

Neurology 2020: Clarifying the diagnosis of acute flaccid myelitis - Anna Jarrett - University of Arkansas

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Statement of the Problem:

Acute flaccid myelitis (AFM) is a serious condition that primarily affects children. AFM is a type of Acute flaccid paralysis, a global terms for AFM and non-AFM etiologies. AFM is diagnosed by gray matter abnormalities in the spinal cord on MRI, or pleocytosis in the cerebral spinal fluid. AFM attacks spinal cord gray matter resulting in lower motor neuron injury and flaccid weakness in the extremities. Although the specific cause of most cases is unknown, viruses, toxins and genetic disorders have been implicated. Stopping the spread of viral infections is crucial to preventing this potentially disabling disease. Simple prevention measures to stress to all patients are: a) hand hygiene by washing your hands, b) control respiratory droplets by coughing/sneezing into your sleeve and then wash your hands, c) stay current with your immunizations, and d) stay away from those who are ill. Identifying patients with AFM is difficult. If suspected, it is important to act quickly with the assistance of local or state health departments in collaboration with the Centers for Disease Control and Prevention (CDC) to determine the causative factor. The CDC provides up-to-date information. Treatment has been unsuccessful using conservative measures, but there is hope for nerve transfer procedures in upper and lower extremities using microsurgery techniques. This is an unfolding story with more to come if this disease cannot be controlled or eradicated.

No definitive cause; could be a variety of causes treatment is supportive. Flaccid paralysis, which means most patients with AFM will have sudden onset of limb weakness and loss of muscle tone and reflexes. Some, in addition to the limb weakness, may also experience one or more of the following symptoms: facial paralysis, oculomotor dysfunction, dysphagia, dysarthria or upper lid ptosis. (blepharoptosis – BLEE FAIR OP TOSIS) ectropion (lower lid ptosis), Numbness or tingling (paresthesia) is rare in patients with AFM, though some patients do experience pain in their arms or legs. Some patients may experience urinary retention.

The most severe symptom of AFM is respiratory failure which can occur when the diaphragm becomes weak. Prevention is crucial to stop disabilities rapid treatment including screening, detection, and diagnosis.

Etiology:

AFM is most often associated with viruses that can cause inflammation and loss of motor and autonomic neurons located in the anterior horn cells of the spinal cord (i.e. front column of gray matter in the spinal cord). The

symptoms are similar despite the etiologic agent and usually include paralysis but sensation is spared. Viruses that have been associated with AFM include: Enteroviruses (both polio and non-polio), Flaviviruses such as West Nile virus (WNV), specifically Japanese encephalitis virus and Saint Louis encephalitis virus, Herpes viruses such as cytomegalovirus and Epstein-Barr virus and the Adenoviruses.

Pathophysiology:

Enteroviruses are small RNA viruses called picornaviruses. They enter the body through the respiratory or gastrointestinal (GI) tract cause cellular protein translation to viral genes by modifying the host cell's translation factors. GI cell surfaces are viral receptors, enabling the enterovirus to replicate in the GI lymphatic tissue. Translocation then occurs to the circulatory system and spreads to major organs.

Poliovirus enters the host via the GI tract and moves to the central nervous system. After exposure, it replicates in the oropharynx and GI tissue. Antibody production occurs in the lymphatic system of the GI tract, prior to invasion of the CNS tissue.

Epidemiology:

Frequency and pattern historically, AFM was associated with polio cases. Since 1988, wild poliovirus cases have dramatically decreased by approximately 99% globally. An increase in AFM cases was noted in North America that occurred with an outbreak of enterovirus D68 in August 2014. Prevalence: U.S. > 1%/ million people. Most AFM cases occur in otherwise healthy individuals under the age of 18 years, with a median age of 7 years, which corresponds to the recent clusters of AFM. Most cases also occur in late summer and fall. Since the initial 2012 outbreak of enterovirus D68, AFM outbreaks tend to be cyclical in nature. It tends to occur biannually and corresponds with increased numbers of confirmed enterovirus D68 cases.

Today, there has been a noted increase in the number of AFM cases that continue to coincide with enterovirus D68.

Transmission:

AFM agents are transmitted through a variety of routes. Enterovirus and adenovirus transmission occurs through the fecal-oral route, contaminated water, and respiratory droplets. Adenovirus, Epstein-Barr virus (EBV) and cytomegalovirus (CMV) transmission may also occur through sexual contact as well as the aforementioned modes of transmission. CMV and EBV are also transmitted by saliva. In addition, CMV transmission occurs through urine and breast milk. In rare case,

EBV has been transmitted through blood transfusions. Flaviviruses Japanese Encephalitis Virus (JEV), St. Louis Encephalitis Virus (SLE), and West Nile Virus (WNV) are primarily transmitted by mosquitoes. SLE and JEV are not transmitted through person-to-person contact, but SNV transmission includes blood transfusions, organ transplants, needle sticks, and mother-to-baby via placenta and breast milk.

Incubation:

Polio enteroviruses have an incubation period of 6 – 20 days with paralysis typically occurring between days 11- 17 in some cases. Non-polio enteroviruses have a 2- 10 day incubation period. From contact to symptoms, flaviviruses known to cause AFM may take from 2- 21 days, with WNV having a very short incubation period of 2-10 days; JEV 5-15 days, and SLE 4-21 days. CMV has a longer incubation period of 3 – 12 weeks, and even though EBV incubation time is unknown, it is understood that it may take up to 50 days for infectious mononucleosis to present.⁵ Adenoviruses may cause respiratory tract infections in 2 -14 days, and GI symptoms typically manifest within 3- 10 days.

Diagnostic Testing and Diagnosis:

Recognition of AFM equips practitioners to order imaging and laboratory testing, initiate treatment, and provide families with accurate information. The clinical picture typically presents an onset of acute flaccid limb weakness. Early signs are more difficult to differentiate. However, if a patient presents with flaccid extremities, the presumptive diagnosis of AFP can be made since poliomyelitis presents as unilateral limb weakness, most commonly in the lower extremities. The precise diagnosis of AFM requires extensive testing. Table 1 presents common clinical presentations of poliomyelitis and other non-polio viruses. Confirmatory evidence of AFM is a magnetic resonance image (MRI) showing spinal cord lesion in gray matter in a vertebral segment, and cerebrospinal fluid (CSF) with pleocytosis, which is quantified as >5 cells/mm³ white blood cells.

A repeat MRI in 72 hours may be necessary to confirm the diagnosis if the initial study is negative because it may take that long for cord lesions to present on MRI. A probable case would include the clinical presentation and pleocytosis on CSF examination. The final case classification is done by experts in national AFM surveillance.

Reporting AFM:

Although AFM reporting is not mandated by CDC, they encourage all providers who see a person presenting with symptoms of AFM to initiate a voluntary reporting mechanism. Mandated reporting may be required by each state health department, so begin by notifying the local or state health department. In addition, as the provider, immediate specimen collection is important. Begin collecting laboratory, stool, and respiratory specimens. This guide illustrates instructions on notifications, specimen collection and storage, diagnostic testing, and additional information needed coordinate the case classification by AFM experts at CDC. To expedite case classification, CDC now encourages sending information on patients who present with clinical presentations of AFM regardless of laboratory or MRI results.

Treatment:

AFM should be considered when assessing a patient with a complaint of extremity weakness, especially after history of febrile respiratory illness. Any child presenting with complaint of head ache, neck pain, and symptoms of facial palsy, diplopia or dysphagia as well as pain in their limbs should be referred to local children's hospital for admission. These patients are at high risk for weakness or paralysis that involves the lungs. Respiratory complications may develop within a few hours of cranial nerve involvement necessitating ventilator support. Specialists at a pediatric inpatient facility should explore alternative diagnosis and confirm diagnosis of AFM.