

Acute-Onset Flaccid Hemiparesis in a 9-Year-Old Boy With Presumed Enteroviral Infection

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Abstract: In the summer and autumn of 2014, a cluster of cases of flaccid paralysis were seen in the United States related to patients infected with enterovirus D68 (EV-D68). We present here a case of acute-onset flaccid hemiparesis in a previously healthy boy with altered mental status, hypothermia, and bowel incontinence.

Key Words: enterovirus, paralysis, cerebral infarction

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Enteroviruses are a broad family of viruses that contain many pathogenic flora commonly seen in the pediatric population including coxsackievirus as well as many numerically named subtypes of enterovirus. Enteroviruses can be acquired by a person directly or indirectly by the ingestion of virus that is shed in the feces or upper respiratory tract of infected contacts.¹ Many people control the infection before major viremia and poliomyelitis or myocarditis develop, and recover with only transient symptoms or are entirely asymptomatic throughout their infective course.¹ We are interested here in the nervous system manifestations of this family of *viridae*.

The pathophysiology of poliovirus is well understood and described in the literature. The virus produces intense inflammation of the leptomeninges and affected gray matter with initial neutrophil infiltration that converts to lymphocyte predominance over time.² In severe cases, macroscopic changes of vascular congestion, petechial hemorrhages, and focal necrosis of the spinal gray matter or brain stem can be seen.² These lesions lead to the acute flaccid paralysis seen in poliovirus infection. Fortunately, due to public health efforts, after a surveillance study across the Western hemisphere, the Americas were declared polio-free on September 29, 1994.³ The pathophysiology of poliovirus can help educate us about how to identify potential new viral causes of these symptoms.

This case report was deemed exempt from review by the institutional review board.

CASE

A 9-year-old boy presented to the emergency department with altered mental status. Per his parents, he had been in his usual state of good health until the day before presentation when he had 2 episodes of vomiting, reported diarrhea, and diffuse muscle aches. Parents reported no recent travel and no known sick contacts. The child was taking Focalin for attention-deficit/hyperactivity disorder,

was developmentally normal, and was in the fourth grade; his sister has epilepsy, and his father reportedly had seizures in childhood. On the morning of presentation, he awoke complaining of headache and vomited. He then attempted to walk to the bathroom, but fell with reported left-sided weakness noted by his father. Shortly after this, he vomited and was incontinent of stool. The family called emergency medical services who responded and evaluated the patient. The family reports that they were reassured that the child likely had “the flu,” ibuprofen was administered and the emergency medical services team left the home. However, his parents remained concerned that the child was having difficulty walking, so they drove him to the hospital. En route, his parents noticed that he was having “trouble breathing.”

The child was brought to the critical care resuscitation bay immediately after arrival to the emergency department. Vital signs were significant for bradycardia to the 60s, hypothermia with a temperature of 32°C, hypotension with systolic blood pressure (BP) below 100 mm Hg. The patient exhibited a shallow breathing pattern. Physical examination was notable for left upper extremity flaccidity, decreased strength in the left lower extremity, 4-mm dilated, equal, reactive pupils. The child had clear breath sounds and no organomegaly. The child found to be only responsive to painful stimuli and was intubated to maintain his airway and received 40 mL/kg of normal saline with improvement in BP, with a systolic BP above 100 mm Hg. Initial laboratory test results were obtained (Table 1), and ceftriaxone was given. Emergent cranial computed tomography showed no evidence of acute intracranial hemorrhage, mass effect, midline shift, or extra axial fluid collections. Gray-white matter interfaces were within normal limits. Shortly after arrival to the Pediatric Intensive Care Unit, the child went for brain magnetic resonance imaging (MRI), which showed multifocal punctate and confluent acute bilateral occipital infarctions, acute left cerebellar lacunar infarctions, and signal abnormality in the left portion of the cervical spinal cord involving both gray and white matter from C2 to C4 level with associated restricted diffusion (Fig. 1). These MRI findings were consistent with regional edema in the setting of recent ischemic injury.

Given the bilateral nature of the infarcts on MRI, there was concern for cardiac embolus or possible coagulopathy. Workup by cardiology and hematology, including echocardiogram and extensive coagulopathy laboratory evaluation, was normal. Cerebrospinal fluid (CSF) obtained by lumbar puncture demonstrated 12 red blood cells, 1 white blood cell, protein of 16, glucose of 76, no microorganisms, and CSF culture and varicella polymerase chain reaction (PCR) were negative. Doppler ultrasound of the abdomen, bilateral neck veins, and bilateral lower extremities all revealed no clots. A diagnostic cerebral angiogram was unremarkable. Follow-up cervical spine MRI performed 2 days after the initial MRI showed evolution and increased conspicuity of the lesion affecting the left hemicord; no abnormal contrast enhancement was present (Fig. 2). A follow-up brain MRI performed 4 days after the initial MRI continued to demonstrate acute posterior circulation infarctions. Ultimately, no uniting etiology was found for the ischemic infarcts seen on MRI. The child had to be reintubated after initial trial of extubation, and there

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TABLE 1. Initial Laboratory Workup

Point of Care Testing–Patient’s Value (Reference Range)		Laboratory Results–Patient’s Value (Reference Range)	
pH	7.149 (7.35–7.45)	Urine drug screen	Negative
PCO ₂ , mm Hg	83.7 (40–50)	Urinalysis	Normal
Bicarbonate, mmol/L	29.2	White blood cell count, K/mcL	8.08 (4.31–11)
Base deficit	2 (1–3)	Hemoglobin, g/dL	11.5 (10.7–13.4)
Sodium, mmol/L	139 (135–144)	Hematocrit, %	34.7 (32.2–39.8)
Potassium, mmol/L	4.1 (3.3–4.7)	Platelet count, K/mcL	234 (206–369)
Ionized calcium, mmol/L	1.28 (1.12–1.37)	Prothrombin time, s	15.0 (12.5–14.7)
Lactate, mmol/L	1.25 (1–2.4)	Activated partial thromboplastin time, s	30.3 (26.6–37.0)
Hemoglobin, g/dL	12.7 (10.5–14)	International normalized ratio	1.14 (0.89–1.11)
Glucose, mg/dL	147 (57–117)	Complete metabolic panel	Normal
		Respiratory viral PCR	Positive for rhinovirus/enterovirus

was some concern that the spinal cord lesions seen on MRI may have affected his diaphragmatic innervation. He was able to extubate to room air during his Pediatric Intensive Care Unit stay and required no respiratory support at the time of discharge. He had improvement in his neurologic function and was discharged to a skilled nursing facility for outpatient rehabilitation. This case

raises interesting questions about the nature of flaccid paralysis in the setting of presumed enteroviral infection.

DISCUSSION

A health advisory issued from the Centers for Disease Control (CDC) in 2014 cautioned clinicians about “an acute

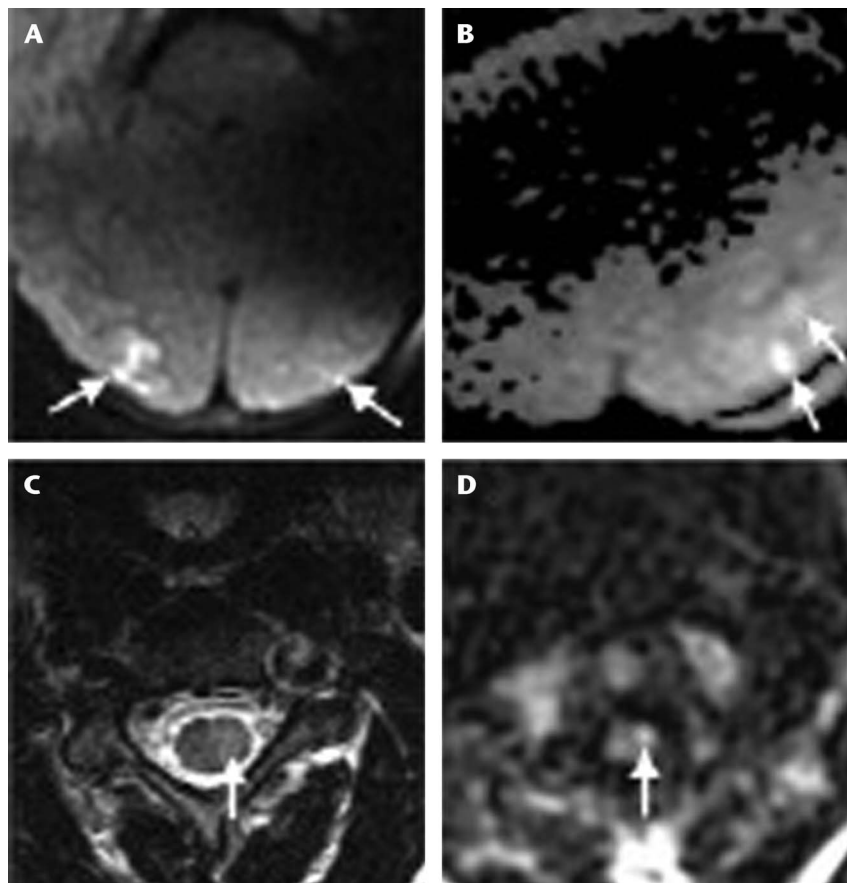


FIGURE 1. Axial diffusion-weighted images (TR/TE, 10000/80 milliseconds) through the occipital lobes (A) and cerebellum (B) reveal multifocal punctate restricted diffusion in the occipital cortices (A) and left cerebellar hemisphere (B) consistent with acute infarctions (arrows). Axial fast spin-echo T2WI (TR/TE, 6000/114 milliseconds) (C) and axial diffusion-weighted image (TR/TE, 10000/80 milliseconds) through the upper cervical spinal cord show ill-defined hyperintense signal and restricted diffusion in the left portion of the spinal cord consistent with edema in the setting of presumed ischemic injury (arrows). Metallic dental hardware artifact degrades the quality of diffusion-weighted images (A, B, and D).

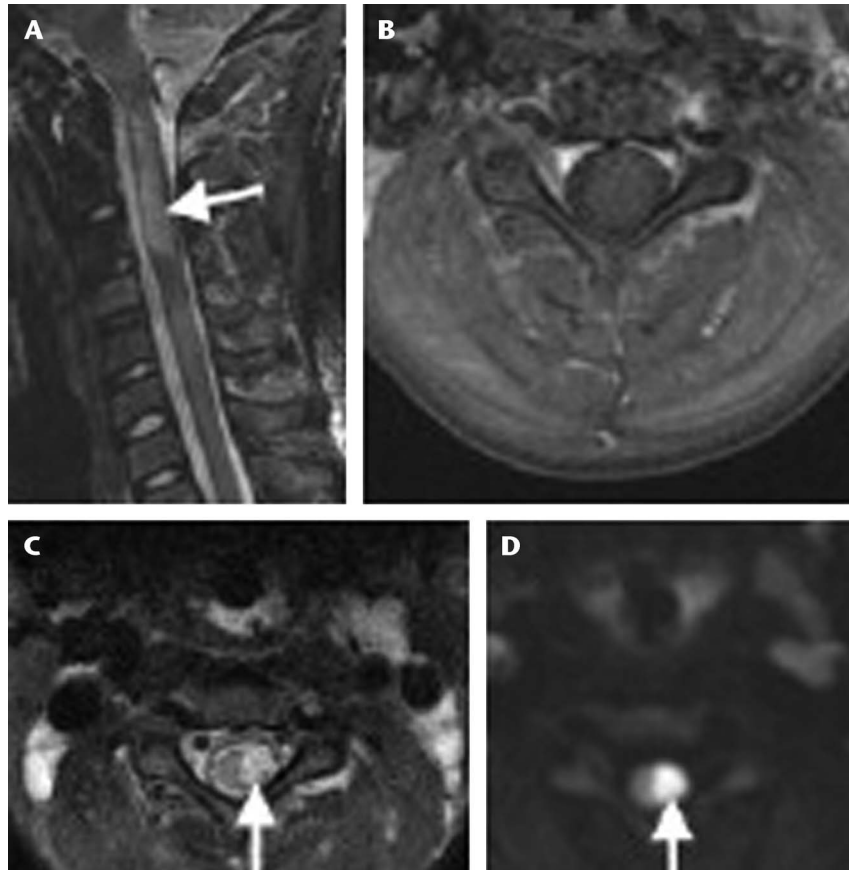


FIGURE 2. Sagittal fast spin-echo inversion recovery (TR/TE/TI; 4618/37/160 milliseconds) (A) and axial fat-saturated T2WI (TR/TE; 5562/80 milliseconds) (C) increased signal in the left half of the upper cervical spinal cord from C1 to C3 (arrows). Marked restricted diffusion is present throughout the lesion (arrow) on the axial diffusion-weighted image (TR/TE, 8000/73 milliseconds). Axial postcontrast fat-saturated T1WI (TR/TE, 385/14 milliseconds) (B) shows no abnormal lesional contrast enhancement.

neurologic illness that features focal limb weakness and abnormalities of the spinal cord gray matter on magnetic resonance imaging (MRI),” particularly MRI of the spinal cord that show nonenhancing lesions largely restricted to the gray matter.⁴ Among cases in a CDC report from Colorado, there was no altered mental status, which our patient exhibited, nor any cortical, subcortical, basal ganglia, or thalamic lesions on MRI,⁵ unlike our patient who did have cortical involvement on MRI. However, as no other etiology was found during his extensive hospital course, his may well be a case of enterovirus D68 (EV-D68)-associated neurologic deficit with a different and more severe clinical picture. Also, our patient, like 6 of the 8 reported by the CDC, tested positive for rhinovirus/enterovirus by nasal PCR. Four of the 6 positive cases in the CDC report were later confirmed EV-D68 positive.⁴ Our patient did not have confirmatory testing.

Other enteroviral case reports include 12 children in Colorado with acute flaccid paralysis and spinal cord lesions involving mostly gray matter on imaging from August to October, 2014.⁶ Seventy-three percent of these children had nasopharyngeal swabs that were positive for rhinovirus and enterovirus.⁶ A retrospective study of children with acute flaccid myelitis in California and Colorado, at the height of the 2014 EV-D68 outbreak, found EV-D68 in the respiratory secretions of 64% of the cases of patients with acute flaccid paralysis.⁷

Similar cases were reported in the literature before 2014. Twenty cases were seen in California in the autumn of 2012, with sudden-onset paralysis with positive PCR for enterovirus 68.⁸ One

case report from 2008 in New Hampshire describes a previously healthy 5-year-old boy presenting with progressive right-sided weakness, eventual inability to walk, bowel and bladder incontinence, and cardiac arrest leading to death.⁹ The sole infectious etiology found at autopsy in this patient was PCR for enterovirus 68 in the CSF.⁹ Microscopic examination of the brain at autopsy showed hypoxic-ischemic injury.⁹ This patient’s presentation resembles that of our patient, with bowel incontinence, inability to walk, and ischemic infarctions on MRI. The underlying cause of the ischemic brain and spinal cord lesions is debatable; regional leptomeningeal inflammation causing vasculitis and secondary arterial and/or venous compromise is a possible etiology.

There were many reported cases of enterovirus 71 in the early 2000s in Asia, causing concern for a possible “new polio.”¹⁰ This outbreak showed rapid progression from a hand, foot, and mouth disease-like prodrome followed by fever and rapid cardiorespiratory failure in some patients.¹⁰ Although our patient did not have a prolonged prodrome and no reported skin findings, his altered mental status and respiratory depression were strikingly similar to the cases reported in Asia. In a sampling of all cases of acute flaccid paralysis from January to September 2003 in Pakistan, 26% were found to be linked to enteroviral infection, and of these, two thirds had asymmetric flaccid paralysis, similar to our patient.¹¹ Forty-one cases of enterovirus 71 were seen in 1998 in Taiwan with a mean patient age of 2.5 years.¹² The pediatric population is also more severely affected by the focal neurologic findings in enteroviral infection.^{11,13} In the Taiwanese patients, 4 had

flaccid paralysis, 3 of whom had findings on MRI in the anterior horn at some level of the spinal cord.¹² Although our patient did not have specific anterior horn involvement, as was seen in these cases, and in the classic description of poliomyelitis, his MRI findings did include significant findings in the spinal cord affecting portions of the anterior horns unilaterally at several cervical levels and his clinical picture fits with this type of pathology. However, spinal cord pathology was not isolated to gray matter in our patient; it also involved the ipsilateral white matter in a diffuse manner.

CONCLUSIONS

This case illustrates a unique and life-threatening presentation of presumed EV-D68 infection. The review of the literature presented here illustrates that the acute flaccid paralysis seen in our patient is not unique to the outbreak seen in the summer and autumn of 2014. This further educates us to recognize the possibility of enteroviral infection in children presenting with acute neurologic symptoms and to consider different strands of enterovirus, including those yet to exhibit poliomyelitis-like symptoms, as multiple strains have caused a similar constellation of symptoms.

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