Neuroradiology (2023) 65:1179–1181
https://doi.org/10.1007/s00234-023-03160-7

SHORT REPORT

MRI of fatal course of acute hemorrhagic leukoencephalitis in a child with SARS-CoV-2 omicron BA 2.0 infection

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Received: 19 October 2022 / Accepted: 3 May 2023 / Published online: 18 May 2023

Abstract

We present a pediatric case of acutehemorrhagic leukoencephalitis associated with SARS-CoV-2 Omicron BA 2.0 infection. A previously healthy girl presented with ataxia and diplopia three weeks after the COVID-19 confirmation from a nasopharyngeal swab. Acute and symmetrical motor weakness and drowsiness ensued within the following 3 days. She then became spastic tetraplegic. MRI revealed multifocal lesions in the cerebral white matter, basal ganglia, and brainstem, with hemorrhagic changes confirmed with T1-hyperintensity and hypointensity on susceptibility-weighted images. Peripheral areas of decreased diffusion, increased blood flow, and rim contrast enhancement were noted in the majority of lesions. She was treated with a combination of intravenous immunoglobulin and methylprednisolone pulse therapy. Neurological deterioration ensued with coma, ataxic respiratory pattern and decerebrate posture. Repeated MRI performed on day 31 revealed progression of abnormalities, hemorrhages and brain herniation. Despite the administration of plasma exchange, she died two months after admission.

Keywords Acute hemorrhagic leukoencephalitis · MRI · SARS-CoV-2 Omicron BA 2.0 Infection · Mortality

Introduction

Acute hemorrhagic leukoencephalitis (AHLE), also known as Hurst disease, is a severe variant of acute disseminated encephalomyelitis (ADEM) which is an uncommon inflammatory disease predominantly affecting the white matter of the CNS [1, 2]. AHLE is characterized by acute onset and rapid progression, having higher rate of morbidity and mortality than ADEM. Reports of severe neurological involvement in children with COVID-19 have emerged, documenting the neuroimaging features of encephalitis, fulminant brain edema, and ADEM [3]. AHLE has been infrequently reported in children, with a mortality rate of 50% [1]. COVID-19 associated AHLE has been rarely reported [4, 5].

We herein reported remarkable MRI findings of AHLE in a 9-year-old girl with SARS-CoV-2 Omicron BA 2.0 and mortality. The imaging findings assessed using advanced MRI techniques may provide pathophysiological insights into AHLE.

Case presentation

A previously healthy 9-year-5-month-old girl had fever (40.3 ℃) for 1 day when she had positive SARS-CoV2 Omicron BA 2.0 real-time-PCR (RT-PCR) from a nasopharyngeal swab. Three weeks later, she had ataxia and diplopia. Acute and symmetrical motor weakness and drowsiness ensued within the following 3 days. No respiratory symptoms had been noticed. At emergency department, she could follow commands. She had isochoric and photoreactive pupils, but presented with crossed eyes and lacked oculocephalic, corneal, cough, and gag reflexes. She had positive Babinski signs and was spastic tetraplegic. Laboratory examination revealed normal C-reactive protein, procalcitonin, and leukocyte count. SARS-CoV-2 RT-PCR was still positive (nasopharyngeal

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swab, cycle threshold value 31.26) on the 5th day of symptoms. Cerebrospinal fluid analysis demonstrated 46.3 mg/dL of protein (<40 mg/dL), 1 cell/uL of white blood cell (<5 cell/uL), 0.33 of IgG index (0.6), and no oligoclonal band. FilmArray Meningitis/Encephalitis panel, RT-PCR for SARS-CoV-2, and fungal and bacterial cultures were all negative. CT revealed multifocal hypodensities in the cerebral white matter, basal ganglia, and brainstem (Fig. 1). MRI performed on day 11 revealed hemorrhagic changes of the lesions, confirmed with hyperintensity on T1-weighted images (T1W) and hypointensity on susceptibility-weighted images (SWI). Peripheral areas of decreased diffusion, increased blood flow on arterial spin-labeling imaging (ASL), and rim contrast enhancement were noted in the majority of lesions. The diagnosis of AHLE was made on the basis of the topography and the imaging characteristics of the abnormalities. She was treated with 2 courses of a combination of intravenous immunoglobulin and methylprednisolone pulse therapy (30 mg/kg/day). She was placed on mechanical ventilation. Neurological deterioration ensued with coma, ataxic respiratory pattern, absent brainstem reflex, and decerebrate posture. Repeated MRI performed on day 31 revealed progression of abnormalities, hemorrhages and brain herniation (Fig. 2). Two cycles of plasma exchange were given. She died two months after admission. Autopsy was not performed because of religious belief of the family.

Discussion

In children with COVID-19 infection, the majority of reported serious neurological complications included, but were not limited to, encephalitis, acute necrotizing encephalopathy, ADEM, cytotoxic lesion of the callosal splenium, posterior reversible encephalopathy syndrome, venous sinus thrombosis, vasculitis and infarction, Guillaine Barre syndrome, transverse myelitis, and myositis [3]. AHLE have been rarely reported in COVID-19, including the first pediatric case reported by Sharma et al. [4, 5]. Comparing with the preceding pediatric case with COVID-19 associated AHLE [5], our patient had a COVID-19 infection with the Omicron BA 2.0 subtype. a more protracted course (died 4 weeks after diagnosis), a more widespread distribution of imaging abnormalities, and ASL and MRA imaging to provide hemodynamic information of the abnormalities.

Characteristic neuroimaging findings of ADEM are multifocal punctate to flocculent, asymmetrical lesions over subcortical and deep white matter regions, with less frequent involvement of the deep gray nuclei, brainstem, and cerebellum [6]. In addition to these findings, AHLE is characterized by the presence of microhemorrhage in the lesions, with the hemorrhage showing hyperintensity on T1W, hypointensity on T2W/FLAIR images and hypointensity with blooming on SWI.

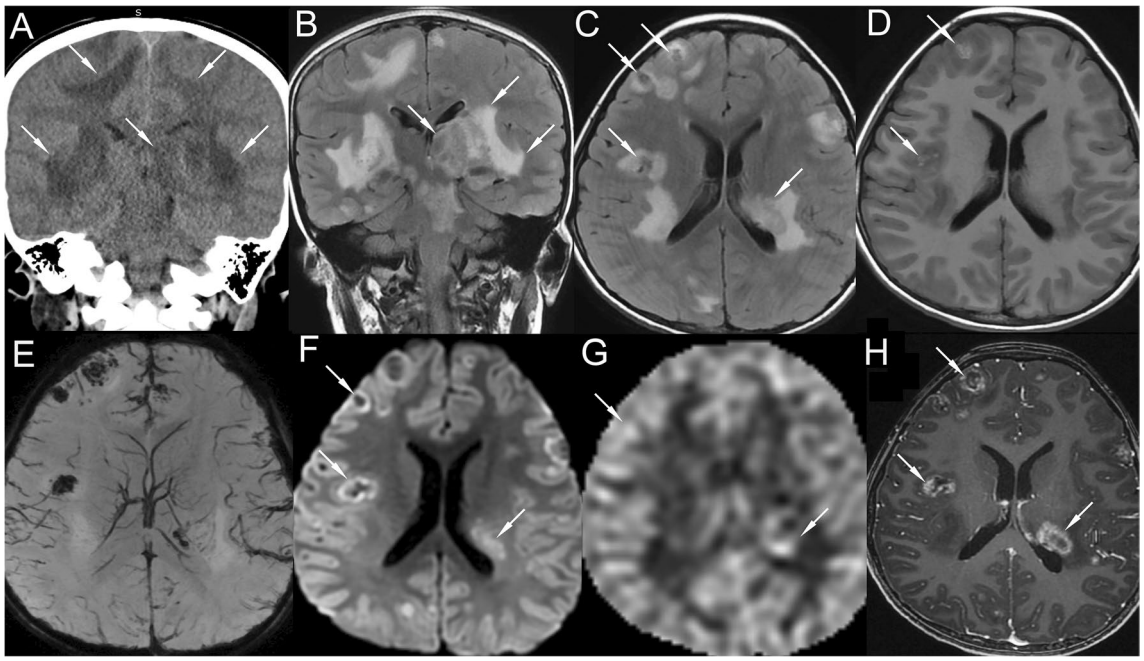

Fig. 1 Acute hemorrhagic leukoencephalitis in a 9-year-and-5-month-old girl presenting with ataxia, diplopia, and drowsiness. (A) Coronal CT image shows patchy hypodensities (arrows) in the cerebral white matter, basal ganglia, thalami, and pons. (B) Coronal and (C) axial FLAIR MR images show patchy hyperintensity mixed with hypointensity in the lesions (arrows), suggesting hemorrhagic change. The hemorrhages are confirmed with hyperintensity (arrows) on axial T1-weighted image (D) and hypointensity on axial susceptibility-weighted image (SWI) (E). The periphery of the lesions shows restricted diffusion (arrows) on axial diffusion-weighted image (F), increased blood flow (arrows) on axial arterial spin-labeling image (G), and contrast enhancement (arrows) on axial post-contrast T1-weighted image (H)

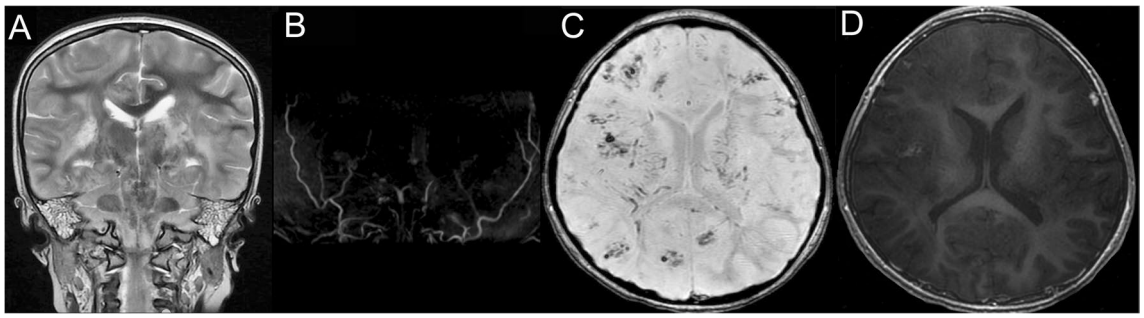

Fig. 2 Repeated MRI performed on day 31 reveals diffuse edema of the brain and progression of the white matter lesions on coronal T2-weighted image (A), loss of vascular flow of the brain on MRA image (B), progression of hemorrhages on axial SWI (C), and loss of the normal intracranial vascular enhancement on axial post-contrast T1-weighted image (D)

Proposed mechanisms of neurological diseases in COVID-19 include both direct damage by the SARS-CoV-2 virus and indirect injury by the cytokine storm [7]. Neuropathological findings included both vascular and demyelinating features, revealing hemorrhagic white matter lesions, vasculitis, and surrounding axonal injury and macrophages [8]. The advanced MRI findings in our patient suggested a pronounced disease activity: the SWI hypointensities indicating hemorrhages, the contrast enhancement representing a blood–brain barrier breakdown and thus a vascular injury, the elevated blood flow on ASL perfusion imaging representing increased vascularity[9], and the reduced diffusion indicating active demyelination[10]. We speculated that these imaging features might reflect the neuropathology of AHLE.

Dismal outcome was observed in our patient (mortality) and in the previously reported child [5] with severe neurological deterioration and mortality. Recognition of the characteristic imaging features of AHLE should alert clinicians of the rapid disease progression and justify earlier intervention using multidisciplinary medical measures.

Author contributions Conceptualization: Alex Mun-Ching Wong, Jainn-Jim Lin; Data curation: Alex Mun-Ching Wong,

Jainn-Jim Lin, Shao-Hsuan Hsia; Formal analysis and investigation: Alex Mun-Ching Wong, Jainn-

Jim Lin, Kuang-Lin Lin; Writing—original draft preparation: Alex Mun-Ching Wong, Jainn-Jim.

Lin; Writing—review and editing: Alex Mun-Ching Wong.

Compliance with ethical standard

Conflict of interest The authors have no competing interests todeclare that are relevant to the content of this article.

Ethical approval No ethical approval for study type.

Patient consent Patient consent obtained for all subjects — no patient identifiable information included in article..

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