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Spinomedullary Weston Hurst Syndrome After COVID-19 and Influenza Co-Infection: A Case Report

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Abstract

The neurological complications of coronavirus disease 2019 (SARS-CoV-2, COVID-19) have so far included a range of para- and post-infectious neuroinflammatory syndromes inclusive of all components of the neuraxis and peripheral neuromuscular system. In comparison to the para-infectious manifestations of anosmia, ageusia, encephalopathy, and encephalitis, cases of post-infectious ADEM have rarely been reported and have most commonly affected the supratentorial component with or without spinal cord involvement. In this report, we describe a case of isolated involvement of the cervicothoracic spinal cord and medulla, occurring in association with microhemorrhages and hemosiderin deposition in the medulla, that presented fulminantly and required aggressive immunotherapy to control the inflammatory attack. We compare and contrast this case against prior reports of acute hemorrhagic leukoencephalitis (Weston Hurst syndrome) and review the atypical features of neuroinflammation reported to occur following COVID-19 infection.

Keywords

Weston hurst disease, acute hemorrhagic leukoencephalitis, COVID-19, influenza, case report

Introduction

The spectrum of neurological disease associated with coronavirus disease 2019 infection (SARS-CoV-2, COVID-19) has so far included a range of para- and post-infectious neuroinflammatory syndromes inclusive of all components of the neuraxis and peripheral neuromuscular system. Para-infectious acute necrotizing encephalopathy and post-infectious acute disseminated encephalomyelitis (ADEM) in association with microhemorrhages have been reported, usually followed only by partial recovery.[1-3] As with other neuroimmunologic disorders, prompt recognition of a post-infectious inflammatory attack holds the greatest potential for treatment to minimize deficit nadir and maximize recovery. To this end, we use this case of hyper-acute hemorrhagic rhombencephalomyelitis (in keeping with Weston Hurst syndrome) to illustrate the atypical features of neuroinflammation following COVID-19 infection and the aggressive immunotherapies that may be necessary to treat it in fulminant cases.

A singular feature of our case is the notable sparing of the upper brainstem and cerebral hemispheres on both MRI and clinical grounds. We additionally present the development and regression of the profound abnormalities in the medulla and spinal cord in the sequential imaging of the neuraxis by MRI.

Case Description

A 22-year-old previously-healthy man presented with rapid sequential development of headache at the skull base, numbness of both arms, and difficulty walking. His condition worsened over the period of 1 hour until finally developing apnea requiring intubation. Two months beforehand, he was infected by both influenza A and COVID-19 (detected by nasopharyngeal PCR) and experienced ageusia, anosmia, myalgias, and dyspnea over the course of 1 week of illness while being managed without complications as an outpatient. He was otherwise healthy in the interim to developing neurologic symptoms.

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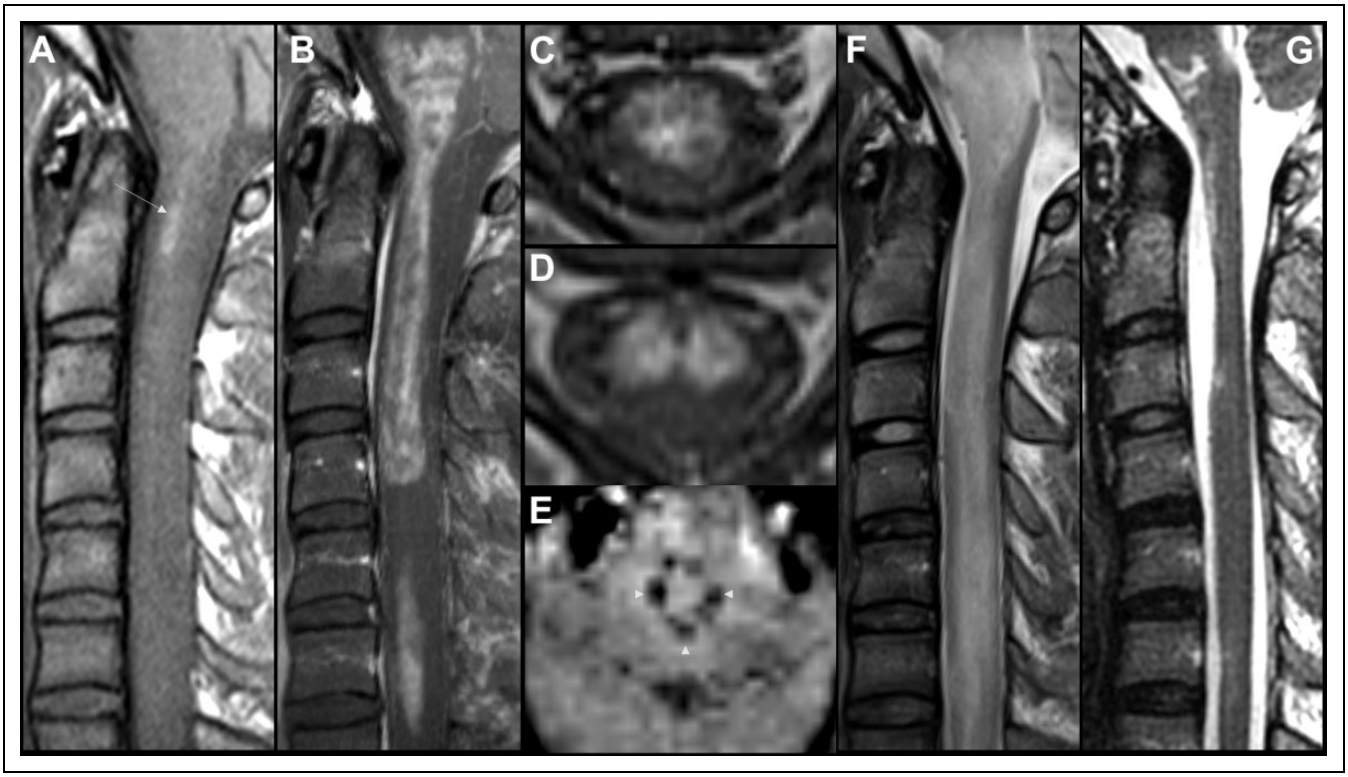

Figure 1. Representative MR images obtained on hospital day ten and 6 weeks after treatment. Sagittal T2-weighted (F) and postcontrast T1-weighted (B) images demonstrate mildly expansile and enhancing lesions affecting nearly the entirety of the medulla and extending throughout the cervical cord. Sagittal pre-contrast T1-weighted (A) and axial susceptibility-weighted (E) images show the presence of intralesional hemorrhagic foci with intrinsic T1 hyperintensity (white arrow) and local susceptibility effect (small arrow heads). Axial postcontrast T1-weighted images (C, D) illustrate the extent of the cross-sectional involvement at the C3 and C6 levels, respectively. Interval improvement with residual T2 hyperintense signal abnormalities associated with mild to moderate volume loss can be appreciated on the sagittal T2-weighted image obtained 6 weeks after treatment (panel G).

CT angiograms of the head and neck were normal in the emergency department. On hospital day two, initial MRIs of the brain and cervical spine were normal. He was initiated on anticoagulation, treated with intravenous methylprednisolone 1000 mg daily for 5 days, and underwent 5 sessions of plasmapheresis administered every other day. By day three, wakefulness and the ability to communicate were restored. On day four, a second round of MRIs revealed extensive and intense abnormalities in the cervicothoracic spinal cord and medulla.

On day ten, repeat MRIs (Figure 1) demonstrated a longitudinally-extensive expansile lesion involving the medulla and cervicothoracic spinal cord associated with heterogeneous enhancement, patchy diffusion restriction, and punctate hemorrhages in the medulla (Figure 1F). The lesion was predominantly central and ventromedial in the medulla (with some extension to the dorsomedial margin). The anterior, lateral, and dorsal columns were involved at various points throughout the spinal cord, both in combination and in isolation depending on the level. The supratentorial brain structures were not involved. An MRA of the spine, and later a cerebral and spinal angiogram, did not reveal a vascular occlusion, dissection, malformation, or arteriovenous fistula.

Extensive testing of the blood and cerebrospinal fluid for inflammatory disorders, infectious diseases, and metabolic derangements was negative (Table 1). CSF testing on 3 occasions was normal (Table 2). Importantly, the common causes of longitudinally extensive transverse myelitis were ruled-out, including testing for AQP4 and MOG autoantibodies (tested negative twice 2 months apart). A body FDG-PET/CT did not reveal any signs of sarcoidosis or malignancy. Mild FDG uptake was noted within the parenchymal signal abnormalities in the medulla and cervical cord.

On day 12, a prolonged episode of non-responsiveness with sustained up-gaze prompted fear for rostral extension of the lesion, leading to the administration of cyclophosphamide and intravenous immunoglobulin, after which he began to stabilize clinically. Follow-up MRIs of the brain and cervicothoracic spine 6 weeks later (Figure 1G) demonstrated marked improvement in the previously seen lesions with residual signal abnormality and susceptibility effect along the ventral aspect of the medulla. There were also scattered residual T2 hyperintense signal abnormalities throughout the cervical cord and significant volume loss of the medulla and cervical cord. At the last clinical follow-up 8 months after the initial attack,

the patient was fully conversant with normal mentation but remained quadriplegic with continued requirement for full ventilatory support. MRIs of the brain and cervicothoracic spinal spine were unchanged 8 months after onset.

Discussion

First described by E. Weston Hurst in 1941, acute hemorrhagic leukoencephalitis (AHLE) is considered the most severe of the central demyelinating diseases.[4] In slight contrast to ADEM which favors children, AHLE typically affects younger adults, usually men.[5] Upper respiratory tract infections are often antecedent triggers.[5] The presentation and progression are fulminant with clinical nadir commonly reached within hours. Risk for death is high in the first week. Demyelination, microhemorrhages, and edema on MRI establish the diagnosis.[6] Isolated involvement of the brainstem and spinal cord without hemispheric lesions, as in this patient, is rare, constituting just 16% of cases.[5] Death occurs in up to 46.5% of cases; full recovery is distinctly uncommon.[1,7] Survivors are often left with significant neurologic disability.[5]

Since the onset of the coronavirus pandemic, a variety of neurological complications have been described in both the para- and post-infectious periods, including stroke, encephalopathy, encephalomyelitis, and variants of Guillain-Barre syndrome.[1,8,9] Cases of supratentorial-predominant ADEM in association with microhemorrhages, some of which additionally involved the spinal cord, have been reported following COVID-19 infection.[10,11] To our knowledge, this is the first case described with isolated involvement of the spinal cord and medulla. Many of its features, including the fulminant presentation and MRI findings, are consistent with a diagnosis of AHLE.

This case highlights several atypical features of post-COVID-19 neuroinflammation. Adult COVID-19 infections have far outpaced pediatric cases, lending itself to the right demographic milieu for AHLE. A fulminant presentation may mimic a vascular process while predominance of spinal cord injury as illustrated by our patient case poses additional diagnostic challenges. Importantly, neurovascular complications related to COVID-19 infection are now well-described and should be considered as a potential mechanism for acute neurologic injury, particularly in younger patients.[11] The demographics, risk factors, MRI features, and angiogram findings are useful in distinguishing the two. However, in many instances, the vascular injury is at the microvascular level beyond angiographic resolution.

Post-COVID-19 neuroinflammatory events can involve any part of the neuraxis and the peripheral neuromuscular components, either in combination or in isolation. Up to 33% of post-COVID patients with white matter lesions may have associated microhemorrhages, which are consistent with prior MRI reports of AHLE patients.[1,5,7] A systematic review of pre-pandemic AHLE patients concluded that elevated protein and pleocytosis were seen in 87% and 65%, respectively, of reported cases.[5] In contrast to most post-infectious neuroinflammatory syndromes, including pre-pandemic AHLE, the CSF of post-COVID-19 patients may appear surprisingly unremarkable with normal cell counts in 36-73% and normal protein in 65%.[1,5,10] At the present time, further study is needed to determine the certainty and potential mechanisms behind these observations in the CSF, including analyzing the potential for this to be a unique feature of neurologic injury specific to the COVID-19 virus.

Case reports comprise the majority of the literature informing the treatment of AHLE, and together, they suggest a role

Table 1. Serum Testing, All Returning Normal or Negative.

Infections
Bacteria: Lyme Ab, RPR, interferon-gamma release assay Viruses: HIV 1/2 Ab/Ag, HTLV 1/2 PCR, coxsackievirus PCR, WNV IgM/IgG, VZV PCR, JCV PCR, CMV PCR, EBV PCR
Autoimmune Disorders
Autoimmunity markers: ANA, ESR, CRP Neuromyelitis optica spectrum disorders: AQP4 x2, MOG x2 Autoimmune encephalomyelitis: gAchR, AGNA-1, amphiphysin, ANNA-1/2/3, n- and p/q type calcium channel, CRMP-5, Yo, CASPR2, DPPX, IgLON5, LG11, NIF, Mglur1, GFAP, Ma, Ta Sarcoidosis: ACE Vasculitis: ANCA Antiphospholipid antibodies Systemic lupus erythematosus: ANA, Lupus anticoagulant Sjögren syndrome: Ro, La Rheumatoid arthritis: rheumatoid factor
Nutritional Deficiencies
B12 Folate Copper

Table 2. Cerebrospinal Fluid Testing, All Returning Normal or Negative.

Hospital day	WBC	RBC	Protein	Glucose	Infectious testing	Autoimmune studies
2	0	283	25	59	WNV PCR, HSV I/II PCR, culture	
5	5	1572	39	82	VDRL, enterovirus PCR, VZV PCR, HSV I/II PCR, culture	
12	2	1025	24	86	WNV IgM/IgG, VZV PCR, culture	OCBs, IgG index/synthesis rate, autoimmune panel

for glucocorticoids, plasmapheresis, and IVIG in its management.[5] In view of AHLE's high mortality rate, more intensive immunotherapy may be an additional consideration when the presentation is truly fulminant, as in our case, which required methylprednisolone, plasmapheresis, IVIG, and cyclophosphamide to arrest the underlying inflammatory process.[12] Exclusion of active COVID-19 infection or complicating superinfections are critically important when immunosuppressants are being considered. Thus far, recovery in those with ADEM phenotypes has most commonly been partial.[1]

Conclusion

Post-infectious central nervous system neuroinflammatory complications of COVID-19 are often associated with microhemorrhages on MRI, the absence of an inflammatory CSF profile, and high risk for permanent neurologic disability.

Authors' Note

Spencer Hutto participated in the longitudinal clinical care of this patient, had a major role in the acquisition of data and its interpretation, drafted the case report and manuscript for intellectual content, and performed the associated literature search to inform the discussion. Otto Rapalino had a major role in the acquisition of data and its interpretation and revised the manuscript for intellectual content. Nagagopal Venna participated in the longitudinal clinical care of this patient, had a major role in the acquisition of data and its interpretation, supervised the creation of the manuscript, and revised the manuscript for intellectual content. All authors have contributed substantively to the conception, design, or analysis and interpretation of the data; contributed substantively to the drafting of the manuscript or critical revision for important intellectual content; given final approval of the version to be published; and agree 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. The patient provided informed consent for publishing. No associated media files contain patient-identifiable images. Approval from our Institutional Review Board was not sought for this case report.

Declaration of Conflicting Interests

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