Clinical Reasoning: A 2-year-old child with acute flaccid paralysis

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SECTION 1

A 2-year-old boy with a history of autism spectrum disorder and speech delay presented with refusal to walk for a day in late December 2014. In addition to leg weakness, he developed constipation and urinary retention for 2 days. There was no history of pain, altered sensorium, cranial nerve deficits, or upper limb weakness. There was no preceding fever, immunizations, sick contacts, travel, or trauma. Birth and family history was unremarkable. He was fully immunized. On neurologic examination, he was awake

and alert without cranial nerve deficits. Muscle tone was normal; he had limited leg movements compared to the upper limbs. Tendon reflexes were diminished at the knees and ankles; plantars were flexor. On sensory examination, he withdrew with tactile stimuli.

Questions for consideration:

1. What is the localization and differential diagnosis for his presentation?
2. What investigations are needed for this patient?

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SECTION 2

This child presented with sudden onset bilateral lower extremity weakness, normal tone, hyporeflexia, and bladder/bowel involvement. Acute flaccid paralysis (AFP) is a clinical syndrome characterized by rapid onset of weakness due to various conditions and the term flaccid indicates lack of corticospinal tract signs on examination (spasticity, hyperreflexia, and extensor plantar responses),¹ as noted in our case. Corticospinal tract signs are typically absent during spinal shock stage, so acute spinal cord lesions can present as flaccid paralysis.

Localization for this presentation can be due to central (upper motor neuron) or peripheral (lower motor neuron) causes (table). Normal sensorium and cranial nerve functions make a diffuse central process like acute disseminated encephalomyelitis (ADEM) less likely. Spinal cord lesion may involve anywhere in the cord above the level of L2 and below T1 (due to sparing of the upper limbs). Presence of

a sensory level is helpful in diagnosing myelopathies, though detection of sensory level in a 2-year-old patient is challenging. Among the various causes of compressive myelopathy, hematoma and epidural abscess seem less likely due to absence of trauma, fever, or pain. Spinal cord tumors typically present insidiously unless there is hemorrhage within a tumor. Among noncompressive myelopathies, demyelinating and vascular lesions can present in this fashion. Acute transverse myelitis presents with weakness and prominent sensory loss, often with a spinal level.² Spinal cord infarction, though rare in children, should be considered in certain high-risk populations (systemic hypoperfusion, fibrocartilaginous embolism, hypercoagulable states, and iatrogenic).²

Among the peripheral lesions, viral infections can involve anterior horn cells acutely. Among the neuropathies, Guillain-Barré syndrome (acute inflammatory polyradiculoneuropathy) and acute intermittent porphyria can present with acute onset weakness but

Table Differential diagnosis of acute flaccid paralysis in children

Site of lesion and clinical conditions	Helpful investigations
Spinal cord	
Compressive myelopathy (trauma, epidural abscess, spinal cord hematoma, spinal cord tumor)	MRI spine ± contrast
Noncompressive myelopathy	
Demyelinating lesions	MRI spine ± MRI brain
Monophasic illnesses: Acute transverse myelitis, ADEM	CSF studies (increased cell count, raised protein, oligoclonal bands, IgG index), serum antibodies for NMO, vasculitis workup
Relapsing-remitting illnesses: Multiple sclerosis, NMO, vasculitis	
Anterior spinal artery infarct	MRI spine with diffusion imaging, vessel imaging (CTA/MRA), TEE or chest CT/MRI for aortic dissection in high-risk population
Fibrocartilaginous embolism	MRI spine with diffusion imaging, vessel imaging (CTA/MRA)
Anterior horn cell	
Viral myelitis affecting gray matter (polio, enterovirus 71, enterovirus D68, West Nile, Japanese encephalitis)	Virologic studies, MRI spine, EMG
Roots and peripheral nerves	
Guillain-Barré syndrome	CSF, EMG, MRI lumbar spine with contrast for nerve root enhancement
Infections (Lyme, diphtheria)	Infectious workup
Metabolic (porphyria)	Urine and stool studies to identify porphyrin metabolism disorders
Tick paralysis	Isolation of tick
Local trauma (e.g., sciatic neuropathy from intramuscular injections)	
Neuromuscular junction	
Myasthenia gravis	EMG, antibodies
Infant botulism	Toxin assay, EMG
Muscle	
Viral myositis	CK
Inflammatory myopathy	CK, EMG, muscle MRI, muscle biopsy
Hypokalemic periodic paralysis	Serum electrolytes

Abbreviations: ADEM = acute disseminated encephalomyelitis; CK = creatine kinase; CTA = CT angiogram; IgG = immunoglobulin G; MRA = magnetic resonance angiogram; NMO = neuromyelitis optica; TEE = transesophageal echocardiogram.

presence of bladder/bowel involvement at onset is uncommon in the former and lack of abdominal pain is uncommon in the latter. Infant botulism presents with rapid onset weakness and severe constipation but lack of oculobulbar symptoms makes botulism or other neuromuscular junction disorders unlikely.

Coming back to our case, the most likely central lesion based upon the history and symptomatology would be a noncompressive myelopathy, although a compressive myelopathy could not be excluded. The most likely peripheral lesions would be disorders affecting the anterior horn cells or peripheral nerves, given weakness and hyporeflexia.

Laboratory studies including blood counts, liver functions, electrolytes, creatine kinase, and inflammatory markers were negative. Abdominal X-ray showed moderate amount of stool. A post-void bladder scan showed a large volume of urine (>200 mL). MRI brain

and entire spine without contrast were unrevealing, thus ruling out ADEM or compressive myelopathy. Diffusion sequences were not obtained, so acute spinal cord infarction could not be excluded. Lumbar puncture was normal (no pleocytosis, normal glucose and protein, negative Gram stain and culture). Assessment of nerve root involvement to support Guillain-Barré syndrome was not possible in the absence of contrast imaging, but lumbar puncture was normal, making this diagnosis unlikely. The patient underwent a bowel cleanout and received laxatives for constipation and intermittent bladder catheterization for urinary retention. He did not receive any specific treatment for leg weakness.

Question for consideration:

1. What other investigation can help to narrow the differential?

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SECTION 3

EMG was performed after 4 weeks. Nerve conduction studies of the lower limbs showed normal sensory responses and low amplitude peroneal motor responses with normal latency and conduction

Figure MRI spine

T2-weighted images show hyperintensities bilaterally at the location of the anterior horn cells at L1 (white arrows).

velocity. Needle EMG showed neurogenic changes (reduced recruitment of longer duration voluntary motor unit potentials) with active denervation (fibrillations and positive sharp waves) in L5 innervated muscles, right more than left. Constellation of these findings suggested subacute focal anterior horn cell or motor axon involvement and ruled out polyradiculoneuropathy.

About 2 months after the onset of the illness, the patient started walking with his right ankle turned in. He continued to receive outpatient physical therapy and used ankle foot orthoses. Follow-up neurologic examination revealed normal muscle tone and anti-gravity movements of the bilateral lower limbs except right ankle dorsiflexor. Knee and ankle reflexes were 2+; right plantar was extensor. Sensation was intact to tactile stimulation. Spine MRI without contrast repeated after 10 months revealed T2 hyperintense foci in the region of the anterior horn cells at L1 bilaterally (figure) and additionally at T12 without cord edema, atrophy, or other lesions.

Question for consideration:

1. Based on these findings, what is the most likely diagnosis?

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SECTION 4

This child presented with AFP with anterior myelitis. The clinical and radiologic picture is reminiscent of poliomyelitis-like presentation from a presumed viral infection (though we could not identify a specific viral etiology).

DISCUSSION AFP is a challenging neurologic emergency in children characterized by abrupt onset of flaccid paralysis in one or more limbs. There are a plethora of causes that can have similar clinical presentation and some can progress rapidly to involve bulbar or respiratory muscle weakness. A logical approach focusing on the history, clinical examination, and investigations help to narrow the differential. In our case, initial diagnosis was not very clear at the onset but EMG showed focal involvement of the anterior horn cells or its motor axons, which was corroborated later by spinal MRI. The child had clinical evidence of myelitis due to bladder/bowel involvement at onset and pyramidal tract signs (right extensor plantar) on follow-up.

Viral myelitis with a predilection of the gray matter is most commonly seen in the setting of wild polio virus infection, typically in children less than 5 years old.¹ There is a febrile illness at the onset followed by rapid progression of asymmetrical limb weakness sparing sensation. Wild poliomyelitis has largely been eliminated globally.³ In areas without circulating polio virus, clusters of AFP in children have been associated with enterovirus 71 and flaviviruses (West Nile and Japanese encephalitis viruses).^{4–6}

The nationwide outbreak of enterovirus D68 in 2014 caused severe respiratory illness.^{2,7,8} A few cases, mostly in children, had a presentation described as acute flaccid myelitis (AFM).⁸ To be considered a confirmed case of AFM, a patient must meet the following criteria: (1) acute onset of focal limb weakness and (2) MRI showing a spinal cord lesion largely restricted to gray matter and spanning one or more spinal segments.⁹ Though the majority of the cases of AFM occurred in 2014, few cases meeting AFM criteria have been reported from 2015 to 2016. However, there are limited data whether enterovirus D68 is an incidental finding or a newly emerging cause of AFM.⁸ A febrile illness and upper respiratory infection prodrome was described in 80% of those cases.⁸ Weakness developed within a week following viral prodrome. Bladder or bowel dysfunction was present in 28% of the patients at onset and neurogenic bladder was noted on long-term follow-up.¹⁰ A similar number of patients had ventilatory or feeding support, underscoring the potential of bulbar and respiratory muscle involvement in these patients. The clinical hallmark of weakness is flaccid limb weakness with hyporeflexia and intact sensation.³ EMG showed normal sensory

conductions with involvement of the anterior horn cells or its motor axons.³ Neuroimaging studies revealed predilection of ventral gray matter of the spinal cord. Ventral root enhancement was detected in about 25% of the patients.³

Electrophysiologic or neuroimaging involvement of the gray matter of the spinal cord was present in 100% of the cases.³ This selective tropism for the ventral gray matter of the spinal cord during this outbreak with enterovirus D68 strain closely resembles the pattern described in poliomyelitis, or enterovirus 71 infections.³ CSF studies showed pleocytosis in 72% of the patients with largely normal protein and glucose.⁸ In this vignette, the child shares most of the features of AFM except febrile illness at the onset and lack of CSF pleocytosis.

Variable modalities of treatment including antiviral agents, corticosteroids, plasmapheresis, and IV immunoglobulin have been tried, with limited success.^{3,8,10} Clinical follow-up at 30 days showed no or limited improvement of limb weakness in the majority of the patients.⁸ On long-term follow-up, most cases had improved with residual motor deficits.¹⁰ For these reasons, close follow-up and continued care with rehabilitative services including physical and occupational therapy is essential. Our patient made substantial recovery with residual deficit at 10 months follow-up.

AFM should be considered in a child presenting with acute onset of lower limb weakness. CSF and virologic studies, MRI spine and EMG, as well the clinical course establish the diagnosis in most cases.

AUTHOR CONTRIBUTIONS

Dr. Ghosh: study concept and design, analysis and interpretation, critical revision of the manuscript for important intellectual content, study supervision. Dr. Al-Ghamdi: acquisition of data, analysis and interpretation.

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