eAppendix 1: Supplementary description of seven cases who required medical and/or surgical ICP management

Cases 1, 6, and 7

These cases have been previously published [1]. An update on their outcomes at follow-up is described in **Table 3** and briefly here. Case 1's MRI brain 4 months following his presentation showed progressive ventriculomegaly with multifocal cystic encephalomalacia most pronounced within the hemispheres. He did not have neuropsychological evaluation due to limited neurological function; per chart review, he was described as having global developmental delay with problems reported in language, attention, and behavior. His anti-MOG-IgG was 1:10000 at onset and remained positive at 1:100 twenty months after onset. He passed away 2 years from onset due to respiratory complications of hypoxic/ischemic injury from MOGAD. Case 6's MRI brain 4 months from her presentation showed evolving atrophy and multifocal gliosis and 5 years later showed stable atrophy. Her longitudinal neuropsychological profile, showing worsening over time, is indicative of "growing into deficits," with her most recent evaluation indicating deficits with nonverbal reasoning, executive functioning, memory, processing speed, and fine-motor skills. She was diagnosed with attention-deficit hyperactivity disorder (ADHD), combined type, as well as learning disorders in reading and math. Her anti-MOG-IgG was positive (1:100) when first tested 7.5 years following disease onset. Case 7's MRI brain 4 months out showed cerebral volume loss with ex-vacuo dilation of the ventricles, multifocal areas of abnormal signal, multifocal parenchymal hemorrhage; 4.5 years later, it showed extensive gliosis and volume loss involving the corpus callosum, both cerebral hemispheres and central gray matter. Neuropsychological evaluation at age 8 (nearly 5 years following disease onset) showed generally global deficits across nonverbal reasoning, visual, motor, expressive language, attention, memory, reading, and math with preserved verbal comprehension. Reading skills and early math concepts were equivalent to that of a 4-year-old. Her anti-MOG-IgG on initial testing 5 years from disease onset was positive (1:100).

Case 2

A 6-year-old Asian boy with a history of asthma was admitted for altered mental status (AMS) in the setting of fever, upper respiratory symptoms, and diarrhea. On admission, he was managed as having bacterial versus viral meningitis, with cerebral spinal fluid (CSF) studies showing 372 white cells and 162 mg/dL protein. Admission head CT head showed mild cerebral edema, and an OP was not recorded. His video electroencephalogram (EEG) on hospital day (HD) 1 showed continuous, generalized slowing and no seizures. He was subsequently transferred to the intensive care unit (ICU) on HD 5 after his clinical status worsened and he became increasingly unresponsive. He was intubated for AMS and hypercapnic respiratory failure. He developed bradycardia, hypertension and pinpoint pupils concerning for elevated ICP, which was supported by changes on follow-up CT imaging showing effacement of the peripheral sulci and basal cisterns. An ICP monitor was placed on HD 5. Subsequent brain MRI on HD 6 showed extensive T2 signal abnormalities and restricted diffusion with predominant involvement of the supra and infratentorial white matter. For ICP management, he received hyperosmolar therapy with mannitol and a hypertonic saline infusion as well as intravenous dexamethasone. Vecuronium and pentobarbital infusions were started on HD 7 and continued until HD 17 and 16, respectively. He had repeat LP on HD 11, with a lumbar drain placement to drain for ICP spikes lasting >5 minutes. Acetazolamide was added on HD 12. The ICP monitor and lumbar drain were removed on HD 22. For acute immunotherapies, he was started on methylprednisolone on HD 6, plasma exchange (PLEX) on HD 7, and intravenous immunoglobulin (IVIG) on HD 21. He was extubated on HD 24. He started recognizing his parents, saying words, and moving his extremities on HD 25. He was transferred to inpatient rehabilitation on HD 34 and had marked improvements in speech and motor skills.

Two and a half months later, at clinic follow-up, he had no further headaches and his acetazolamide was tapered off over the next month. MRI brain 3 months following his presentation

showed significant interval improvement, with scattered areas of subcortical gliosis and persistent abnormal signal intensity in the right hippocampus with evolving right mesial temporal sclerosis. MRI brain 4 years later showed persistent abnormal signal in right hippocampus with mild interval decrease in degree of white matter signal abnormality. Longitudinal neuropsychological evaluation showed reductions in performance over time, most notably in attention, working memory, and fine-motor skills. His most recent neuropsychological evaluation 4 years later showed above average intelligence and intact academic skills in math and reading. Deficits were noted in attention, executive functioning, fine-motor skills, motor-based processing speed, and academic skills fluency. He was diagnosed with ADHD, combined type. Anti-MOG-IgG titer was 1:1000 at onset and remained positive at 1:40 four years later.

Case 3

A 3-year-old African American boy with a history of laryngomalacia, recurrent otitis media, and gastric reflux was admitted for new onset seizures in the setting of fever. He was given lorazepam and started on levetiracetam for maintenance therapy. Initial routine EEG showed generalized delta slowing. On HD 2, an MRI showed multifocal cerebral and spinal lesions, and LP showed an elevated OP of 42.5 cmH_2O. He was transferred to the ICU on HD 2 for closer neurologic monitoring. He had breakthrough seizures on HD 3 and was noted to have a new left hemiparesis. A head CT suggested progression of cerebral edema and he was intubated on HD 3. For ICP management, he was given hypertonic saline boluses with a serum sodium goal >145 mEq/L. He was started on methylprednisolone on HD 2, PLEX on HD 4, and IVIG on HD 13. He was extubated on HD 7. His course was complicated by involuntary abnormal movements for which he was treated with valium and gabapentin and started on baclofen and botulinum toxin for spasticity. He was transferred to inpatient rehabilitation on HD 23.

MRI brain 3 months later showed interval decrease in T2 signal abnormalities, with new areas of gliosis and small areas of encephalomalacia in both frontal lobes. His levetiracetam, valium, gabapentin and baclofen were tapered off by his 12-month follow-up. His neuropsychological evaluation after 20 months showed intact nonverbal intelligence with deficits noted in language, attention, memory, and fine-motor skills. He continued to meet criteria for a language disorder. Anti-MOG-IgG titer was 1:1000 at onset and negative 15 months later.

Case 4

A 10-year-old African American boy with a history of chromosomal 6p16 deletion, developmental delay, asthma, and obesity was admitted for AMS and seizures in setting of fever, headaches, and body aches. On arrival to the ED, he was noted to be unresponsive with eye deviation. Seizures were treated with benzodiazepines, and he was intubated. A head CT was concerning for diffuse cerebral edema. Hypertonic saline was given, and he was admitted to the ICU. On HD 1, a brain MRI showed multifocal lesions of restricted diffusion involving the bilateral frontal lobes, parietal lobes, temporal lobes, and left occipital lobe with associated leptomeningeal enhancement. Initial video EEG showed subclinical status epilepticus, for which he was treated with multiple anti-seizure medications (diazepam, lacosamide, fosphenytoin) followed by midazolam boluses and infusion on HD 1 and 2. LP was done with interventional radiology (IR) guidance on HD 2, with no OP measurement. While in the IR suite, he was noted to have bradycardia to 70s and hypertension with systolic blood pressure of 150 mmHg. A repeat head CT showed worsened cerebral edema with downward cerebral herniation without tonsillar herniation. Due to presumed elevated ICP and continued abnormal EEG, he was started on pentobarbital on HD 3 but this was discontinued on HD 4 due to development of lactic acidosis and concern for propylene glycol toxicity. He was restarted on midazolam infusion until HD 7 and continued lacosamide and levetiracetam for maintenance therapy. For immunotherapy, methylprednisolone was started on HD 3 and IVIG on HD 8. After anti-MOG-IgG returned positive (1:1000) on HD 17, he was

started on a 7-week oral steroid taper. He was extubated on HD 13 and transferred to inpatient rehab on HD 25.

He was seen in clinic 10 days after discharge. Prior to admission, he was able to carry on basic conversations, add and subtract double digits, feed himself, walk and run. Due to behavioral presentation in the rehabilitation setting, he was unable to engage in inpatient neuropsychological evaluation. Post-hospitalization, he was non-verbal, required assistance with feeds, and could ambulate independently for short distances. Follow-up MRI 3 months later showed multifocal cortical encephalomalacia, global atrophy and compensatory dilatation of the ventricular system. Anti-MOG-IgG titer remained positive 5 months later at 1:100.

Case 5

An 11-year-old African American/Hispanic twin with a history of dyslexia was admitted for headaches, neck pain, increased sleepiness and decreased oral intake. Admission head CT showed mild cerebral edema, and LP showed 39 white cells in the CSF with no OP measured. He became increasingly obtunded and was intubated and transferred to ICU on HD 2. A brain MRI showed widespread cerebral edema and restricted diffusion involving the cerebral cortex, with additional lesions involving the right anterior corpus callosum, thalami, and brainstem. He was treated with methylprednisolone starting on HD 2 and PLEX on HD 3. He was noted to have unequal pupils on HD 4, with a head CT showing mild mass effect and more pronounced left to right subfalcine shift. He was given hypertonic saline boluses. He was extubated on HD 8, transferred to the floor on HD 9, and discharged home shortly after.

His neuropsychological evaluation at 3 months out showed he had intact skills in many areas, with some mild weakness in working memory, fine-motor coordination, and performance speed. Of note, he had a premorbid diagnosis of learning disorder in reading. MRI brain 4 months later showed significant improvement with faint residual T2 prolongation in the left frontal lobe, insula, and anterior temporal lobe. Anti-MOG-IgG titer was 1:100 at onset and remained positive at 1:20 eight months later.

eTable 1. Comparison between those for whom opening pressure was or was not available.

	Opening pressure not available (n=42)	Opening pressure available (n=43)	P-value
Age at onset, median (IQR) (years)	7.2 (3.9-11.9)	9.9 (4.9-13.2)	0.070
Female gender, n (%)	20 (52.4%)	23 (46.5%)	0.589
Headache on admission, n (%)	11 (26.9%) (n=41)	14 (32.6%)	0.522
GCS ≤12 on admission, n (%)	4 (9.5%)	2 (4.7%)	0.379
ADEM, n (%)	17 (4.0%)	14 (32.6%)	0.447
ICU stay, n (%)	11 (26.2%)	10 (23.3%)	0.757

eTable 2. Additional details on the cases who required acute medical and/or surgical ICP management. MRI, magnetic resonance imaging; CSF, cerebral spinal fluid; WBC, white blood cell; RBC, red blood cell; EEG, electroencephalogram; CYC, cyclophosphamide; RTX, rituximab; MMF, mycophenolate mofetil; IVIG, intravenous immunoglobulin.

	Case 1[a]	Case 2	Case 3	Case 4	Case 5	Case 6[a]	Case 7[a]
Year at presentation	2018	2018	2019	2022	2019	2010	2013
Presenting symptoms	Somnolence, altered mental status, sore throat, nausea, fever	Somnolence, altered mental status, unable to walk, fever	Seizures, fever	Altered mental status, seizure, fever	Headaches, neck pain, ataxia, increased sleepiness, decreased oral intake	Somnolence, altered mental status, vomiting	Seizure, fever
MRI spine on admission	Normal	Normal	Abnormal cord signal at T1/T2 and T8	Normal	Multifocal abnormal central cord and conus signal, with subtle patchy enhancement and long segment thoracic cord involvement	Normal	Not done
CSF findings on admission	WBC 16 (32% lymphocytes), RBC 0, protein 30, glucose 62	WBC 372 (49% lymphocytes), RBC 2, protein 136, glucose 63	WBC 8 (50% lymphocytes), RBC 1, protein 20, glucose 59.	WBC 213 (87% lymphocytes), RBC 1, protein 88, glucose 68	WBC 39 (81% lymphocyte), RBC 2, protein 25, glucose 69	WBC 20 (18% lymphocytes), RBC 12, protein 44, glucose 90	WBC 56 (24% lymphocytes), RBC 1, protein 23, glucose 48
EEG on admission	Generalized electrodecremental segment and polymorphic delta slowing	Generalized, polymorphic delta and theta slowing	Generalized, polymorphic delta slowing	Generalized slowing with relative attenuation over right hemisphere, lateralized periodic discharges with overlying sharps that showed evolution consistent with ictal-interictal continuum	Not done	Generalized slowing	Generalized slowing

Number of days intubated	38	20	5	13	7	17	17
Discharge exam	Visually tracks, blinks or intermittently nods/shakes his head to answer, sits with support and holds his head upright for up to 30 seconds, grasps and releases various objects, has gastrotomy tube, breathing on room air	Speaks in sentences, carries out activities of daily living with mild assistance, ambulates independently for short distances, has nasogastric tube, breathing on room air	Speaks 1-2 word phrases, ambulates independently for short distances, has nasogastric tube, breathing on room air	Difficulty initiating speech and unable to request wants/needs, ambulates independently for short distances, full oral intake, breathing on room air	Speaks in sentences, ambulates independently, full oral intake, breathing on room air	Speaks in sentences, ambulates independent for short distances, full oral intake, breathing on room air	Non-verbal, inconsistent visual tracking, minimal ability to follow commands, non-purposeful movements, has nasogastric tube, breathing on room air
Additional Immunosuppressive regimen	CYC, RTX during admission	No	No	No	No	RTX → MMF due to relapse → IVIG → MMF due to side effects	RTX
Exam at last follow-up	Speaks some words, sits and stands with support, on enteral feeds	Normal speech, strength, coordination, and gait, full oral intake	Speaks in several word phrases with some articulation issues, gait normal, full oral intake	Same as discharged exam	Normal speech, strength, coordination, and gait	Normal speech, strength, coordination, and gait.	Speech dysarthric but fluent and intelligible, ambulate independently with abnormal gait
Anti-MOG-IgG titer at last follow-up (live cell-based assay)	1:100	1:40	Negative	1:100	1:20	Not done	1:100