

First Adult Case of Echovirus 21–Associated Poliomyelitis-Like Myelitis Presenting with Flaccid Asymmetric Tetraparesis

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Abstract

Background

Non-polio enterovirus–associated myelitis is a rare condition causing acute flaccid paralysis due to anterior horn cell injury. While most cases occur in children, reports in adults are exceedingly uncommon.

Methods

We report the first known case in a 63-year-old woman with relapsed/refractory mantle cell lymphoma (MCL) after second-line therapy with rituximab and ibrutinib. Following leukapheresis for planned CAR-T-cell therapy, she received bridging chemotherapy with bendamustine, cytarabine, and rituximab. During prolonged neutropenia and lymphopenia, she developed sudden asymmetric tetraparesis. Diagnostic workup included brain and spinal MRI, cerebrospinal fluid (CSF) analysis with cytology and flow cytometry, nerve conduction studies (NCS), and electromyography (EMG).

Results

NCS and EMG demonstrated a predominantly axonal neuropathy with acute denervation. Spinal MRI revealed cervical intramedullary T2 hyperintensities with a characteristic “snake-eye” sign involving the anterior horns. CSF analysis showed normal cell counts and protein levels without lymphoma involvement. Multiplex PCR detected enteroviruses, subsequently identified as Echovirus-21. Initial treatment with intravenous immunoglobulins for suspected Guillain–Barré syndrome was discontinued after confirmation of enterovirus-associated myelitis, and supportive care was provided.

Discussion

Although rare in adults, enterovirus-associated myelitis should be considered in immunosuppressed patients presenting with acute flaccid paralysis. Early diagnosis using spinal MRI, CSF PCR, and electrodiagnostic studies is essential to avoid misdiagnosis and inappropriate treatment.

Introduction

Non-polio enterovirus–associated myelitis is a rare condition that predominantly affects infants and young children and typically presents with acute flaccid paralysis(1). Enteroviruses – including echovirus serotypes – have been described as important pathogens in this context, most commonly enterovirus D68 and enterovirus A71(2). Echovirus-21, a member of the enterovirus B group, has generally been associated with meningitis, hepatitis, and gastroenteritis, but polio-like myelitis has not previously been reported in association with this serotype(3). Clinically, affected patients often develop rapidly

progressive flaccid paralysis, sometimes accompanied by cranial nerve involvement. Here, we report the first adult case of Echovirus-21 –associated acute flaccid paralysis, characterized by rapidly progressive asymmetric weakness and spinal MRI findings showing predominant gray matter involvement consistent with poliomyelitis-like anterior horn cell injury(1). This case underscores the importance of considering rare enterovirus serotypes in adults presenting with acute spinal motor neuron syndromes and highlights the diagnostic value of early CSF enterovirus PCR and spinal MRI.

Case Presentation

A 63-year-old woman with a long-standing history of stage IV A mantle cell lymphoma (MCL), with a blastic variant and high-risk MIPI score, presented at our hospital for CAR-T-cell therapy with Brexucabtagen-autoleucel (Brexu-cel). First-line therapy comprised alternating R-CHOP/R-DHAP induction, followed by high-dose chemotherapy (R-BEAM) and autologous stem cell support five years before the current disease episode. At the time of presentation, she suffered from relapsed/refractory MCL following second-line therapy with rituximab and ibrutinib, which was initiated at first relapse in 2021. At the time of leukapheresis, an abdominal bulk in the pelvic region and malignant ascites were the predominant sites of lymphoma. Because of the bulky disease, bridging-therapy with Rituximab, Cytarabine, and Bendamustin was administered after leukapheresis.

In the weeks leading up to her planned CAR-T cell infusion, she developed rapidly progressive weakness of the lower limbs. A lumbar spine MRI performed at our center excluded mechanical compression but showed contrast-enhancing, thickened cauda equina fibers. At the time of her inpatient admission for CAR-T preparation, she described a 2–3-day history of worsening of bilateral leg weakness as well as areflexia without sensory symptoms, fever, or B-symptoms. Examination revealed a flaccid paraplegia with intact cranial nerves and preserved sphincter control. Of note, no weakness or sensory symptoms of the upper extremities were evident at this time. Lymphodepleting chemotherapy was initiated suspecting progredient lymphoma affecting the cauda equina fibres, according to the previously performed MRI. Over the following two days, the weakness rapidly ascended to involve the upper extremities. Despite chemotherapy and corticosteroids a flaccid tetraparesis with diaphragmatic weakness, though swallowing remained unimpaired, was observed. A whole-spine MRI performed during this progression demonstrated new leptomeningeal enhancement along the lower thoracic cord and cauda fibers, as well as mild intramedullary T2 signal changes in the cervical cord "snake eye sign" (Fig. 1).

Lumbar puncture was performed and, given the differential diagnosis of central nervous system lymphoma involvement versus Guillain–Barré syndrome (GBS), we administered intrathecal methotrexate and dexamethasone. Two days later, autologous CAR T cells were infused. Cerebrospinal fluid (CSF) analysis revealed an acellular CSF with normal protein levels (Table 1); however, PCR was positive for enterovirus. Other neurotropic pathogens – including *Escherichia coli* K1, *Haemophilus influenzae*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Streptococcus agalactiae*, *Streptococcus pneumoniae*, Cytomegalovirus, Herpes Simplex virus type 1 and 2, human Herpesvirus 6, human

Parechovirus, Varicella-Zoster virus, and Cryptococcus neoformans/gattii – were not detected. Malignant cells were not identified. PCR for early summer meningoencephalitis (ESME) virus as well as West Nile virus IgM and IgG antibodies were negative in the CSF. At that time, there was no evidence of specific paraneoplastic antibodies (LGI1, CASPR2, NMDAR, GlyR, IgLON5, AMPAR1/2, GABABBR, GABA.AAR, GAD65, DPPX, mGluR5, mGluR1, Hu, Ma2/Ta, Ri, Yo, SOX1, CV2, DNER/Tr, Zic4, Amphiphysin, Recoverin, Titin, ANNA-3, Purkinje cell antibodies, GFAP, Adenylate Kinase 5, Neurexin-3α IgG) or ganglioside antibodies (GQ1b, GM1, GM2, GM3, GD1a, GD1b, GT1b IgG) in serum or CSF. Flow cytometric analysis of the CSF revealed no abnormal lymphoid population and no evidence of leptomeningeal lymphoma involvement. Initial nerve conduction studies demonstrated an axonal motor Neuropathy with absent F-waves and minimal demyelinating features, raising suspicion for a polio-like anterior horn cell disorder rather than classic AIDP/GBS. From a differential therapeutic perspective, IVIG was administered to avoid overlooking the less suspected GBS.

Table 1
CSF analysis:

Parameter	Normal range	Unit	Result
Protein	20.0–50.0	mg/dl	27
Glucose	30–80	mg/dl	65
Lactat	10.0–20.0	mg/dl	22
Oligoclonal bands	Negative		Negative
Leucocytes	< 4	/μl	3
Erythrocytes	0	10^3/μl	0.00

Based on the rapidly progressive flaccid paralysis, characteristic MRI findings, axonal neurophysiology, enterovirus PCR positivity, and confirmatory typing from a reference laboratory, we diagnosed an enterovirus ECHO21–associated polio-like myelitis. Repeated electrophysiology approximately two weeks later showed florid denervation without evidence of reinnervation.

The subsequent disease course was complicated by grade 2 cytokine release syndrome (CRS), mild ICANS, prolonged severe cytopenias requiring a CD34 + stem-cell boost, and a subdural hematoma that required surgical evacuation. Although her hematologic parameters eventually recovered and infectious complications resolved, she remained severely tetraparetic. After several weeks of stabilization, multidisciplinary management, and supportive therapy, she was transferred from our hospital to a specialized neurological rehabilitation facility.

Discussion

The case highlights a rare adult manifestation of Echovirus-21 causing a polio-like anterior horn cell dysfunction. Such a presentation is exceedingly rare and has previously been attributed almost

exclusively to EV-D68 and EV-A71, but has not yet been described in association with Echovirus-21(1, 4). Echovirus-21 belongs to the Enterovirus B family, a single-stranded, positive-sense RNA virus that predominantly targets the intestinal tract but can also cause systemic and neurological disease(5). While published reports have linked Echovirus-21 mainly to meningitis(6), acute hepatitis, and gastroenteritis(7) — primarily in infants and young children — there are no available data describing acute flaccid paralysis caused by Echovirus-21, neither in children nor in adults.

Enteroviruses reach the central nervous system either through hematogenous spread or via retrograde axonal transport, crossing the blood–brain barrier. Once in the CNS, they demonstrate tropism for anterior horn cells, where they replicate and cause cell lysis, ultimately leading to the loss of motor neurons(8). These infections are seen predominantly in children because their immune systems are less mature and provide weaker barriers against enteroviral replication and dissemination—particularly before full development of cell-mediated immunity and before vaccination schedules offer protection against related viruses. Young children, especially those under five years of age, have not yet encountered or developed immunity to the wide range of enterovirus serotypes, making them more susceptible to primary infection and severe neurological manifestations(9, 8). The manifestation in adults is rare and usually associated with immunosuppression, as in our case.

Recent large-scale surveillance studies, including Bubba et al. (2020) and de Schrijver et al. (2025), have highlighted the rising incidence of neurological manifestations due to non-polio enteroviruses, especially among immunocompromised individuals, reinforcing the relevance of early diagnosis in such populations. While Echovirus-21 has not been commonly linked to poliomyelitis-like myelitis, the emerging patterns in Europe highlight the growing recognition of its neurological implications. As demonstrated in Bubba et al. (2020), the incidence of neurological symptoms among those infected with enteroviruses such as Echovirus-30 underscores the importance of considering less commonly implicated serotypes like Echovirus-21 in similar presentations. The emerging trends in de Schrijver et al. (2025) further suggest that cyclic outbreaks of enterovirus infections may lead to increasing cases of neurological complications(10, 11).

Diagnosis plays a central role when dealing with such rare conditions, particularly in the presence of concomitant diseases. In our patient, the differential diagnosis of Guillain–Barré syndrome (GBS) was not supported electrophysiologically, as the electrodiagnostic findings demonstrated an axonal rather than a demyelinating pattern. The cerebrospinal fluid profile was also not consistent with cytoalbuminous dissociation. Lymphomatous meningitis was another relevant differential diagnosis; however, this was considered unlikely because the CSF showed normal routine parameters—especially normal protein levels—and cytology did not reveal malignant cells. Although repeated lumbar punctures are generally required to exclude lymphomatous meningitis, the identification of a causative pathogen made this diagnosis unlikely. Nerve conduction studies further argue against this diagnosis, as meningeosis typically presents with a sensorimotor neuropathy, whereas a predominantly motor axonal neuropathy was observed. In addition, the MRI findings in our patient demonstrated a myelopathic signal selectively affecting the anterior horn cells with "snake eye" sign, which does not correlate with

leptomeningeal diseases(12), where diffuse or nodular leptomeningeal enhancement is expected. The “snake-eye sign” has been described in disorders affecting the anterior horn, including early summer meningoencephalitis (ESME), acute flaccid myelitis (AFM), and amyotrophic lateral sclerosis (ALS)(13). Autoimmune myelopathies such as NMOSD or MOGAD were also deemed unlikely, as their characteristic imaging patterns (longitudinally extensive lesions, dorsal/central cord involvement, or conus lesions) did not match the MRI findings in this case. Radiculopathies caused by pathogens such as herpes simplex virus or *Borrelia burgdorferi* were excluded by CSF testing and would typically present with nerve-root enhancement rather than pure anterior horn involvement.

Another challenging issue concerns the management of non-polio enterovirus–associated myelitis. There are no disease-specific treatments, and therapeutic strategies remain largely supportive. Intensive care monitoring and early rehabilitation are the main pillars of care. A few reports have suggested potential benefit from intravenous immunoglobulin (IVIG) in non-polio enterovirus myelitis, particularly in acute flaccid myelitis (AFM) caused by EV-D68 or EV-A71(14). Experimental data from rodent models indicate that early IVIG administration can reduce progression to neuroinvasive disease and paralysis(15); however, in humans, the clinical efficacy appears limited and has not been systematically demonstrated. Thus, evidence for IVIG remains inconclusive, and no standardized immunotherapy currently exists for these conditions. A limitation of our case is the lack of follow-up spinal imaging, which might have provided additional insights into the temporal evolution of anterior horn cell injury. Clinical follow-up was also unavailable, as the patient unfortunately died shortly after presentation due to pneumonia.

In summary, echovirus-21 should be considered in adults presenting with acute asymmetric flaccid paralysis, particularly when MRI demonstrates gray-matter–predominant spinal cord lesions. Early enterovirus PCR testing is crucial to avoid misdiagnosis and unnecessary immunomodulatory treatments.

Declarations

Disclosures:

I. Farhood, L. Schönlau, T. Mika, R. Schroers, A. Katsounas, A. Nashtar, C. Seliger have no disclosures relevant to the manuscript.

Ethics approval and consent to participate

According to the regulations of the Ethics Committee of the Medical Association of Westphalia-Lippe, formal ethical approval was not required for this single-patient case report. The case report was conducted in accordance with the guidelines and regulations of the Ethics Committee of the Medical Association of Westphalia-Lippe and the principles of the Declaration of Helsinki.

Consent for publication

Written informed consent for publication was obtained from the patient's husband, as the patient had died.

Competing interests

The authors declare that they have no competing interests.

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The authors report no targeted funding.

Author Contribution

I.F. conceptualized the case report, collected and interpreted the clinical data, performed the literature review, and drafted the manuscript. L.S., T.M., R.S., A.K., and M.A.N. contributed to the clinical management of the patient, interpretation of the clinical findings, and critical revision of the manuscript. C.S. supervised the work, contributed to the interpretation of the findings, and critically revised the manuscript. All authors read and approved the final manuscript.

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

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Figures

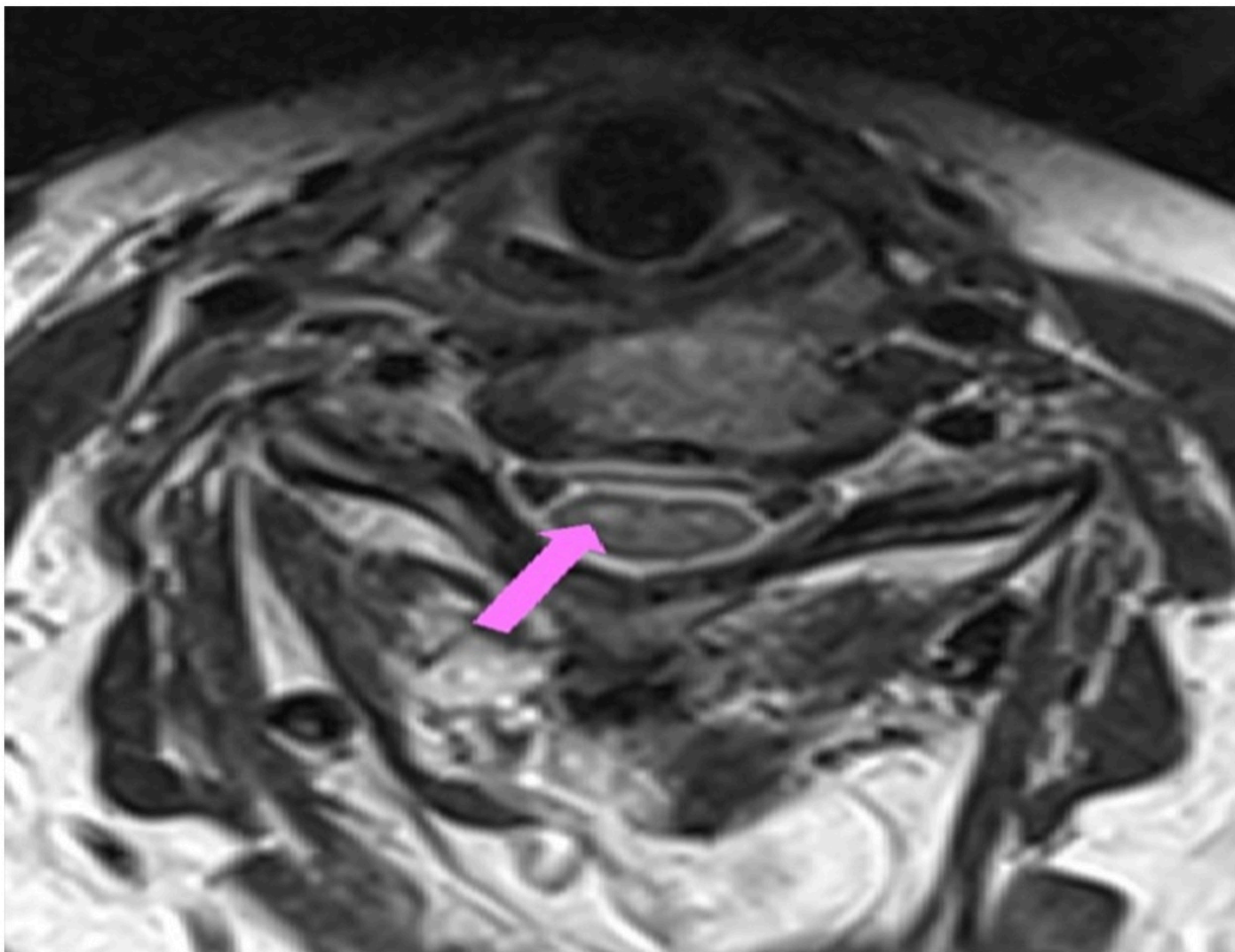


Figure 1

Axial T2-weighted MRI of the cervical spinal cord demonstrating the **"snake-eye sign"** (bilateral symmetric hyperintense foci in the anterior horn regions, arrow).