NEUROIMAGING HIGHLIGHT

Extensive Neuromyelitis Optica Spectrum Disorder at First Presentation

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A 66-year-old Caucasian man with hypertension and atrial fibrillation developed persistent dry cough without fever. Medications included rivaroxaban, ramipril, bisoprolol, and hydrochlorothiazide. Ramipril was stopped and he was started on moxifloxacin as chest radiograph in the community showed multifocal infiltrates. One month later, he presented to hospital with persistent nonproductive cough, intractable hiccups, fatigue, and anorexia. On initial presentation, he had fluctuating hypothermia with temperature as low as 35 degrees Celsius, but otherwise normal vital signs. Nasopharyngeal swab for COVID-19 and extended respiratory virus panel was negative. Bloodwork revealed hyponatremia (sodium 110 mmol/L; ref 135–145) and markedly elevated C-reactive protein (84.5 mg/L; ref < 10) with negative blood cultures. Despite slow sodium correction (less than 8 mmol/L per day), he developed rapidly progressive quadriparesis and was intubated for airway protection.

Magnetic resonance imaging (MRI) of the neuraxis demonstrated diffuse abnormalities in the left temporal lobe, hypothalamus, midbrain, area postrema, and longitudinally extensive cord lesion spanning the cervicomedullary junction to the lower thoracic spine without conus involvement (Figure 1). Lumbar puncture showed markedly elevated protein (3.90 g/L; ref 0.12–0.60) and neutrophilic (83%) pleocytosis (717 × 10^6 cells/L; ref 0–5), with no oligoclonal bands or malignant cells on cytology. He was treated with broad-spectrum antimicrobials until culture and viral studies returned negative. Given high suspicion for a florid inflammatory process, he was then treated with 5 days of high-dose IV methylprednisolone–without improvement–and subsequently transferred to our institution for consideration of plasma exchange (PLEX). After five sessions of PLEX, he had marked improvement in his upper extremity strength and was extubated uneventfully. Serum cell-based immunofluorescence assay performed at Mitogen Advanced Diagnostic Laboratories (Calgary, Alberta) returned high-positive for anti-aquaporin-4 (AQP4) IgG (titre not reported), establishing a diagnosis of neuromyelitis optica spectrum disorder (NMOSD).

Historically, the classic presentation of neuromyelitis optica (Devic's disease) featured severe optic neuritis with a longitudinally extensive transverse myelitis (LETM)[1]; however, other presentations have been recognized, expanding the clinical spectrum under a single set of diagnostic criteria for NMOSD (Table 1A).[2] NMOSD is an autoimmune inflammatory disease of the central nervous system (CNS) characterized by at least one of six core clinical presentations (Table 1B). The antibody responsible is produced against AQP4, a water channel expressed throughout the CNS, especially around pial and ependymal surfaces in periventricular areas.[3] The diagnosis can still be established without anti-AQP4-IgG antibodies so long as at least two core clinical features are present, one of which is either LETM, optic neuritis, or area postrema syndrome (Table 1B), and additional MRI requirements are fulfilled (Table 1C).[2] MRI characteristics of NMOSD include extensive periependymal lesions which may run immediately parallel to the ventricles (Figure 1A)—as opposed to perpendicular as typically seen in multiple sclerosis[4]—and long, diffuse, heterogenous or edematous lesions involving the length of the corpus callosum[2] (Figure 1A), lesions involving the hypothalamus (Figure 1B), confluent unilateral or bilateral, cortical, subcortical or deep white matter lesions[2] (Figure 1B), small and localized lesions involving the area postrema in the dorsal medulla (Figure 1D), and in the spinal cord longitudinally extensive involvement with a central gray matter predominance and cord expansion/edema extending more than three vertebral segments which may have rostral extension into the brain stem (Figure 1E and F).[2]

This case uniquely highlights many characteristic imaging findings of NMOSD with involvement of area postrema, hypothalamus, cerebral deep white matter, and extensive spinal cord involvement with edema (Figure 1) in a single patient at first clinical presentation. This patient tested positive for AQP4-IgG antibodies and met four core clinical criteria with supportive neuroimaging satisfying the diagnostic criteria. Whereas

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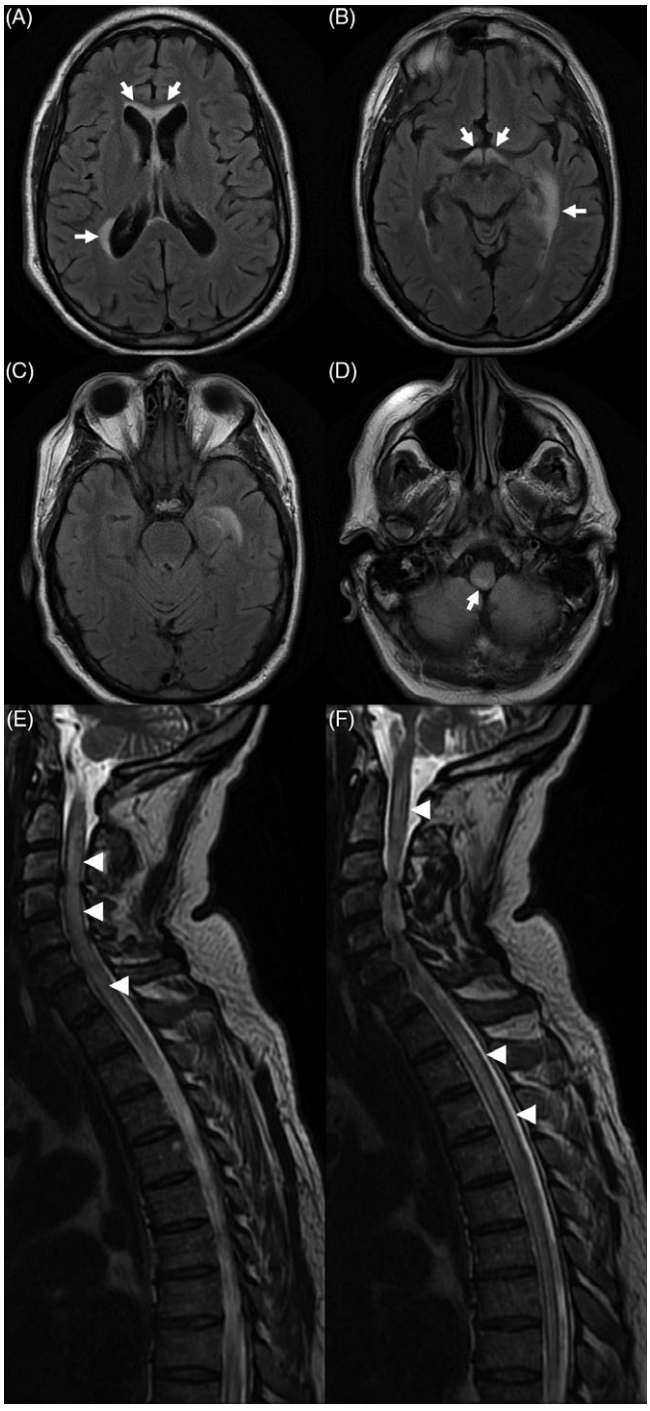

Figure 1: *MRI at initial presentation. Brain axial T2-FLAIR sequences demonstrating hyperintensities throughout the corpus callosum and periependymal surfaces which run parallel as opposed to perpendicular to the ventricles (A, arrows), hypothalamus and left mesial temporal lobe deep white matter (B, arrows), sparing the optic nerves and chiasm (C) but involving the area postrema in the dorsal medulla (D, arrow). Spine sagittal T2 sequences demonstrating longitudinally extensive cord hyperintensity with expansion/edema extending from the cervicomedullary junction to the lower thoracic spine (E, F; arrowheads). MRI = magnetic resonance imaging, FLAIR = fluid-attenuated inversion recovery.*

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Table 1: (A) 2015 diagnostic criteria for NMOSD from the International Panel for NMO diagnosis, (B) core clinical characteristics of NMOSD, and (C) additional MRI requirements for NMOSD.[2]

A) Diagnostic criteria for NMOSD with AQP4-IgG
1. At least one core clinical characteristic
2. Positive test for AQP4-IgG using best available detection method
3. Exclusion of alternative diagnoses
Diagnostic criteria for NMOSD without AQP4-IgG or NMOSD with unknown AQP4-IgG status
1. At least two core clinical characteristics occurring as a result of one or more clinical attacks and meeting all of the following requirements:
a. At least one core clinical characteristic must be optic neuritis, acute myelitis with LETM, or area postrema syndrome
b. Dissemination in space (two or more different core clinical characteristics)
c. Fulfillment of additional MRI requirements, as applicable
2. Negative tests for AQP4-IgG using best available detection method, or testing unavailable
3. Exclusion of alternative diagnoses
B) Core clinical characteristics of NMOSD
1. Optic neuritis 2. Acute myelitis 3. Area postrema syndrome: episode of otherwise unexplained hiccups or nausea and vomiting 4. Acute brain stem syndrome 5. Symptomatic narcolepsy or acute diencephalic clinical syndrome with NMOSD typical diencephalic MRI lesions 6. Symptomatic cerebral syndrome with NMOSD typical brain lesions
C) Additional MRI requirements for NMOSD without AQP4-IgG and NMOSD with unknown AQP4-IgG status
1. Acute optic neuritis requires brain MRI showing (a) normal findings or only nonspecific white matter lesions, OR (b) optic nerve MRI with T2-hyperintense lesion or T1-weighted gadolinium enhancing lesion extending over 1/2 optic nerve length or involving optic chiasm 2. Acute myelitis requires associated intramedullary MRI lesion extending over ≥3 contiguous segments (LETM) OR ≥ 3 contiguous segments of focal spinal cord atrophy in patients with history compatible with acute myelitis 3. Area postrema syndrome requires associated dorsal medulla/area postrema lesions 4. Acute brain stem syndrome requires associated periependymal brain stem lesions

intractable nausea and hiccups are more typical of area postrema involvement in NMOSD, intractable cough has been reported and speculated as being similarly related to involvement of the nearby nucleus solitarius.[5]

Disclosures

T. L. Feng reports no disclosures. A. Plecash reports no disclosures. T. Chen reports no disclosures.

Statement of Authorship

TLF, AP, and TC contributed equally to the manuscript.

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