New Cluster of Acute Flaccid Myelitis in Western Pennsylvania

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Acute flaccid myelitis is a debilitating illness characterized by acute onset of limb weakness, with one or more spinal segments displaying magnetic resonance imaging–confirmed gray matter lesions. Since the first outbreak in 2014, tracking by the Centers for Disease Control and Prevention has demonstrated biennial epidemics in the United States, with a current outbreak occurring in 2018. The cases of 3 children with acute flaccid myelitis who were initially thought to have common nonneurologic diagnoses are presented. Emergency physicians need to be vigilant to recognize the subtleties of acute flaccid myelitis because the illness progression is rapid and therapy is nuanced. [Ann Emerg Med. 2019;74:503-508.]

0196-0644/$-see front matter

https://doi.org/10.1016/j.annemergmed.2019.01.024

INTRODUCTION

Viral-mediated pathogenesis for acute flaccid myelitis has been suggested, given similarities to poliovirus, associations with enterovirus D68, and seasonal variation.[1,2] There have been a total of 440 cases recorded, with 116 in 2018 alone.[2] Acute flaccid myelitis typically begins with a constitutional prodrome and most patients present in early childhood.[1,3] Weakness develops and is often asymmetric, with one or more limbs involved. Diminished reflexes are appreciated.[1] The site most affected is the cervical spine.[1] Gray matter lesions are initially diffuse but become more localized to the anterior horn cells. Enhancement is observed in the minority of patients.[1,4] Cerebrospinal fluid pleocytosis is typical.[1] A high degree of suspicion is required to promptly identify cases of acute flaccid myelitis in patients with a constitutional prodrome, focal motor deficit, and decreased reflexes to prevent additional morbidity and establish early neurorehabilitative efforts.

CASE REPORTS

On September 28 to 30, 2018, 3 previously healthy immunized children younger than 5 years and from the Pittsburgh area presented with acute flaccid myelitis (Figure 1 and Table 1).

Case 1

A 3-year-old boy presented to the emergency department (ED) with 3 days of fever, fatigue, and pharyngitis, and 24 hours of vomiting, with generalized weakness. Vital signs were notable for fever and tachycardia. The patient was unable to sit up but was able to move all extremities. He was mildly hypoglycemic but was noted to have improved strength after intravenous fluids. The patient was admitted with the assumption that the weakness was a result of sepsis, dehydration, and hypoglycemia. Within hours of admission, he was noted to have decreased spontaneous movements. Inpatient neurology consultation demonstrated weakness in all extremities (power grade 1/5 in the left upper extremity and 3/5 in all other extremities). There was no difference in proximal or distal muscle strength. Light touch sensation was intact. Deep tendon reflexes were 1+ throughout and symmetric. His examination worsened over 10 hours from admission to flaccid quadriplegia and respiratory failure, prompting emergency intubation. Magnetic resonance image (MRI) demonstrated increased T2 signal in the central gray matter of the cervical spine and thoracic spine (vertebrae levels 7 to 10), as well as the dorsal pons and midbrain. Because of initial concern for transverse myelitis, intravenous methylprednisolone (30 mg/kg) was administered. On further deliberation, acute flaccid myelitis was diagnosed and human intravenous immunoglobulin (2 g/kg) was administered 5 days after prodromal onset. Cerebrospinal fluid obtained after imaging and steroid administration was notable for a lymphocytic pleocytosis. He was transferred to inpatient rehabilitation on hospital day 9. At 2 weeks after transfer, he demonstrated minimal improvement in head control but otherwise continued to have severe functional motor impairment.

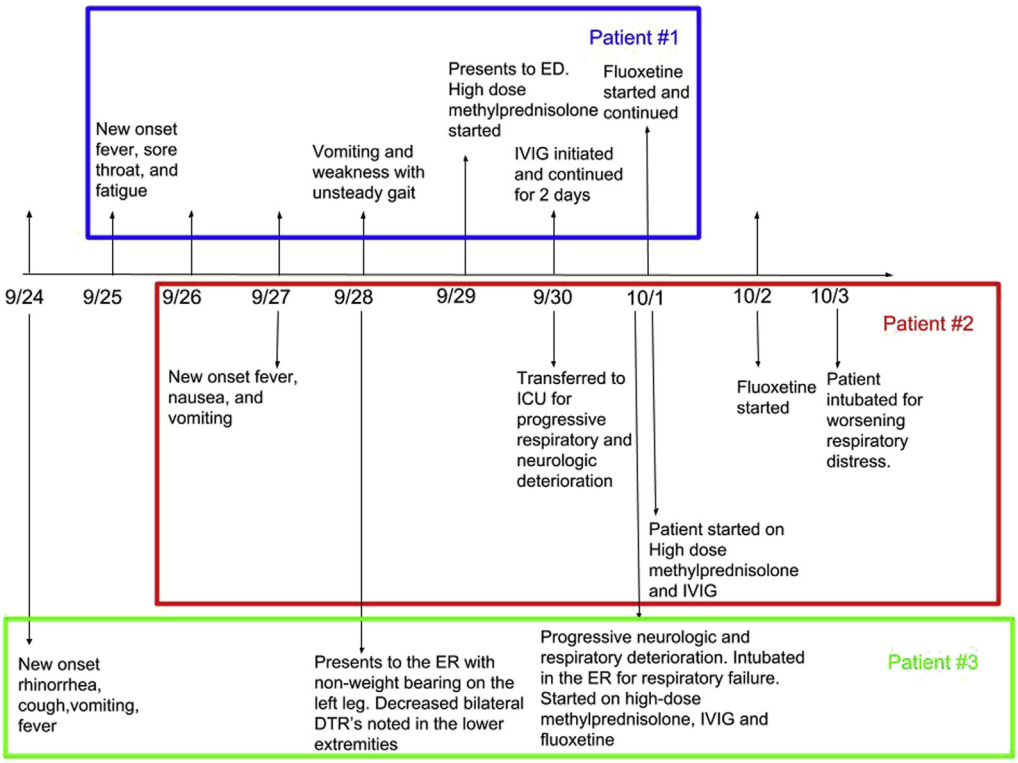

Figure 1. Illness time course for the 3 patients. IVIG, Intravenous immunoglobulin; DTR, deep tendon reflexes.

Case 2

An 11-month-old female infant was treated at urgent care for fever with emesis and received a diagnosis of acute otitis media. She presented the following day to an outlying facility, with difficulty with walking (compared with her baseline ability for age), poor head control, and weak cry. Because of progressive weakness, she was transferred as an inpatient to a tertiary ICU. In the ICU, she was hypotonic with poor head control, lacked spontaneous movements, and was lying in frog-leg positioning. Pupillary reflex and light touch sensation were intact. Tendon reflexes were diminished or absent in all except right patellar and bilateral Achilles tendons, where they were normal. Transverse myelitis was initially considered, and empiric methylprednisolone (30 mg/kg) was recommended. An MRI result was notable for subtle T2 hyperintensities without enhancement in the medullary tegmentum, dentate nuclei, and the central spinal gray matter at the level of cervical vertebrae 2 to 6, as well as the level of the 12th thoracic vertebrae. Cerebrospinal fluid obtained after imaging and steroid administration displayed pleocytosis. A diagnosis of acute flaccid myelitis was made, and human intravenous immunoglobulin (2 g/kg) was administered after the fourth day of illness onset. Within 2 days of ICU admission, she developed respiratory failure, necessitating intubation. She underwent tracheostomy and gastrostomy tube placement for persistent weakness and subsequently was transferred to inpatient rehabilitation. At 2 weeks after her transfer, she demonstrated some improvement with head control and activation of fingers, toes, and wrists bilaterally. However, marked functional impairment persisted.

Case 3

A 2-year-old boy presented to the ED with 2 days of left lower extremity limp, fever, emesis, and rhinorrhea. Examination result was notable for areflexia of the left lower extremity. He was discharged with presumed transient synovitis after an evaluation was negative for septic arthritis. The patient returned to care in 48 hours for persistent fever and new-onset truncal weakness. Pupillary light reflex was normal. There was poor neck control, flaccid paralysis of both lower extremities, and decreased strength (power grade 3/5) in his upper extremities. Deep tendon reflexes were absent in the bilateral lower extremities and left upper extremity, and were 1+ in the right upper extremity. Within 3 hours of presentation, he developed bulbar weakness manifesting as an inability to swallow secretions, prompting emergency intubation in the ED. Transverse myelitis was considered and empiric methylprednisolone (30 mg/kg) was administered.

Table 1. Laboratory and imaging results of the 3 patients.

Laboratory and Imaging Results	Patient 1	Patient 2	Patient 3*
Brain and total spine MRI with and without contrast	Increased T2 signal in the central gray matter from C1 to C7 and T7 to 10, as well as the dorsal pons and midbrain without enhancement	Subtle T2 hyperintensities in the medullary tegmentum, dentate nuclei, and the central gray matter of the cervical cord from C2 to C6, as well as an indistinct region at T12 without enhancement	Increased T2 signal within the central gray matter of the entire spinal cord, as well as the dorsal pons without enhancement
Cerebrospinal fluid	62 WBCs/high-power field	111 WBCs/high-power field	129 WBCs/high-power field
WBC count	66% lymphocyte	42% neutrophils, 41% lymphocyte	82% lymphocyte
Differential	Protein, 36 mg/dL	Protein, 32 mg/dL	Protein, 48 mg/dL
Protein count	Glucose, 97 mg/dL	Glucose, 80 mg/dL	Glucose, 67 mg/dL
Glucose count	0.83 IgG index	0.82 IgG index	0.72 IgG index
IgG index (normal <0.70)	0 oligoclonal bands	0 oligoclonal bands	0 oligoclonal bands
Oligoclonal bands	Aquaporin 4 antibody negative	Aquaporin 4 antibody negative	Aquaporin 4 antibody negative
Local enterovirus PCR serum/stool/CSF	-/-/-	-/-/-	-/-/-
Herpes simplex viral PCR CSF	-	-	-
Respiratory viral panel	+ Rhinovirus/enterovirus	+ Rhinovirus/enterovirus	-
CDC testing	Enterovirus D68 PCR positive, sequencing negative	-	Coxsackie A2 stool positive
Lyme serology	-	-	-
Bartonella serology	-	-	Not tested
Chlamydophila pneumoniae PCR	-	-	-
Mycoplasma pneumoniae PCR	-	-	-
Epstein-Barr virus PCR	Not tested	-	-
Legionella PCR	Not tested	-	-

C1-C7, Cervical spine; *T7-T12*, thoracic spine; *IgG*, immunoglobulin G; *PCR*, polymerase chain reaction; *CDC*, Centers for Disease Control and Prevention; -/-/-, serum, stool, and CSF studies negative; -, negative; +, positive.
*Patient 3 had a positive West Nile virus IgG antibody result, but it was obtained after human intravenous immunoglobulin was administered and therefore was unreliable. Repeated testing result on saved pre–human intravenous immunoglobulin serum was negative.

An MRI demonstrated increased T2 signal within the central gray matter of the entire spinal cord, as well as the dorsal pons without enhancement (Figure 2). Cerebrospinal fluid obtained after imaging and steroid administration displayed lymphocytic pleocytosis. Acute flaccid myelitis was diagnosed and human intravenous immunoglobulin (2 g/kg)

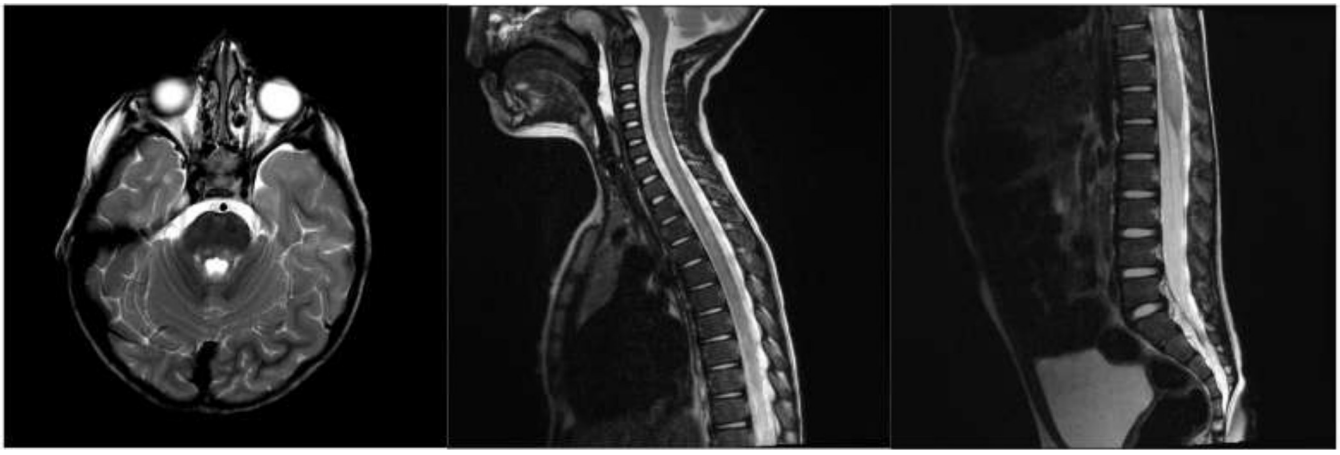

Figure 2. MRI images of patient 3, displaying increased T2 signal within the central gray matter of the entire spinal cord, as well as the dorsal pons (the image on the left was enlarged to match the size of the other 2).

Table 2. Differential diagnosis of acute flaccid myelitis and defining characteristics.[1,3,5,6,8,10,11]

Defining Characteristics	Acute Flaccid Myelitis	Transverse Myelitis	Guillain-Barré Syndrome	Infantile Botulism	Acute Disseminated Encephalomyelitis	Spinal Cord Infarct
Age (typical) Illness timing	Early childhood Prodrome typically within a week of weakness onset Acute weakness Often with concurrent fever	Late childhood/ early adolescence Acute or subacute weakness (deterioration up to 10 days)	Early childhood, most occurring at <10 y Prodrome during preceding weeks (2–4) Acute weakness	Typically <6 mo Subacute (constipation can occur weeks before bulbar dysfunction)	Early childhood Acute or subacute	Early adolescence Hyperacute (up to 24 h) Most cases of nonidiopathic spinal cord infarct are related to congenital cardiac anomalies or trauma disrupting blood flow.
Encephalopathy	–	–	–	–	++	–
Cranial nerve abnormalities	+/–	–	+/–	++ (nonreactive pupils, ptosis, weak cough/ gag)	Variable	–
Tone	↓	↓ (acute) ↑ (chronic)	↓	↓	Variable	↓
Motor	Wide range, monoplegia to tetraplegia, asymmetric onset	Wide range, monoplegia to quadriplegia, often symmetric	Ascending symmetric paralysis	Descending paralysis, weak cry/gag	Variable	Variable, depending on site of insult
Sensory	–	++ (with sensory level)	Dysesthesia, no anesthesia	–	Variable	+ (classic complete form presents with dissociative anesthesia [loss of pain and sensation below the level of insult with preservation of proprioception and vibration sense]. Back pain often present. The incomplete form is pseudo poliomyelitis with only gray matter involvement, resulting in isolated motor deficits.
Reflexes	↓	↓ (acute) ↑ (chronic)	Absent (ascending)	↓	Variable	↓
MRI	Central cord T2 hyperintensity, no contrast enhancement. Unlikely to have supratentorial lesions.	T2 hyperintensity >two thirds cross-sectional area of spinal cord, variable enhancement	Ventral nerve root enhancement only	Normal	Multifocal brain lesions. White matter, deep gray nuclei, and cortical gray matter T2 hyperintense lesions.	"Owls eye" pattern and "pencil-like" T2 hyperintensity Thoracolumbar region most commonly affected Diffusion-weighted imaging can display restriction, depending on the timing of the imaging.
CSF Pleocytosis	+	+	–	–	+	–
CSF protein	+/–	+/–	++ unless done early (albuminocytologic dissociation)	–	+	–

–, Not consistent with the diagnosis; ++, strongly associated with diagnosis; +/–, sometimes found with diagnosis; +, occurs often with diagnosis; *CSF*, cerebrospinal fluid.

was administered 5 days after illness onset. The patient underwent tracheostomy and gastrostomy tube placement. He was transferred to inpatient rehabilitation after 4 weeks. At 2 months after his transfer, he remained ventilator dependent, with persistent functional motor impairment.

DISCUSSION

The 3 patients were initially thought to have nonneurologic diagnoses. Conversely, a recent study has shown that up to a quarter of patients who have received a diagnosis of acute flaccid myelitis actually suffered alternate illnesses, most often transverse myelitis or spinal cord infarct.[3] Eliciting specific historical information, performing a detailed neurologic examination with an emphasis on reflexes, and recognizing the typical findings on imaging can aid in diagnostic differentiation. Table 2 describes various causes of acute weakness and differentiating points. The following are some highlights:

Transverse myelitis displays variable gadolinium enhancement, with both gray and white matter lesions evident on MRI, unlike the isolated gray matter lesions in acute flaccid myelitis.[5] The examination result of transverse myelitis displays a sensory-level deficit along with symmetric motor dysfunction.[3,6] Cranial nerve palsy is not typically found in transverse myelitis because as it is in Guillain-Barré Syndrome and acute flaccid myelitis.[7] Additionally, transverse myelitis causes neurogenic bladder and bowel, which occurs less frequently in acute flaccid myelitis.[6,8,9] The difficulty in differentiating transverse myelitis from acute flaccid myelitis arises from inconclusive sensory examination results in young patients.

Infantile botulism typically occurs between aged 10 days and 6 months. Often, an exposure such as nearby construction or honey ingestion is discovered. There is no constitutional prodrome as in other causes of weakness. Patients display bulbar weakness represented as feeding difficulty. Significant constipation and sluggish pupils develop. Cerebrospinal fluid pleocytosis does not occur. In an older child, one should suspect an alternate diagnosis of weakness.[6,10]

Ascending symmetric weakness, occasional autonomic lability, and pain represent classic symptoms of GBS.[6,11] Conversely, acute flaccid myelitis weakness is initially asymmetric.[3] Cerebrospinal fluid in GBS displays albuminocytologic dissociation, with protein values typically between 80 and 200 mg/dL and normal leukocyte counts.[6] Conversely, a lymphocytic pleocytosis is more consistent with acute flaccid myelitis and transverse myelitis.[1,8] Altered mental status and multifocal brain lesions are found in acute disseminated encephalomyelitis, whereas supratentorial lesions are not common in acute flaccid myelitis.[12,13]

Patients with spinal cord infarct present with sudden onset of back pain, followed by deficits that typically manifest within 4 hours. The insult often results in anterior spinal artery syndrome. Classic anterior spinal artery syndrome differs from acute flaccid myelitis because there is spinothalamic deficit in addition to motor deficits. Cerebrospinal fluid is normal as opposed to that from other causes of weakness.[14,15]

Progression to respiratory failure in acute flaccid myelitis is rapid. Forced vital capacity and negative inspiratory force should be checked.[16] The Centers for Disease Control and Prevention does not recommend or discourage any particular treatment because nothing has shown clear benefit or harm in human beings.[2] Because of negative outcomes from animal testing, the efficacy and safety of steroids have been questioned. In contrast, human intravenous immunoglobulin has shown positive results in animal models, particularly when administered early in the disease course.[17]

Complete recovery in acute flaccid myelitis is rare, and all 3 patients have sustained significant neurologic disability.[1] Early neurologic consultation and rehabilitative efforts in suspected cases are likely to allow for the best possible outcome.[16] Emergency physicians need to identify the subtleties of acute weakness in children because the institutionally recommended therapies may differ, depending on the presumed cause.

Drs. Cramer and Munjal contributed equally to this work.

Supervising editor: Lise E. Nigrovic, MD, MPH. Specific detailed information about possible conflict of interest for individual editors is available at https://www.annemergmed.com/editors.

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Authorship: All authors attest to meeting the four ICMJE.org authorship criteria: (1) Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND (2) Drafting the work or revising it critically for important intellectual content; AND (3) Final approval of the version to be published; AND (4) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding and support: By *Annals* policy, all authors are required to disclose any and all commercial, financial, and other relationships in any way related to the subject of this article as per ICMJE conflict of interest guidelines (see www.icmje.org). The authors have stated that no such relationships exist.

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IMAGES IN EMERGENCY MEDICINE

(continued from p. 491)

DIAGNOSIS:

Cecal volvulus. The CT findings demonstrated grossly dilated bowel (Figure 1) and a "whirl" sign (Figure 2) consistent with cecal volvulus. The whirl sign has a sensitivity of 73% and specificity of 100% for cecal volvulus.[1] It corresponds to the area in which loops of bowel and mesenteric vessels have undergone torsion. Colonic volvulus is the third leading cause of intestinal obstruction worldwide, with cecal volvulus preferentially affecting younger women.[2] Long-distance running is a known risk for cecal volvulus. The repetitive vertical displacement of the colon during long-distance running is thought to cause permanent elongation of colonic tissue, creating independent risk for cecal volvulus.[3] Emergency physicians should consider eliciting this social history from patients presenting with complaints of concerning abdominal pain because early diagnosis and surgical intervention of cecal volvulus are vital to decreasing mortality, which increases to 30% to 40% when strangulation results in gangrenous bowel.[4]

The patient underwent reduction of the volvulus and right hemicolectomy with primary ileocolostomy and recovered well.

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