Acute Flaccid Myelitis (AFM): Clinical Presentation

Last updated April 4, 2019

Objectives

- **Describe for patients with AFM:**
  - Clinical presentation
  - Initial evaluation
  - Treatment considerations
  - Reporting patients to public health

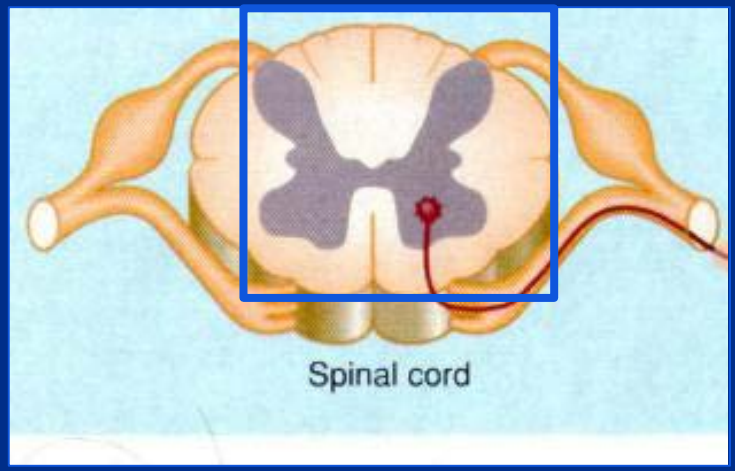
- **The primary audience for this presentation is clinicians.**

Slide 2 notes

This presentation provides information about what Acute Flaccid Myelitis is, and the clinical presentation, initial evaluation, and treatment considerations for patients with AFM, as well as reporting patients that meet the clinical criteria for AFM to public health authorities. The primary audience for this presentation is clinicians.

Acute flaccid myelitis (AFM)

- **The term "AFM" was coined 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



Slide 4 notes

The term Acute Flaccid Myelitis or AFM was coined in the fall of 2014 to describe patients who had developed sudden onset of limb weakness with no known cause.

AFM is identical in clinical presentation to paralytic poliomyelitis and affects the same region of the spinal cord, specifically the gray matter, or motor neurons as shown here in the blue box.

There may be other viral causes of AFM aside from poliovirus including: non-polio enteroviruses (for example enterovirus (EV) 71), flaviviruses like West Nile virus or Japanese encephalitis virus, herpesviruses, and adenoviruses.

HOW DO YOU SUSPECT AFM?

Slide 6 notes

What clinical characteristics would make you suspect AFM?

AFM 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

Slide 8 notes

Here are some of the clinical characteristics of patients who have AFM.

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

These symptoms include fever, rhinorrhea, cough, and may include vomiting or diarrhea although those are less common.

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

Weakness occurs in one or more limbs, and may be accompanied by stiff neck, headache or pain in the affected limbs. Many patients also complain of neck, shoulder or back pain prior to weakness onset.

Cranial nerve abnormalities may be present and include facial or eyelid droop, difficulty swallowing or speaking, and a hoarse or weak cry.

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

Slide 10 notes

Hospitalization is recommended for patients suspected to have AFM.

This will ensure the clinician is able to:

- 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 for suspected AFM

- **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 changes

Slide 12 notes

Many patients present to urgent care, or the emergency room for limb weakness. In an urgent care or emergency setting, it is important to ask the following questions about their medical history to narrow the differential diagnosis.

Details about any illness in the past 2 to 3 weeks should be collected, including respiratory symptoms and gastrointestinal symptoms, and fever.

Ask about hand-foot-mouth lesions, as we know that viruses associated with hand-foot-mouth disease are also associated with AFM, such as EV-A71.

Other symptoms to ask about 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 changes, particularly constipation

Initial evaluation for suspected AFM

- **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)

Slide 14 notes

On examination, it is important to note tone and reflexes in each extremity, and to look for asymmetry in muscle strength and gait. Parents often report that their child appears clumsy when trying to pick up objects, or they notice a foot is dragging or the child is limping.

Conduct a thorough cranial nerve assessment to look for any facial, palatal or shoulder strength asymmetry, and assess hoarseness or hypophonia.

Sensory exam is often normal.

It is very important to assess the ability of the child to protect his or her airway, and to document respiratory sufficiency. Negative inspiratory force may be used if the child is old enough and able to cooperate.

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, Elrick 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

Slide 16 notes

Rapid specimen collection is essential to increase the chance of pathogen detection.

Testing at the hospital or clinic should include:

- Nasopharyngeal and oropharyngeal swabs for respiratory multiplex testing and enterovirus (EV) PCR
- Rectal swab for EV PCR
- 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

It is important to note that in addition to hospital based testing, nasopharyngeal (or oropharyngeal), serum, CSF, and stool specimens should be routed through the state health department to CDC for further testing.

Additional pathogen specific testing (e.g., West Nile Virus, EBV, Lyme) should be considered based on seasonality, exposures, and geography.

MR Imaging for suspected AFM

- **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 brainstem or total brain MRI should be considered
  - Although lesions are predominantly grey matter, some patients with AFM may have white matter involvement

Slide 18 notes

Here are some guidelines for imaging patients suspected of having AFM. Imaging should be guided by clinical presentation.

We know that imaging within the first 72hrs after limb weakness onset may be normal, and should be repeated if clinically indicated.

Axial and sagittal images are most helpful in identifying lesions

Since multiple levels of the spinal cord are often involved, imaging of the entire spinal cord can help confirm AFM.

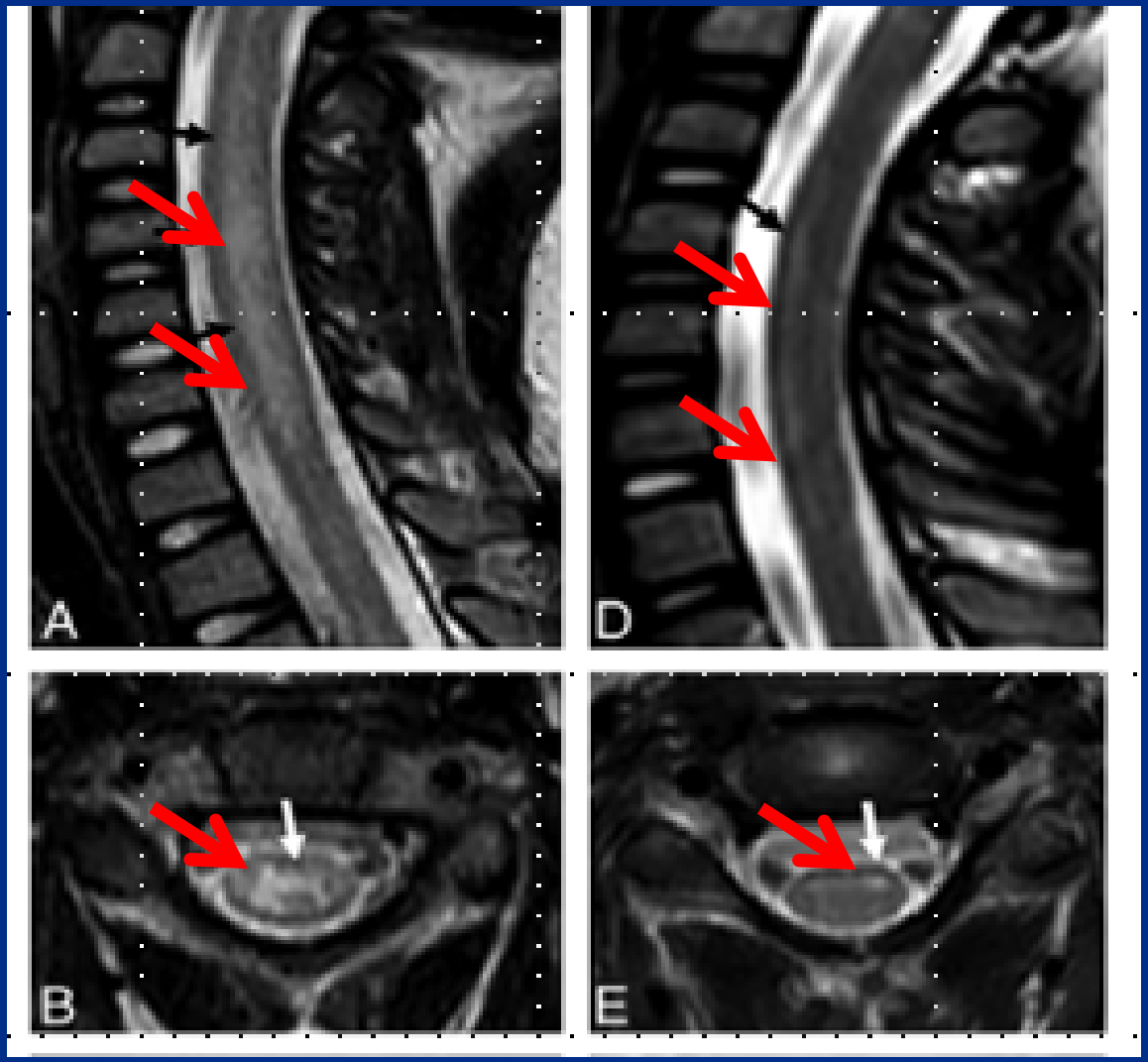
In patients with cranial nerve deficits, high cuts of brainstem or a total brain MRI should be considered

Although lesions are predominantly in the grey matter, some patient with AFM may present with some 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

Slide 20 notes

These MRI images provide examples of the characteristic MRI findings among patients presenting with AFM.

A and B present sagittal and axial images that demonstrate the hyperintensity of the entire central gray matter of the thoracic spinal cord (as indicated by the arrows in panel A) and the characteristic “H” shape pattern (indicated by the red arrow in panel B).

Panels D and E present the sagittal and axial images demonstrating T2 hyperintensity that is confined to the left anterior horn cells. This is best demonstrated in panel E, indicated by the red arrow.

AFM-differential diagnosis of limb weakness

- **AFM may resemble:**
  - Synovitis
  - Neuritis
  - Limb injury
  - Guillain-Barre syndrome (GBS)
  - Transverse myelitis
  - Stroke, including spinal stroke
  - Tumor
  - Acute cord compression
  - Conversiondisorder
- **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 symptoms**

Slide 22 notes

The differential diagnosis of limb weakness is broad and can affect multiple areas of the central nervous system. Clinicians who have initial contact with a patient with limb weakness should consider synovitis, neuritis, limb injury, Guillain-Barre syndrome, transverse myelitis, stroke (including spinal stroke), tumor, acute cord compression and conversion disorder as possible causes

A careful examination and laboratory testing can help guide the diagnosis and distinguish AFM from other conditions.

However, AFM must be high on the differential diagnosis in the late summer or early fall time frame, especially in patients with preceding viral symptoms.

Interim Clinical Considerations for AFM

- **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**
  - Reviewof 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/acute-flaccid-myelitis/index.html**

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In November 2014, CDC developed a summary of treatment approaches that providers could use to help manage patients with AFM. Experts from infectious diseases, neurology, pediatrics, critical care medicine, public health epidemiology, and virology were consulted during this process. The opinions from these individual consultations formed the basis of the "Interim Considerations for Clinical Management of AFM" document drafted in 2014.

In 2016 and 2017, CDC continued to solicit input from clinical experts with experience in treating AFM patients.

CDC updated the summary in 2018, following consultation with national experts and review of the peer-reviewed, published literature.

The 2018 update is available as a link on the CDC AFM website.

Specific treatments for AFM

- **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 bypotential 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 ofAFM

www.cdc.gov/afm

Slide 26 notes

For three main treatments used for AFM, 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.

The potential benefits of using corticosteroids for spinal cord edema or white matter involvement must be balanced by the 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 AFM.

Specific treatments for AFM

- **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 neurologicoutcomes
  - 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**

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Slide 28 notes

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There is no indication that fluoxetine should be used for the treatment of AFM.

For other anti-viral medications or interferon, there are no data to indicate benefit for patients with AFM

Reporting patients 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/

Slide 30 notes

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. The clinical criteria for AFM are the presence of sudden onset of flaccid limb weakness.

Reporting to the health department should be done as soon as flaccid weakness is recognized in order to increase the chances of obtaining early biological specimens for etiologic testing.

No additional laboratory results or MRI findings are necessary to report the patient to the health department.

CDC has a dedicated webpage on recognizing and reporting AFM , which can be found at this link.

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**

Slide 32 notes

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 and initiate a workup that includes laboratory testing and MR imaging. Clinicians should also consult with neurology and infectious diseases specialists to assist with patient management

There is currently no indication that any specific targeted therapy or intervention should be preferred or avoided in the treatment of AFM. The current clinical considerations are available on the CDC website and will updated as additional evidence becomes available.

Remember to report all patients meeting the clinical criteria for AFM, acute flaccid limb weakness, to your local or state health department. Every case counts-each case reported contributes to our understanding of AFM, which will lead to the development of treatment and prevention strategies.

For additional information visit:

www.cdc.gov/afm

Contact CDC at: AFMinfo@cdc.gov