Acute Flaccid Myelitis Among Hospitalized Children in Texas, 2016

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Introduction

Background: This is a multisite study of pediatric patients with acute flaccid myelitis (AFM) in Texas during the year 2016 among 6 children's hospitals. AFM is a poorly understood disease. Data describing pathogenesis, treatment, and recovery are limited.

- AFM is a central nervous system/spinal cord disease, characterized by limb paralysis, CSF pleocytosis and MRI findings with gray matter edema of spinal cord in previously healthy children, often with preceding or concurrent viral illness.
- Outbreaks occurred in the U.S. in 2014 and 2016. Prognosis in 2014 was poor; 80-90% with permanent paralysis.
- There is no known cause, but it is believed infectious or post-infectious; linked to enterovirus D68 in 2014 cases.
- Anti-inflammatory treatment during 2014 did not appear effective and the CDC later advised against use. There is no recommended medical treatment.
- AFM is not a nationally notifiable condition and therefore, many cases are not reported.

Study Objective:

Form a collaborative database of Texas cases of AFM that occurred during the 2016 outbreak, creating the largest cohort of regional 2016 case data. Research goals included describing disease presentation, treatments used, response to medical intervention, pathogens identified, long-term outcome data, and any variables associated with prognosis.

Methods

- Study Design & Setting: Retrospective chart review of hospitalized patients meeting inclusion criteria among 6 Texas children's hospitals in 4 major metropolitan areas. (Austin, Dallas/Ft. Worth, Houston, San Antonio). This study was IRB approved for all participating hospitals.
- Inclusion Criteria: Patients age 0-18 years hospitalized between January 1- December 31, 2016 identified by each participating hospital according to the following Texas Department of Health and Human Services and definition of confirmed AFM:

  An illness with onset of acute focal limb weakness AND
  - a magnetic resonance image (MRI) showing spinal cord lesion largely restricted to gray matter and spanning one or more spinal segments.

- Variables: Detailed chart review included the following: demographics, patient medical history, prodromal illness, vaccine history, neurologic exam at nadir of illness, imaging of brain and spine, laboratory data, medical treatments, physical therapy, degree of improvement following treatments, and outpatient visits up to 18 months.

Results

- 22 cases of AFM were seen in children in Texas in the midst of a second nationwide epidemic of AFM in the US in 2016. Characteristics described in Table 1.
- A plausible pathogen was identified in 50% of cases (Table 2).
- 95% (21) showed some degree of improvement as of the last follow up (94% (17) with and 100% (4) without treatment) (fig 1 & 3).
- 45% (10) had recovery of function (ability to perform activities of daily living); 32% (7) had full recovery of strength and function (fig 3)
- Among the 8 patients with all extremities involved, 6 had significant residual weakness, ranging from flaccidity in one extremity to complete caregiver dependence. One was lost to follow up after discharge.
- None of the three patients with enterovirus D-68 made a full recovery, and all three remain completely or largely dependent on caregivers.

Table 1. Illness Characteristics Among Children Hospitalized with AFM, Texas 2016 (N=22)

Characteristics	No. (%)
Age onset (median, range)	4.9 yrs (6.8 mos-15 yrs)
Seasonality	
May-Nov	19 (86)
Dec-April	3 (14)
Preceding prodromal illness	19 (86)
Upper respiratory infection	14 (64)
Gastrointestinal infection	7 (32)
Fever	13 (59)
Onset to nadir: median days; quantile (range)	3; 1-5 (0-27)
Weakness	
Upper extremity	17 (77)
Lower extremity	14 (64)
All extremities	8 (36)
Asymmetric	19 (86)
Reflexes	
Decreased	14 (64)
Normal	5 (23)
Increased	3 (14)
Illness course and symptoms	
Sensory deficit	4 (18)
Pain	12 (55)
Cranial nerve palsies	7 (32)
Change in mental status on exam	6 (27)
Respiratory failure	7 (32)
MRI Findings	
Cervical/thoracic spinal levels involved, median (range)	17.5 (1-20)
Brain stem lesions on MRI[a]	14 (64)
CSF Studies	
Pleocytosis (>5 WBC/mm3)[b]	19 (90)
CSF WBC, median; quantile (range)[b]	43; 17-151 (2-301)
CSF Protein median (range)[c]	35 (20-75)
CSF glucose median (range)[c]	55 (46-83)

[a]Largely Pons/Medulla
[b]Rate in 21/22 cases with value for CSF WBC
[c]Rate in 19/22 cases with result for CSF protein/glucose

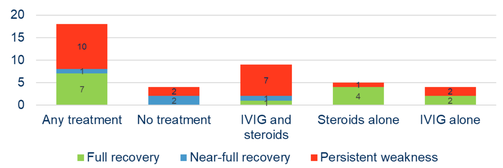

Figure 1. Treatment Used and Outcome

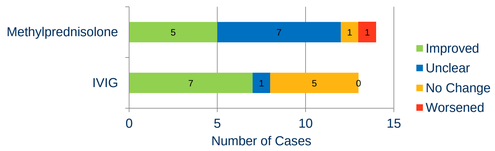

Figure 2. Direct Response Reported Following IVIG and Methylprednisolone

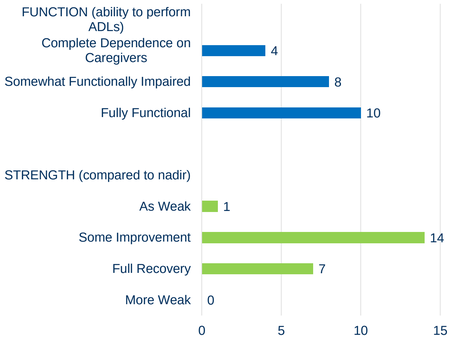

Figure 3. Strength and Function at Last Follow Up (median 254 Days)

Table 2. Pathogens Identified

Pathogen Identified	N (specimen)	Test
Enterovirus[a]	5	PCR
Enterovirus D68	3 (1 CSF; 2 NP)	PCR
Non-D68 enterovirus	2 (2 NP, 1 stool)	PCR
Human parechovirus	2 (1 NP, 3 stool, 1 blood)	PCR, culture[b]
Rhinovirus A58	1 (NP)	PCR
Human herpesvirus 6	1 (CSF)	PCR
Mycoplasma pneumoniae	1 (CSF & NP)	PCR
Bartonella henselae	1 (serum)	IgG/IgM
Influenza B	1 (NP)	PCR
No pathogen Identified	11	

[a]21 (95%) cases tested for enterovirus
[b]Case 1-stool culture and PCR from stool, NP, and blood; Case 2-stool PCR

Conclusions

- Our cases were similar to those described across the U.S. in 2014.
- Clinical outcomes were markedly better than those seen in 2014.
- Associated viral infections were varied, but included cases of enterovirus D68.
- We were unable to find a consistent correlation between a specific treatment and improvement or recovery, therefore it is unclear if the use of anti-inflammatory treatment like IV methylprednisolone and IVIG is beneficial (fig 2).
- We did not see complications overall due to anti-inflammatory therapy.
- Patients with all extremities involved or enterovirus D68 identified appear to have poorer outcomes.

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