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Clinical Letter

Acute Fulminant Cerebellitis in Children with COVID-19 Infection: A Rare But Treatable Complication

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The past year, coronavirus disease 2019 (COVID-19) has displayed widespread systemic manifestations including neurological features (up to 36%) such as stroke, myelitis, and encephalitis.[1,2] We draw attention to two children with COVID-19-associated acute fulminant cerebellitis and discuss the treatment challenges.

Patient 1 is a 12-year-old boy who presented with headache and altered mental status for 15 days along with short-duration fever and projectile vomiting. He was drowsy with fluctuating alertness but had no focal deficits or incoordination in bed. Computed tomography of the head showed ill-defined right cerebellar hemispheric hypodensity with compression of fourth ventricle and resultant obstructive hydrocephalus (Fig A). In view of bradycardia and increasing drowsiness, an external ventricular drain (EVD) was placed in the right lateral ventricle through the right frontal Kocher point burr hole, resulting in improvemed sensorium and now evident gait ataxia. Magnetic resonance imaging (MRI) of the head revealed confluent asymmetric (right > left) hyperintensities involving both cerebellar hemispheres with faint folial enhancement, without restricted diffusion or microhemorrhages (Fig B).

Patient 2 is a 10-year-old boy who presented with new-onset, severe occipital headache for two days and nonprojectile vomiting. He was drowsy, highly irritable and exhibited mild left-sided dysmetria, dysdiadochokinesia, and gait ataxia. Computed tomography of the head revealed ill-defined hypodensity involving both cerebellar hemispheres (left > right) with effacement of the fourth ventricle leading to supratentorial ventriculomegaly (Fig D). A temporary EVD was placed for three days. MRI of the brain confirmed cerebellar hyperintensities on T2 and fluid-attenuated inversion recovery (FLAIR) without hemorrhages (Figs E and F).

In both patients, imaging features were consistent with isolated cerebellitis. Nasopharyngeal swab was positive for reverse transcription-polymerase chain reaction (RT-PCR) for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Hematologic, biochemical, serologic, and ancillary tests ruled out endemic causes of cerebellitis such as malaria, dengue, and typhoid. Lumbar puncture was not attempted in either patient but ventricular cerebrospinal fluid (CSF) was analyzed. Patient 1 had 5

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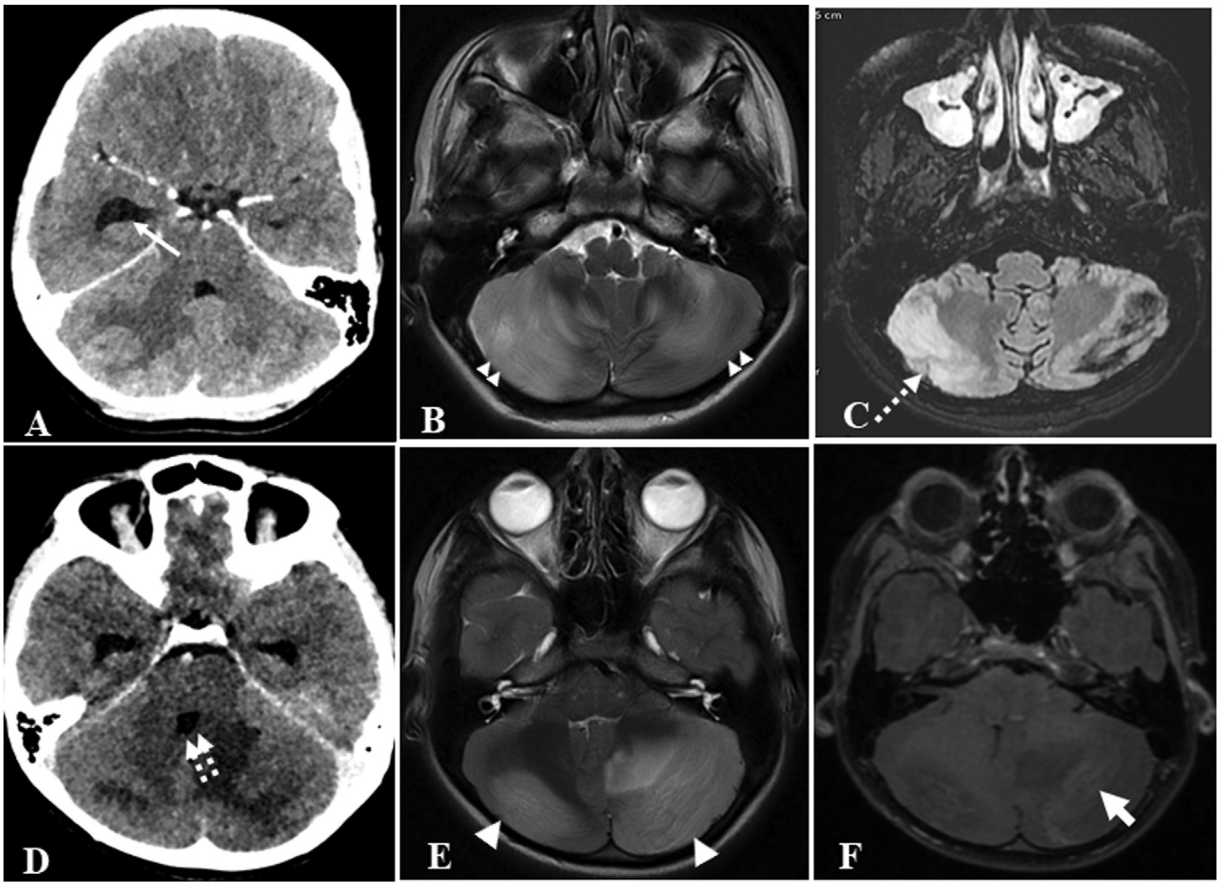

FIGURE. (A) Axial noncontrast computed tomographic (CT) brain image from Patient 1 shows asymmetric hypodensity involving the cerebellar hemispheres (right > left) with displacement of the fourth ventricle toward the right and a dilated temporal horn (white arrow). (B) Axial T2 MRI confirms confluent cerebellar hyperintensity (small double arrowheads) with compression of the fourth ventricle and mild ventricular prominence (after external ventricular drain placement). (C) Follow-up axial T2 image shows residual minimal signal changes in the right cerebellar hemisphere (dashed arrow) after six weeks. (D) Axial noncontrast CT brain image from Patient 2 shows asymmetric hypodensity involving the cerebellar hemispheres (left > right) displacing fourth ventricle toward right (double dashed arrows). (E) Axial T2 MRI confirms confluent cerebellar involvement (arrowheads) and compression of fourth ventricle. (F) Contrast-enhanced T1 image shows patchy folial enhancement (thick white arrow).

lymphomocytes/mm^3; protein, 8 mg/dL; and glucose, 75 mg/dL (corresponding blood glucose 108) and Patient 2 had protein, 15 mg/dL; glucose, 89 mg/dL (corresponding blood glucose 115 mg/dL); and 5 lymphocytes/mm^3. CSF Gram, India ink, and acid-fast bacilli stains; aerobic culture; and fungal cultures were negative, as was the analysis for adenovirus, enteroviruses, Epstein-Barr virus, human herpesvirus-7, human herpesvirus-6, human parechovirus, parvovirus B19, varicella zoster virus, cytomegalovirus, herpes simplex virus 1 (HSV-1), and HSV-2. CSF was also negative for RT-PCR for SARS-CoV-2. Both children improved and maintained sensorium with temporary EVD without need for posterior fossa decompression. In addition, steroids and acyclovir were administered for 14 days despite negative CSF-PCR for HSV and other neurotropic viruses because of rapid and dramatic improvement. The patients had recovered without sequelae at six weeks (Fig C) and three months, respectively, with radiological resolution of cerebellar signal changes.

These patients highlight moderate to severe acute cerebellitis as a rare presentation of COVID-19, which, if left unattended, can be fatal. Acute cerebellitis in children has been documented with varicella zoster, herpes simplex, Epstein-Barr, rotavirus, echovirus, coxsackie, mumps, measles, and rubella; affected individuals can exhibit both cerebellar and extracerebellar manifestations.[3] Acute cerebellitis and parainfectious/postinfectious or postvaccinial cerebellar ataxia form a clinical spectrum of cerebellar ataxia in relation to infection. Clinicoradiological differentiation between them includes the timeline of presentation, altered sensorium, signal abnormalities and edema on MRI, and significant clinical and radiological asymmetry.[3] In our patients, SARS-CoV2 is a possible cause for cerebellitis due to positive nasopharyngeal RT-PCR at admission, reiterating its neurotropic and neuroinvasive potential even though neuropathologic evidence of encephalitis or cerebellitis in COVID-19 is lacking.

There are only two reports of acute COVID-19-related cerebellitis, although ataxia due to stroke, Miller Fisher syndrome, or demyelination has been documented.[1,4,5] The previous patients with cerebellitis were both adults (47 and 30 years) who had ataxia and mild, medication-responsive extracerebellar symptoms.[4,5] The severity of acute cerebellitis ranges from a benign, self-limiting illness to more fulminant disease. Our children had more fulminant disease, acute cerebellar inflammation and swelling leading to brainstem compression, acute hydrocephalus, and altered sensorium.[6] The presence of acute increased intracranial pressure with inflammation is a life-

threatening situation requiring urgent surgical intervention with CSF diversion in order to avoid brainstem compression and herniation.[6] It is important to avoid lumbar puncture in order to avoid catastrophic brain herniation.

Although steroids and antiviral agents may be beneficial in cerebellitis, trial medications like lopinavir have been given to some individuals with COVID-19 encephalitis and cerebellitis with improvement, whereas others improved without specific antivirals.[2,4,5] At this point, it is not possible to distinguish COVID-19-related cerebellitis from that related to other viruses. I Our pediatric patients with severe COVID-19 cerebellitis had a good outcome with aggressive management.

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