Central Nervous System Demyelinating Disease Diagnostic Algorithm*

Clinical presentation suspicious of central nervous system (CNS) demyelinating disease: Perform magnetic resonance imaging (MRI)

MRI of head, orbit: Abnormal, consistent with optic neuritis

Classic MS brain/spine lesions present without atypical features
→ Diagnosis: multiple sclerosis (MS)

Classic MS brain/spine lesions absent
→ Optic neuritis
→ Order CDS1 / CNS Demyelinating Disease Evaluation, Serum

POSITIVE

MOG-IgG: high titer (≥1:100)
→ Diagnosis: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD)

MOG-IgG: low titer (1:20 or 1:40)
→ Possible MOGAD diagnosis
→ Red flags for alternative diagnoses or MS?
  - PRESENT → Confirm alternative diagnosis or MS
  - ABSENT → Diagnosis: MOGAD

AQP4-IgG: any abnormal titer
→ Diagnosis: Aquaporin-4-IgG seropositive neuromyelitis optica spectrum disorder (NMOSD)

NEGATIVE
→ Reassess for alternative diagnosis

MRI: Normal or reveals changes suggestive of demyelination, bilateral or unilateral encephalitis

Assess for cerebrospinal fluid (CSF) inflammation and order all of the following:
- MSP3
- ENS2 / Encephalopathy, Autoimmune/Paraneoplastic Evaluation, Serum
- ENC2 / Encephalopathy, Autoimmune/Paraneoplastic Evaluation, Spinal Fluid

If encephalitis including acute disseminated encephalomyelitis (ADEM) or unilateral encephalitis/meningoencephalitis is suspected, consider also ordering CDS1 evaluation

NEGATIVE
→ Reassess for alternative diagnosis

POSITIVE

MOG-IgG: high titer (≥1:100)
→ Diagnosis: MOGAD

MOG-IgG: low titer (1:20 or 1:40)
→ Possible MOGAD diagnosis
→ Red flags for alternative diagnoses or MS?
  - PRESENT → Confirm alternative diagnosis or MS
  - ABSENT → Diagnosis: MOGAD

AQP4-IgG: any abnormal titer
→ Diagnosis: Aquaporin-4-IgG seropositive NMOSD

Any other antibody positive
→ Antibody associated autoimmune or paraneoplastic CNS disorder confirmed

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MRI: Abnormal, suggestive of possible demyelination (eg, brainstem syndrome); order MSP3 / Multiple Sclerosis (MS) Profile, Serum and Spinal Fluid

No classic MS brain lesions, negative oligoclonal bands (OCB) or kappa-free light chains (KFLC), and absent peripheral spinal cord lesions
→ Order CDS1 evaluation
  - If coexisting encephalitis exists, consider ordering both ENS2 and ENC2.
  - If coexisting ataxia or movement disorder exists, consider ordering both MDS2 / Movement Disorder, Autoimmune/ Paraneoplastic Evaluation, Serum and MDC2 / Movement Disorder, Autoimmune/ Paraneoplastic Evaluation, Spinal fluid.

Classic MS brain lesions, elevated KFLC, positive OCB, and multiple spinal cord lesions
→ Diagnosis: MS

NEGATIVE

MRI of spine: Abnormal spinal cord T2-lesion; order MSP3

Short T2 lesion
→ No classic MS brain lesions, negative OCB or KFLC, and absent of peripheral spinal cord lesions

Longitudinally extensive T2 lesion
→ Transverse myelitis

→ Order either: CDS1 evaluation OR MAS1 / Myelopathy, Autoimmune/ Paraneoplastic Evaluation, Serum AND MAC1 / Myelopathy Autoimmune/ Paraneoplastic Evaluation, Spinal Fluid

NEGATIVE
→ Reassess for alternative diagnosis

POSITIVE

MOG-IgG: high titer (≥1:100)
→ Diagnosis: MOGAD

MOG-IgG: low titer (1:20 or 1:40)
→ Possible MOGAD diagnosis
→ Red flags for alternative diagnoses or MS?
  - PRESENT → Confirm alternative diagnosis or MS
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AQP4-IgG: any abnormal titer
→ Diagnosis: Aquaporin-4-IgG seropositive NMOSD

Any other antibody positive
→ Antibody associated autoimmune or paraneoplastic myelopathy confirmed

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*For diagnosis of pediatric patients, see the Pediatric Autoimmune Central Nervous System Demyelinating Disease Diagnostic Algorithm