  - Initiate a workup including laboratory testing and MR imaging
  - Consult with neurology and infectious diseases specialists
- There is currently no indication that any specific targeted therapy or intervention should be preferred or avoided in the treatment of AFM
- Report all patients meeting the clinical criteria for AFM to your state or local health department

For additional Information

www.cdc.gov/afm

Contact CDC at:
AFMinfo@cdc.gov

THANK YOU!