Neurocrit Care (2019) 31:559–561
https://doi.org/10.1007/s12028-019-00801-9

NEUROCRITICAL CARE SOCIETY

PRACTICAL PEARL

Cerebellitis with Mass Effect: A-Not-So-Everyday Problem for the Neurointensivist

Lauren Jackson[1], Edison Cano Cevallos[2] and Eelco Wijdicks[1*]

Keywords: Cerebellitis, Ataxia, Edema, Hydrocephalus

Case Presentation

A 25-year-old woman had otherwise been in normal health until approximately 1 week earlier, when she presented to her primary care provider with a 2-day history of painful mouth ulcers, sore throat, and watery diarrhea. She denied any fever or upper respiratory symptoms, such as cough or rhinorrhea, at that time. She denied any other rashes. She had reported that her nephew had been diagnosed with hand–foot–mouth disease earlier that month; otherwise, she denied any sick contacts. She was treated conservatively by her physician.

Approximately 7 days after initial symptoms, she developed an acute progressive holocephalic headache, accompanied by nausea and vomiting, and progressed to full-body myalgias. She presented to the emergency department several times for the above symptoms and ultimately underwent a computed tomography (CT) scan without contrast of the brain, which was negative for any abnormalities. Her headache persisted, and she was admitted to the outside hospital a week later. Initially, she was treated with acetaminophen, ketorolac, morphine, oxycodone, and ondansetron. Magnetic resonance imaging (MRI) with and without contrast was done on admission, which demonstrated meningeal enhancement predominantly involving the posterior fossa.

A lumbar puncture done the next day demonstrated opening pressure of 38 mmHg. Total nucleated cell count in cerebrospinal fluid (CSF) was 201, with lymphocytic predominance (88%), monocytes 9%, red blood cell count 8, glucose 56, and protein 141. CSF polymerase chain reaction (PCR) studies were negative for enterovirus, cytomegalovirus, human herpesvirus 6, *Cryptococcus*, *Haemophilus influenzae*, *Listeria monocytogenes*, *Neisseria meningitidis*, *Streptococcus pneumoniae*, varicella zoster virus, and herpes simplex virus 1 and 2. CSF bacterial and fungal cultures were all negative. Influenza A and B antigens from a nasal swab were negative. Further studies reportedly included human immunodeficiency virus antibodies, arbovirus serologies, and West Nile serologies, all of which were negative.

She developed progressive dysarthria and diplopia. A repeat CT demonstrated mild cerebellar edema, although the 4th ventricle remained patent. A repeat MRI demonstrated diffusion restriction of cerebellum, left greater than right, as well as ongoing leptomeningeal enhancement predominantly involving the posterior fossa (Fig. 1). She was given 10 mg of dexamethasone and transferred to the intensive care unit for further care.

Her examination was notable for saccadic eye movements, left sixth nerve palsy, ataxic dysarthria, overshoot on Holmes rebound testing, and intention tremor noted with finger-to-nose testing and heel-to-opposite shin testing. Head titubation seen in predominately midline lesions was absent (Video I). Acyclovir was continued for 24 h until viral studies were confirmed negative in the CSF. She was continued on dexamethasone, 4 mg

*Correspondence: wijde@mayo.edu
[1] Department of Neurology, Mayo Clinic, 200 First Street SW, Rochester, MN 55905, USA
Full list of author information is available at the end of the article

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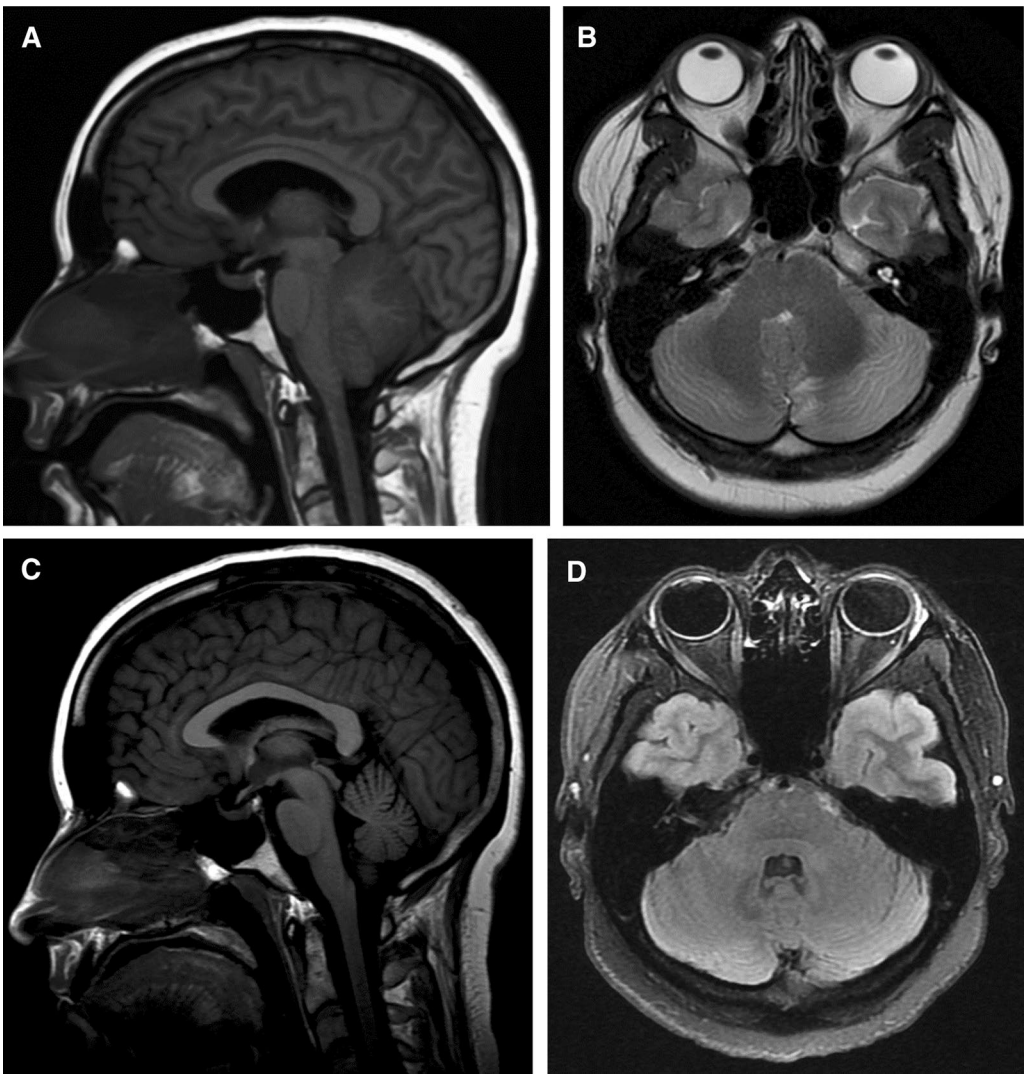

Fig. 1 MRI scans. From left to right, up to down: **a** T1 sequence, showing hypointense, edematous cerebellar hemispheres with significant bowing of the pons, compression of the quadrigeminal plate and full obliteration of the aqueduct and 4th ventricle. **b** T2 sequence, showing hyperintense cerebellar hemispheres. **c** T1 fluid attenuated inversion recovery (FLAIR) showing atrophy of the cerebellar hemispheres. **d** T2 FLAIR sequence, showing normalized hyperintensity

every 4 h, and continued to exhibit clinical improvement throughout her stay.

A serum paraneoplastic panel demonstrated borderline positivity of GAD-65 but was otherwise negative for all other antibodies. Infectious disease consultants recommended additional testing for enteroviruses in the blood and stool. Her serum *Mycoplasma pneumoniae* IgG was positive; IgM was reactive, but confirmatory immunofluorescence assay was negative. Mycoplasma pneumoniae PCR from CSF was negative. Further molecular testing sent to the Centers for Disease Control came back negative for enteroviruses including pan-enterovirus real-time molecular assay, pan-parechovirus real-time molecular assay and pan-EV molecular assay targeting the viral protein 1 (VP1) region.

Neurosurgery recommended conservative management. The patient continued to improve over the next week, and she was discharged home with outpatient physical therapy. She was seen back in clinic in 3-month follow-up with essential resolution in her symptoms. A repeat MRI demonstrated mild cerebellar atrophy with resolution of the previously seen areas of T2 hyperintensity and leptomeningeal enhancement (Fig. 1).

Discussion

We present a patient with viral cerebellitis, who had severe involvement of the brainstem and cerebellum and who presented with profound headache, nausea, diplopia, and ataxia. Brain MRI initially demonstrated diffuse cerebellar edema and mild hydrocephalus. She exhibited clinical improvement over the course of 3 months despite cerebellar atrophy noted on follow-up MRI. Infectious disease testing was extensive and ultimately negative for an etiology. Given negative viral serologies and molecular tests in the CSF, blood, and feces, a parainfectious etiology secondary to a systemic viral infection was considered the most likely cause. Due to her history of prior exposure to suspected coxsackievirus, this was ultimately determined to be the source of infection.

Viral cerebellitis is a rare disease characterized by symptoms associated with pancerebellar syndrome. Acute cerebellitis has been reported in association with varicella, Epstein–Barr virus, mycoplasma pneumoniae, rotavirus, human herpesvirus 7, and influenza. A majority of cerebellitis cases are described in children, and little is known about the characteristics and outcomes of cerebellitis in adults. Overall, the most common etiologies in adults are unknown (34%), medication-induced (11%), paraneoplastic (9%), and parainfectious (6%) [1]. The cerebellum is an immunologic target, possibly because Purkinje cells express multiple antigens [2]. Interestingly, in our patient, GAD-65 was borderline positive, and there is a known degree of heterotypic cross-reactivity between coxsackievirus B4 nonstructural p2C antibodies and GAD65 antibodies, further supporting the hypothesis that coxsackie virus was the precipitating viral illness [3]. CSF studies can be helpful to work up infectious etiologies; the risk of herniation must be considered in patients who have significant cerebellar edema. CSF leukocytes can vary widely in adults with cerebellitis (0–797 leukocytes) [1]. Though imaging can be normal, 80% of cases display abnormalities on FLAIR, diffusion weight imaging, and T1 post-gadolinium sequences [1]. Due to risk of developing hydrocephalus, patients will often need admission to an intensive care unit for monitoring and should be treated with steroids to temporize further swelling. In a prior case series, hydrocephalus was noted in 26% of cases of acute cerebellitis, with 7/9 requiring neurosurgical intervention with extra-ventricular drain placement [4]. Of note, no reported cases have required suboccipital decompressive craniotomy. At least three-quarters of adult patients with cerebellitis have cerebellar atrophy noted on follow-up MRI, and half of all patients suffer residual neurologic symptoms [2, 5].

In summary, acute cerebellitis is characterized by acute-onset headache and ataxia and is often diagnosed on MRI, although CSF studies can be helpful in working up infectious etiologies. Steroids should be used in the acute setting when cerebellar edema is present, and ICU monitoring should be considered in the acute phase in case of deterioration and need for neurosurgical intervention and in most instances a ventriculostomy. We were unable to find a documented case of suboccipital decompressive craniotomy in the literature, but our case also demonstrates that close and expert monitoring of clinical signs can be sufficient. To intervene solely on the basis of MRI studies alone—even impressive studies—is currently not supported by evidence. Outcomes are variable, but a majority of cases have long-lasting cerebellar atrophy noted on follow-up imaging.

Electronic supplementary material
The online version of this article (https://doi.org/10.1007/s12028-019-00801-9) contains supplementary material, which is available to authorized users.

Author details
[1] Department of Neurology, Mayo Clinic, 200 First Street SW, Rochester, MN 55905, USA. [2] Department of Infectious Diseases, Mayo Clinic, Rochester, MN, USA.

Author's Contributions
LJ was involved in study concept and design, acquisition of data, analysis and interpretation, and drafting of the manuscript. ECC was involved in analysis and interpretation and drafting of the manuscript. EW was involved in study concept and design, analysis and interpretation, and critical revision of the manuscript for important intellectual content.

Source of Support
No source of support was used to fund this report.

Conflicts of Interest
All authors declare that they have no conflicts of interest.

Informed Consent
Informed consent was obtained from the patient.

Publisher's Note

Published online: 1 August 2019

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