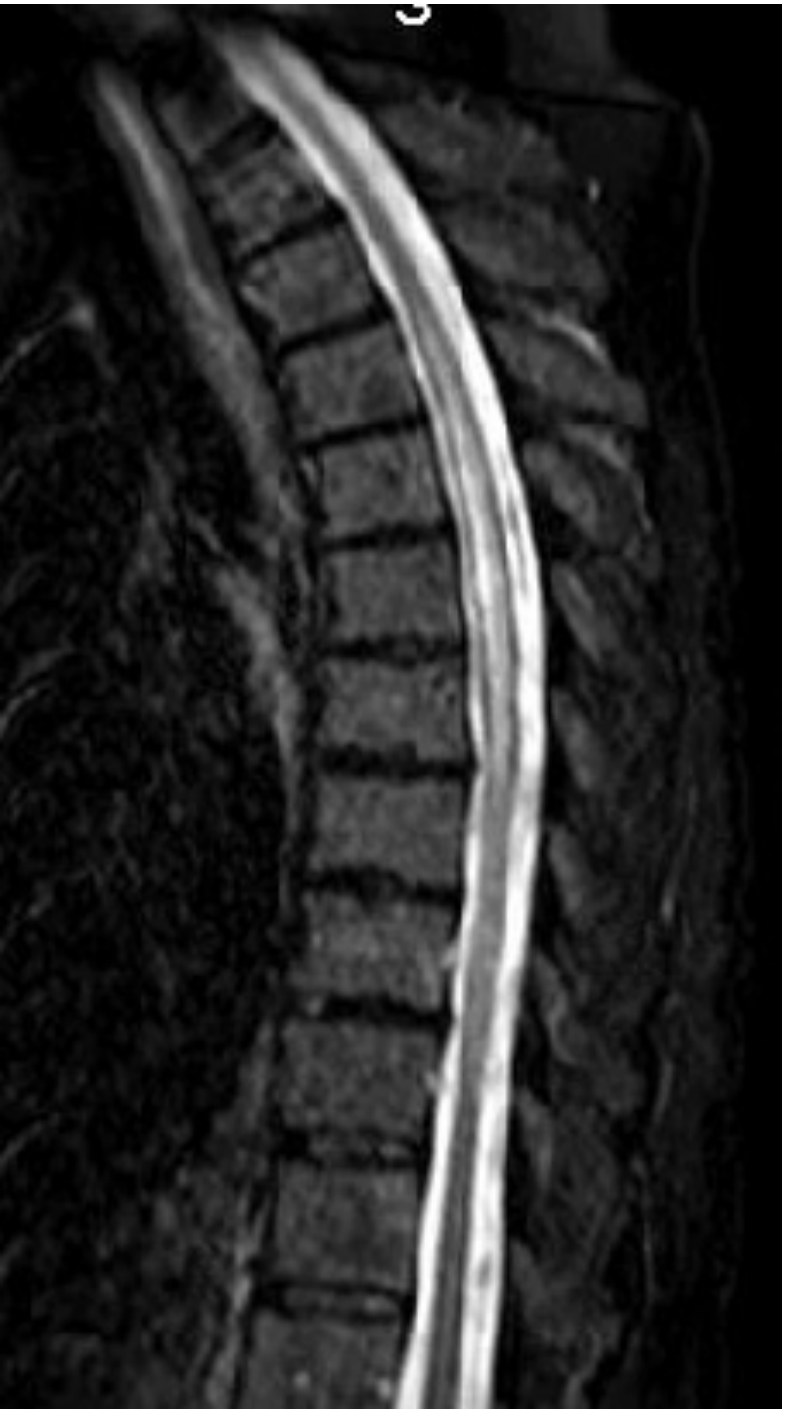
CASE

A 38 year old woman presented with acute urinary retention and progressive paraplegia over 48 hours. She has a history of bilateral vision loss one year ago. MRI is on the next slide:



The antibody test you send is located where?

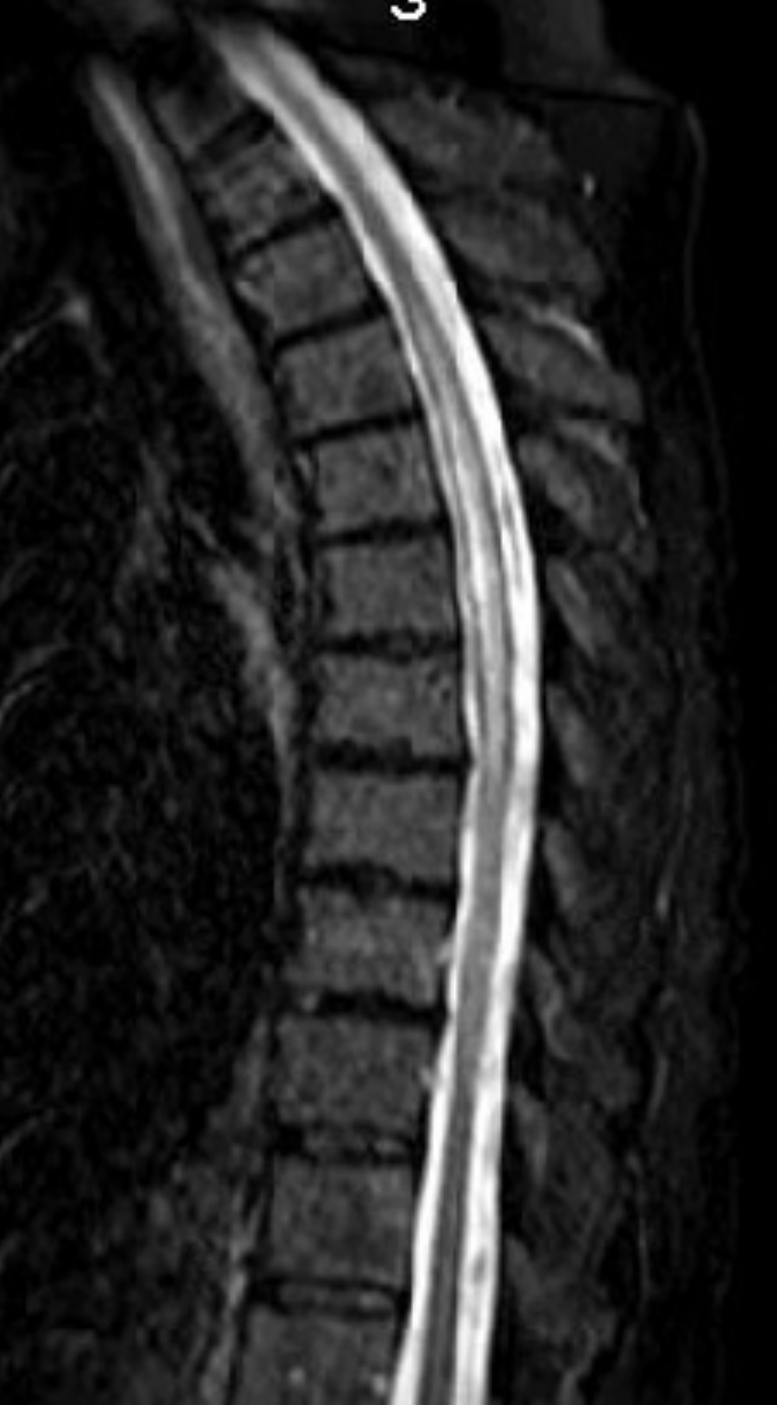
A.) Neuronal Dendrites

B.) Astrocytes

C.) Ventricular lining

D.) Microglia

E.) Myelin basic protein



The antibody test you send is directed against what?

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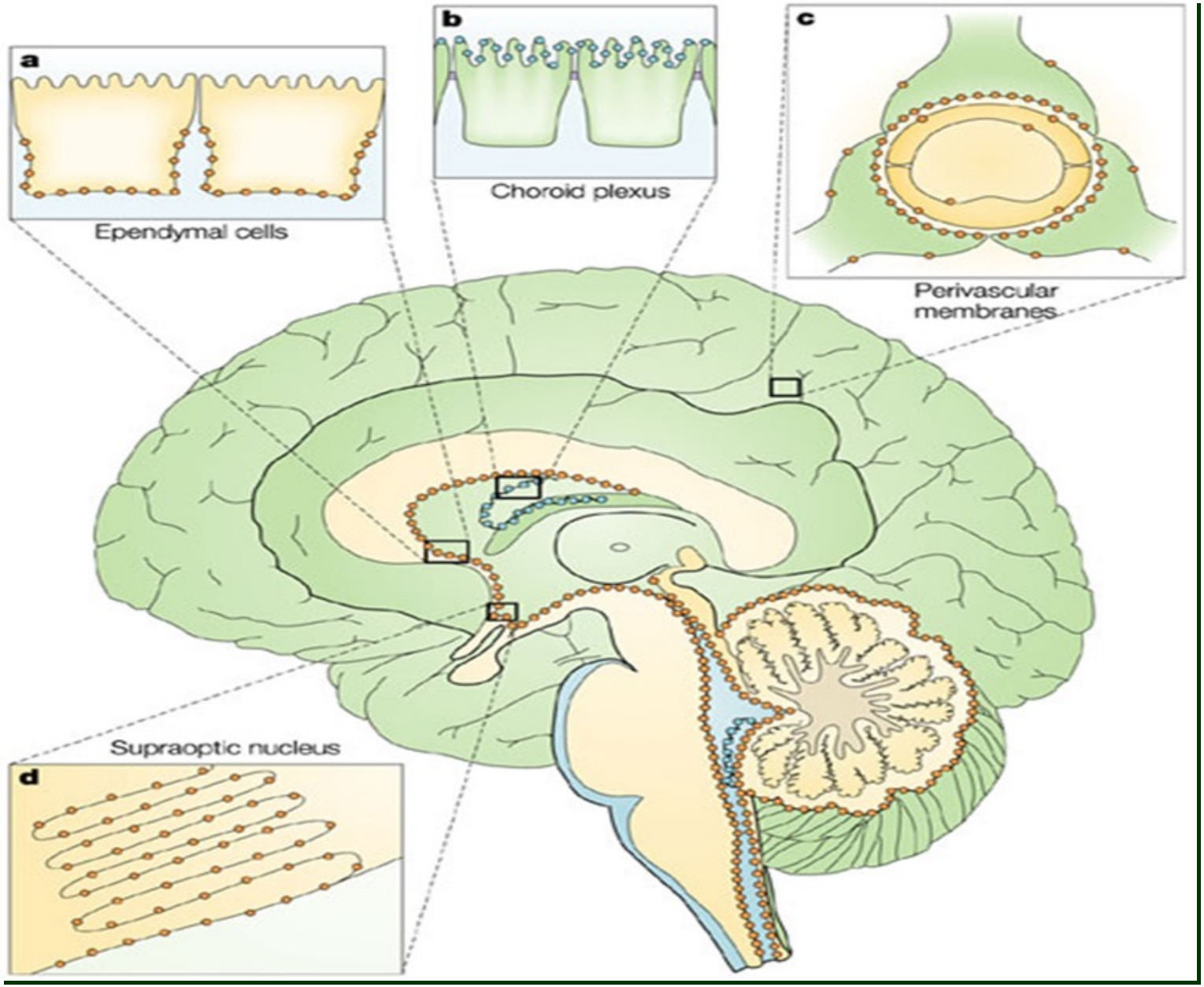
Neuromyelitis Optica Spectrum Disorder

- Antibodies against aquaporin-4 are present in 80% of cases
  - IgG1
  - Aquaporin-4 is a transmembrane protein located on astrocyte foot processes in contact with brain capillaries.
  - It is the predominant water channel in the CNS


a
Ependymal cells
b
Choroid plexus
c
Perivascular membranes
Supraoptic nucleus
d

Neuromyelitis Optica Spectrum Disorder (NMOSD)

- NMOSD: unified term
  - Stratified by serostatus NMOSD with AQP4-IgG
  - NMOSD without AQP4-IgG (or testing unavailable)
    - Allows for future revisions e.g. discovery and validation of other antibodies associated with NMOSD clinical phenotype

Revised Diagnostic Criteria:
NMOSD with AQP4-IgG

Requirements

- At least 1 core clinical characteristic
- Positive test for AQP4-IgG
- No better explanation
  - Clinical and MRI red flags

Core Clinical Characteristics

- Optic neuritis
- Acute myelitis
- Area postrema syndrome:
  - nausea/vomiting/hiccups
- Other brain stem syndrome
- Symptomatic narcolepsy or acute diencephalic syndrome with MRI lesion(s)
- Symptomatic cerebral syndrome with MRI lesion(s)

Revised Diagnostic Criteria:
NMOSD without AQP4-Ig (or unavailable)

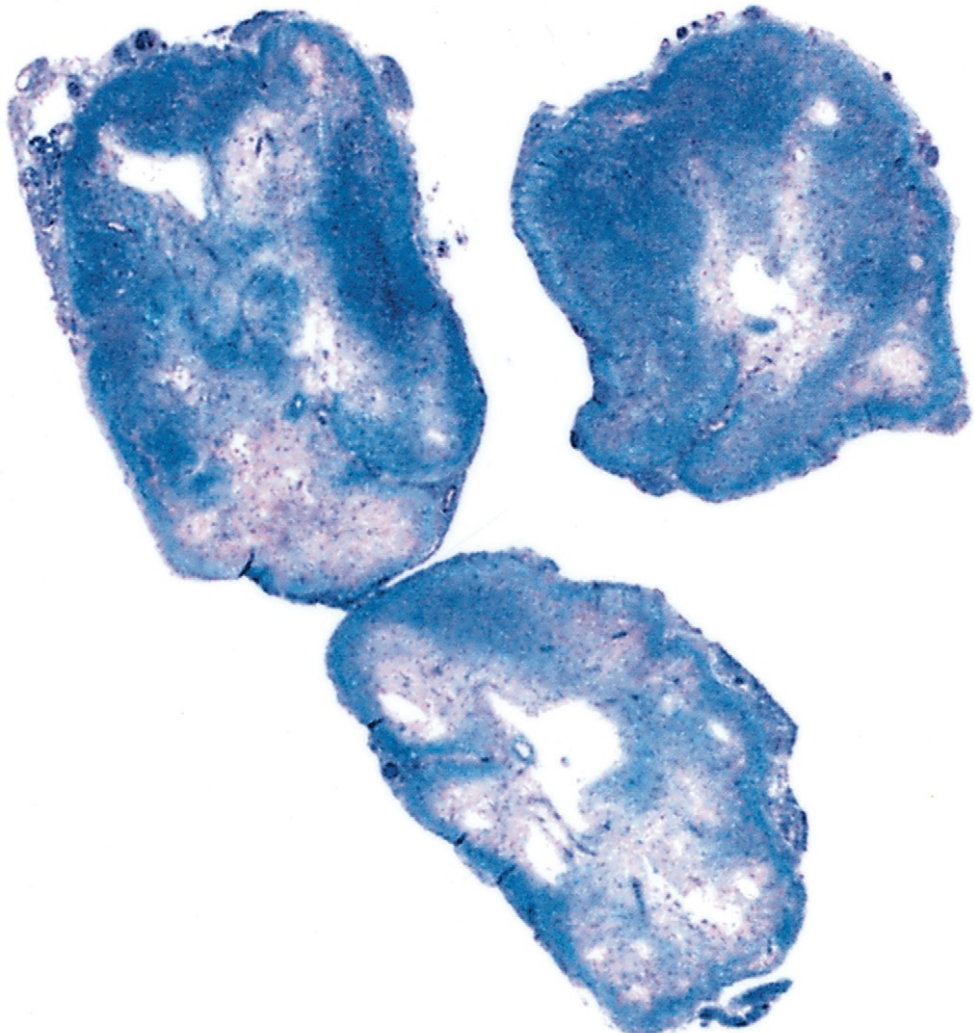
- At least 2 core clinical characteristics all satisfying:
  - 1 of ON, myelitis, or area postrema syndrome
  - Dissemination in space
    - Isolated recurrent ON or recurrent TM do not qualify
  - Additional MRI requirements
    - AP syndrome: dorsal medulla lesion
    - Myelitis: LETM
    - ON: normal brain MRI ***OR*** >1/2 ON ***OR*** chiasm lesion
  - Negative test(s) for AQP4-IgG using best available assay, or testing unavailable
- No better explanation for the clinical syndrome

Neuromyelitis Optica Spectrum Disorder (NMOSD)

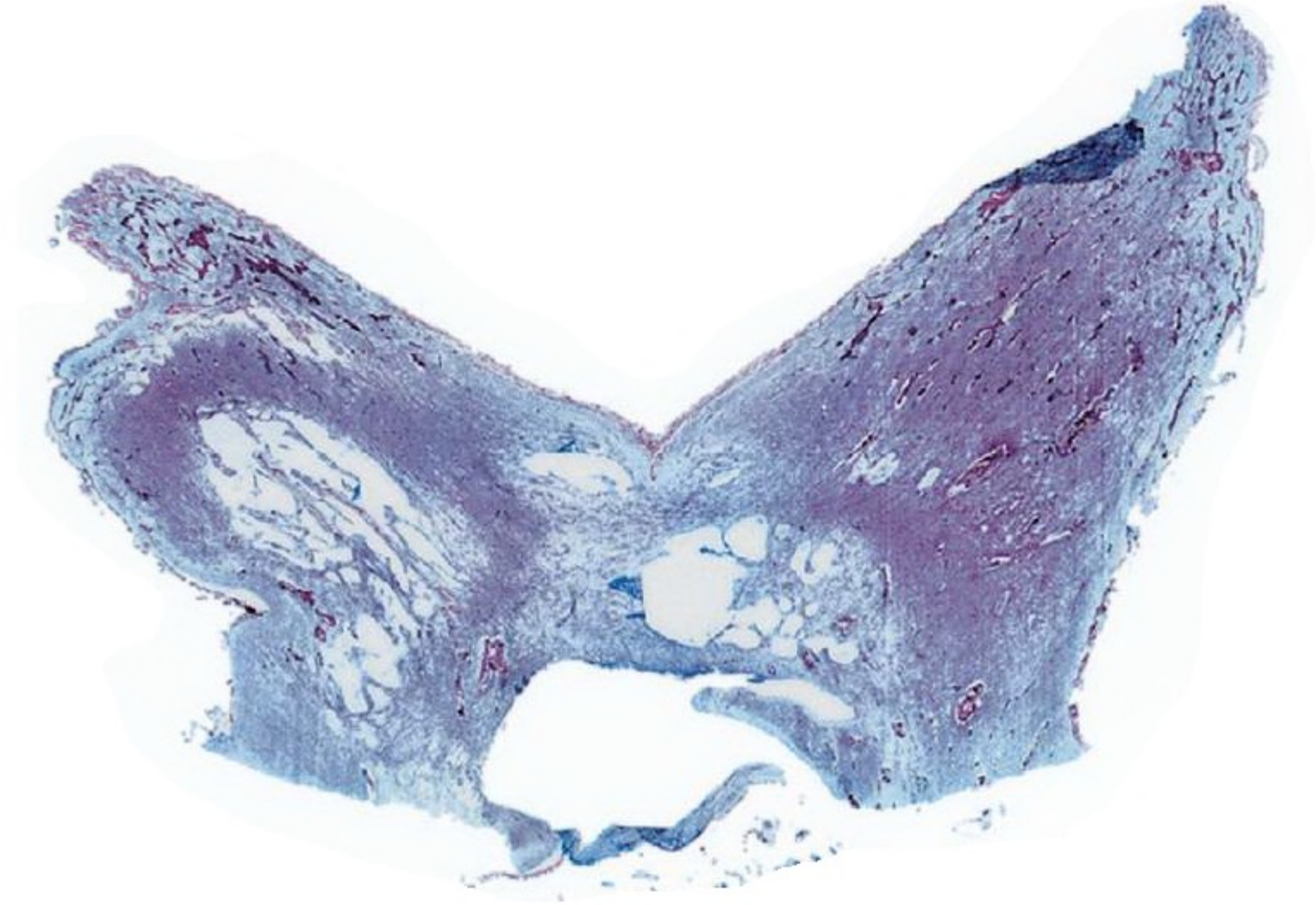
- Gross findings:
  - Swollen cord in acute phase
  - Tissue damage over multiple cord segments
  - Cord and optic nerve atrophy in later stages of the disease

Neuromyelitis Optica Spectrum Disorder (NMOSD)

Devic disease (neuromyelitis optica) at autopsy classically manifests severe necrotic lesions involving several levels of spinal cord.



Neuromyelitis Optica Spectrum Disorder (NMOSD) - ON



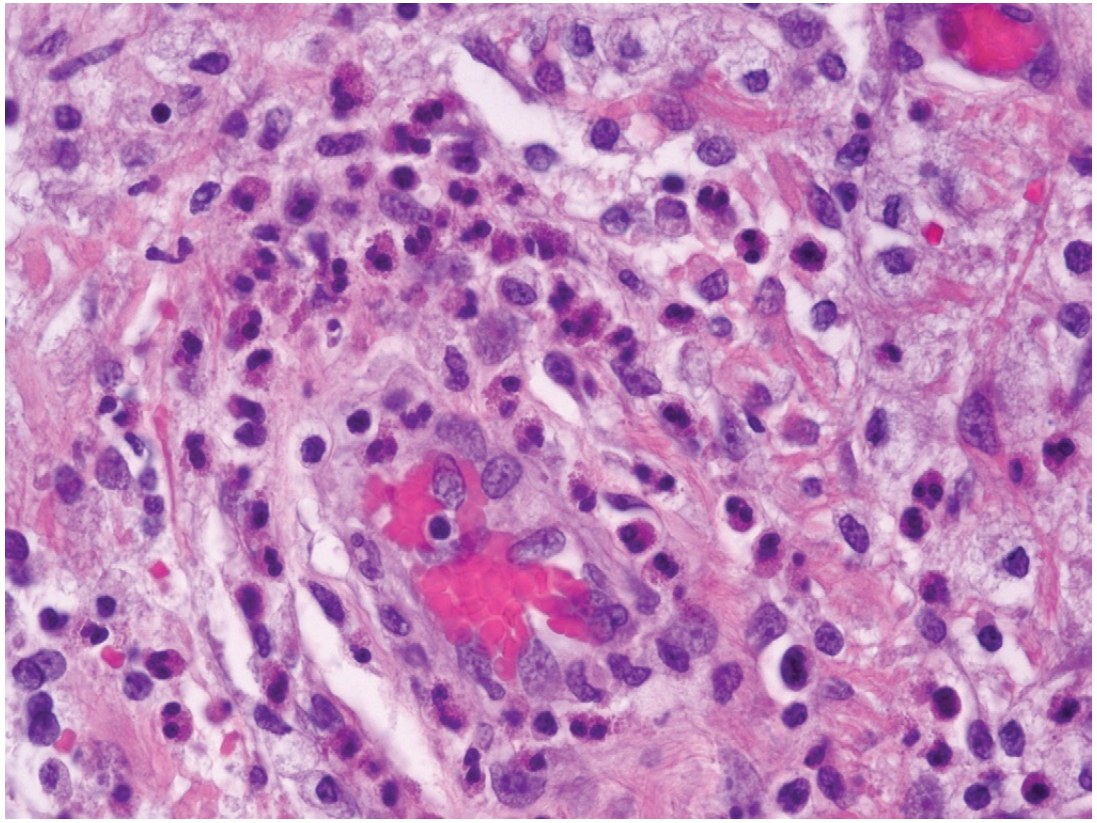
Neuromyelitis Optica Spectrum Disorder (NMOSD)

- Microscopic features
  - Cavitary lesions may contain sheets of macrophages
  - Some cases show greater B cell, eosinophil, and neurophil inflammatory components than typical MS
  - Blood vessles in lesions are thickened and hyalinized

Neuromyelitis Optica Spectrum Disorder (NMOSD)

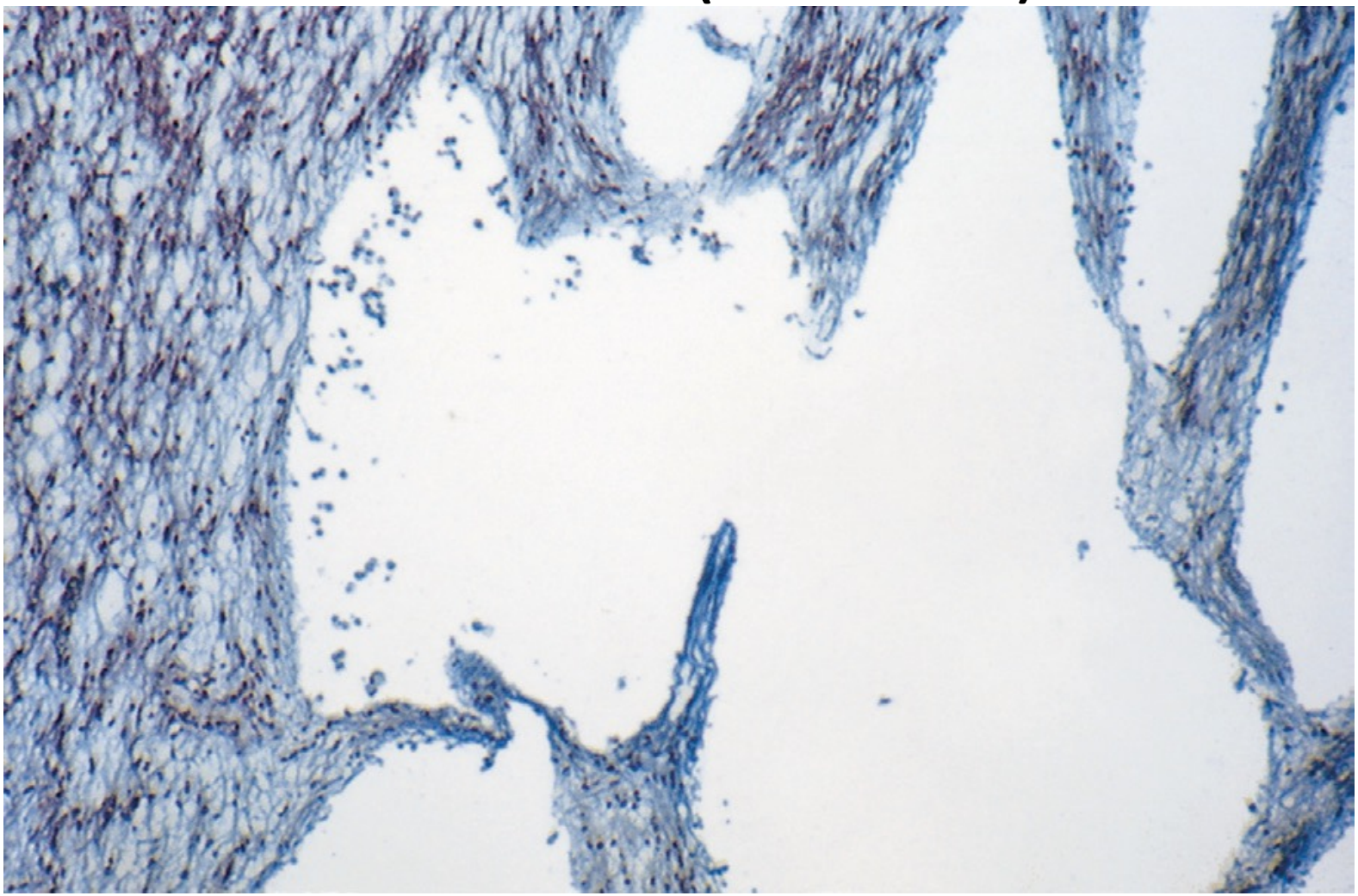
- Immunohistochemical features
  - Desposits of IgG and IgM with complement activation in vasocentric pattern
  - Loss of immuno-staining for Aquaporin-4

Neuromyelitis Optica Spectrum Disorder (NMOSD)



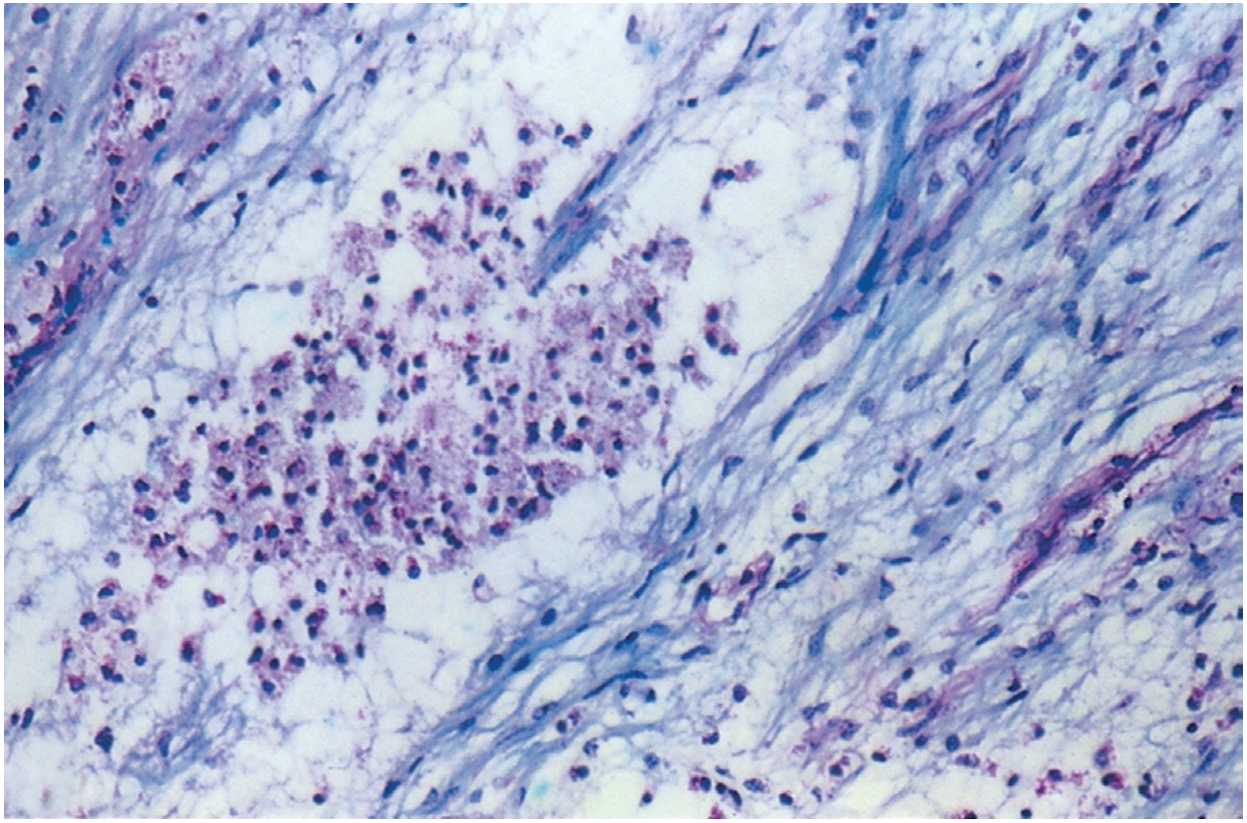
Eosinophils may also be seen in lesions of neuromyelitis optica but are rare in MS.

Neuromyelitis Optica Spectrum Disorder (NMOSD)



optic chiasm on a whole-mount section (A), with significant axonal loss (B) with significant axonal loss

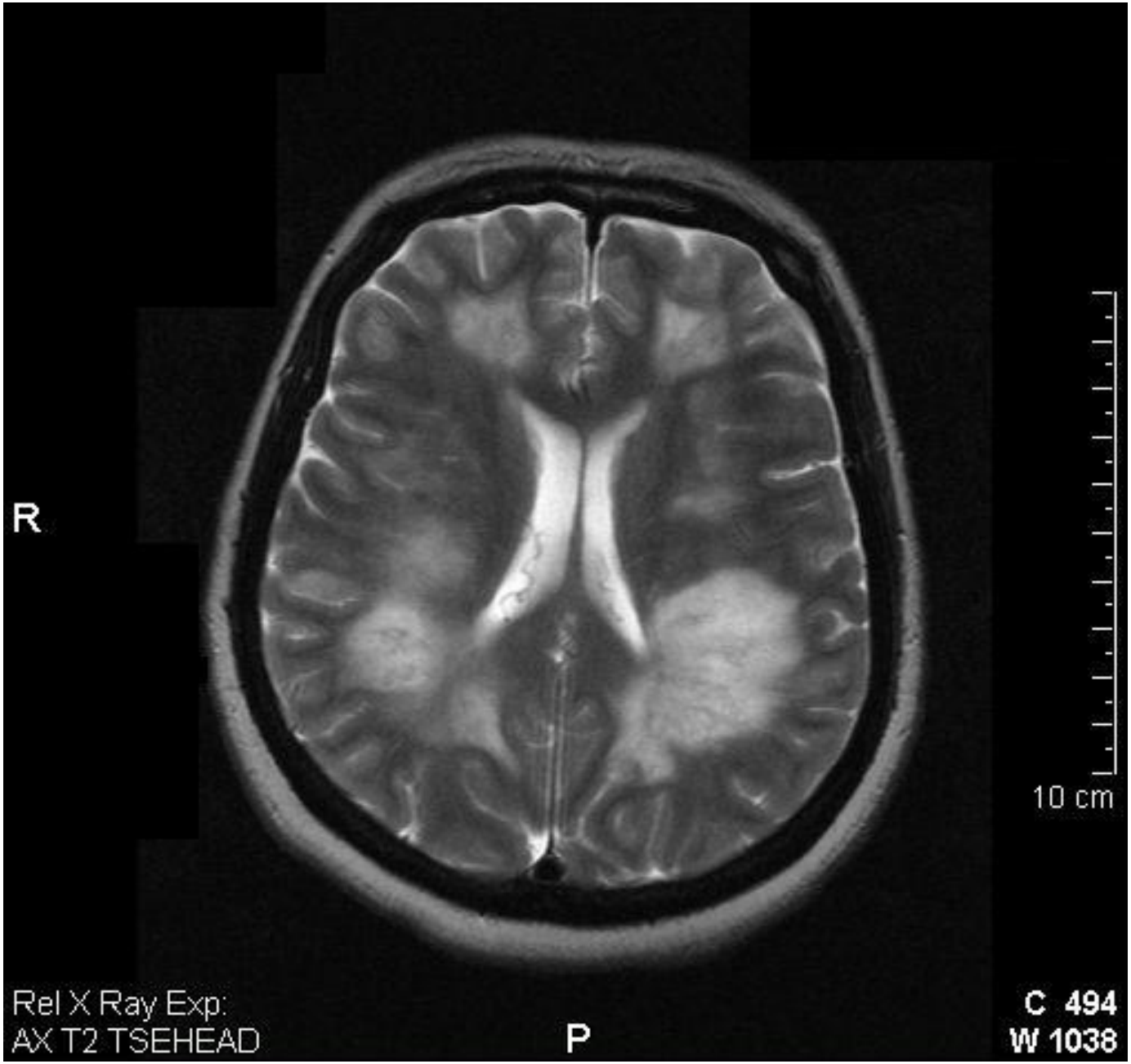
Neuromyelitis Optica Spectrum Disorder (NMOSD)



cavitary lesions containing macrophages

CASE

- A 14 year old girl comes into the CHP ED after developing confusion and fevers which after several hours is complicated by seizures and ataxia. MRI is shown on the next slide. She received a vaccination last week.


R
10 cm
Rel X Ray Exp:
AX T2 TSEHEAD
P
C 494
W 1038

- Microscopic features of this condition include:
  - A.) Eosinophil infiltration
  - B.) Loss of aquaporin-4
  - C.) Narrow cuffs of myelin loss around venules
  - D.) Confluent areas of myelin loss around arterioles

- Microscopic features of this condition include:
  - A.) Eosinophil infiltration
  - B.) Loss of aquaporin-4
  - **C.) Narrow cuffs of myelin loss around venules**
  - D.) Confluent areas of myelin loss around arterioles

Acute Disseminated Encephalomyelitis (ADEM)

- A/w infection or immunization
  - Lag of 2-10 days, may be 4 weeks
- Signs:
  - Pyramidal signs (60- 90%)
  - Acute hemiplegia (76%)
  - Seizures (35%)
  - Fevers, headaches, AMS

Acute Disseminated Encephalomyelitis (ADEM)

- Typically a monophasic source
- Recovery is typically rapid, within a week after onset

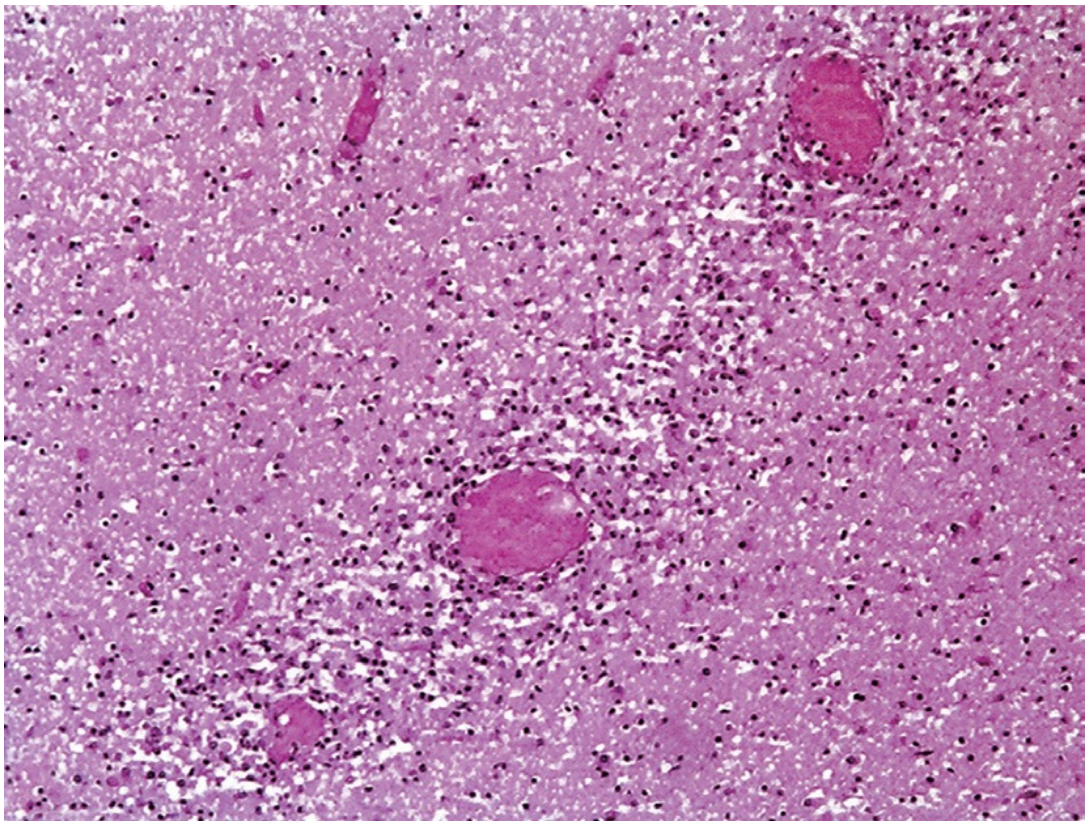
Acute Disseminated Encephalomyelitis (ADEM)

- Gross
  - Patients dying in acute phases have diffuse cerebral edema and herniations
  - Demyelination is not obvious grossly

Acute Disseminated Encephalomyelitis (ADEM)

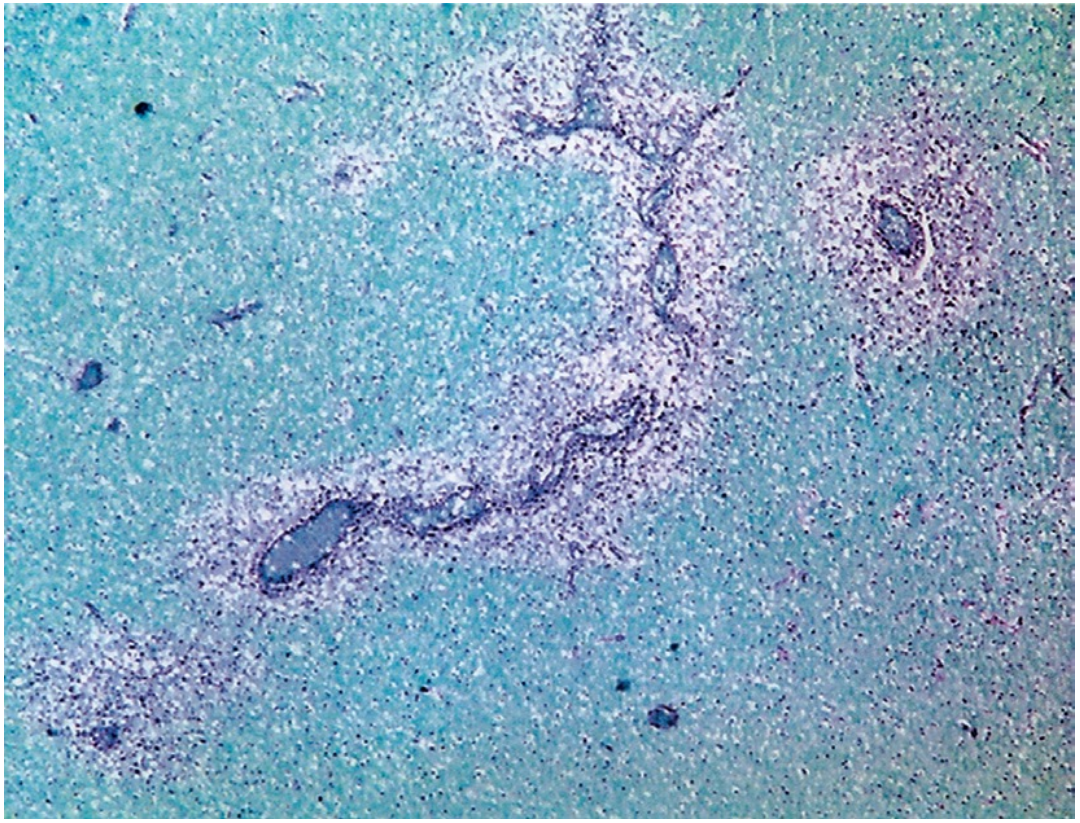
- Microscopic features
  - Characteristic narrow cuffs or sleeves of myelin loss around small veins/venules
  - Lesions involve white matter, cortical gray matter and deep gray matters
  - **Lesions are all the same age**
- Immunohistochemistry: no specific features

Acute Disseminated Encephalomyelitis (ADEM)



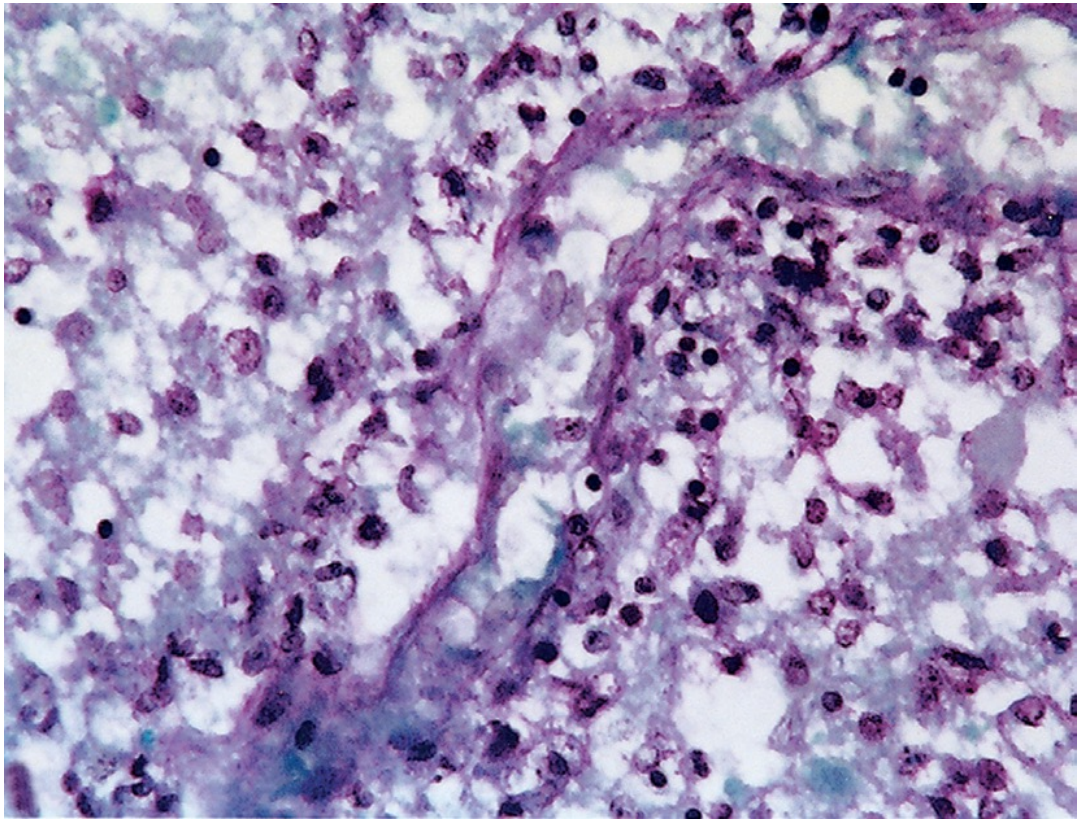
Acute disseminated encephalomyelitis shows hypercellular perivenular lesions

Acute Disseminated Encephalomyelitis (ADEM)



demyelination best appreciated on LFB-PAS staining

Acute Disseminated Encephalomyelitis (ADEM)



perivascular lymphocytes and macrophages (LFB-PAS stain).