Interactive Cases: Demyelinating Diseases and Mimics

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Case 1
* 25 yo F with nystagmus; look for tumor

What do you suspect?
A. Demyelinating disease
B. Malignancy
C. PRES
D. Septic emboli
E. Stroke

Disclosures
* None

What do you suspect?
A. Demyelinating disease
B. Malignancy
C. PRES
D. Septic emboli
E. Stroke
Multiple sclerosis

- Classic lesions:
  - Multiple ovoid perivenular *pericallosal* (i.e. within corona radiata)
  - *Callosoptal interface* (inferior edge of CC)
  - Middle cerebellar peduncle
  - Brainstem

DDx

- Acute disseminated encephalomyelitis (ADEM)
- Neuromyelitis optica (NMO)
- Vasculitis
- CADASIL
- Lyme disease
- Susac syndrome

Case 2

- 27 yo F with headache, left eye blurriness, mild confusion

- Branch retinal artery occlusion found on funduscopic exam
**What additional clinical finding would you expect in this patient?**

A. Aquaporin-4 antibody  
B. Hearing loss  
C. NOTCH3 mutation  
D. Rash  
E. Viral prodrome

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**Susac syndrome**

- Rare autoimmune disease affecting small vessels of brain, cochlea, retina  
- **Classic triad**: encephalopathy, branch retinal artery occlusion, sensorineural hearing loss  
- 20-40 yo, F > M  
- Lesions in middle layers of corpus callosum

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**Case 3**

- 31 yo F with decreased vision in left eye

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**What additional clinical finding would you expect in this patient?**

A. Aquaporin-4 antibody  
B. Hearing loss  
C. NOTCH3 mutation  
D. Rash  
E. Viral prodrome

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**Susac syndrome**

- Lesions in middle layers of corpus callosum

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**Case 3**

- Patient has a family history of CADASIL and multiple sclerosis
What additional clinical finding would you expect in this patient?
A. Aquaporin-4 antibody
B. Hearing loss
C. NOTCH3 mutation
D. Rash
E. Viral prodrome

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CADASIL*
• Hereditary small vessel disease with NOTCH3 mutation
• Dementia, mood disorders, migraine, strokes in young to middle-aged adults
• Anterior temporal lobes, external capsule, parasagittal high frontal lobe
• BG and subcortical lacunar infarcts

* Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy

Companion case
• 69 yo M with rapidly progressive dementia

* After extensive workup, initially diagnosed with limbic encephalitis
• Symptoms and imaging worsened so biopsy performed
• Pathology: anaplastic astrocytoma (!)
Case 4
• 61 yo F with seizures, memory loss

Most likely diagnosis?
A. CADASIL
B. Chronic microvascular ischemic disease
C. Multiple sclerosis
D. Reversible cerebral vasoconstriction syndrome (RCVS)
E. Vasculitis

Case 4
• Workup positive for several auto-antibodies (ANA, centromere, B2GP-1)

Case 4
Most likely diagnosis?
A. CADASIL
B. Chronic microvascular ischemic disease
C. Multiple sclerosis
D. Reversible cerebral vasoconstriction syndrome (RCVS)
E. Vasculitis

Systemic lupus erythematosus
• Many types and causes of CNS vasculitis, with broad spectrum of imaging findings
• Neuropsychiatric lupus in 50% of SLE; psychosis, stroke, seizure, HA, cognitive
• Small WM lesions (most common), diffuse atrophy, infarcts, hemorrhage
• Vessel imaging: stenosis, beading, occlusions in pattern atypical for athero

Case 5
• 63 yo F with progressive dementia & falls
Most likely diagnosis?
A. Cavernous malformations
B. Cerebral amyloid angiopathy
C. Diffuse axonal injury
D. Hemorrhagic metastatic disease
E. Hypertensive microhemorrhages

Cerebral amyloid angiopathy
• Deposition of β-amyloid in walls of small and mid-sized arteries → dementia, hemorrhage
• Microhemorrhages most commonly at GW junction
• Inflammatory CAA: uncommon variant; patchy or confluent WM hyperintensity; responsive to steroids

• Could this case be inflammatory CAA?

Case 6
• 35 yo F with transient left eye vision loss
What additional clinical finding would you expect in this patient?
A. Aquaporin-4 antibody  
B. Hearing loss  
C. NOTCH3 mutation  
D. Rash  
E. Viral prodrome

Neuromyelitis optica (NMO)
- Demyelinating disease with optic neuritis and longitudinally extensive (>3 segments) myelitis
- Brain lesions also common, e.g. periventricular in hypothalamus, thalamus, brainstem; full thickness of CC
- NMO and MS managed differently

Case 7
- 53 yo M from Ghana with progressive weakness and mild confusion
Most likely diagnosis?
A. Canavan disease
B. Chronic hypertensive encephalopathy
C. CO poisoning
D. HIV encephalopathy
E. Progressive multifocal leukoencephalopathy (PML)

HIV encephalopathy
- Clinical: HIV associated dementia
- Diffuse cerebral atrophy and symmetric diffuse WM abnormality
- No enhancement or diffusion restriction
- DDx: PML
  - Opportunistic infection by JC virus
  - WM lesions can be solitary, multifocal, or confluent and bilateral but asymmetric

Companion case: PML
- Initial scan (FLAIR)
- 2 months later

Case 8
- 31 yo F with acute encephalopathy, h/o bipolar disorder

FLAIR

DWI

ADC
Most likely diagnosis?
A. Canavan disease
B. CO poisoning
C. HIV encephalopathy
D. Post-anoxic leukoencephalopathy
E. Toxic leukoencephalopathy

Toxic leukoencephalopathy (acute)
- Diffuse symmetric WM DWI+ (> FLAIR hyperintensity); can be reversible
- Many causes: drugs of abuse (inhaled opiates), chemotherapy, organic solvents
- DDx: post-anoxic leukoencephalopathy, congenital metabolic disorders (leukodystrophies), CO; history is key!

Case 9
- 60 yo M with acute left-sided weakness
**Most likely diagnosis?**
A. Demyelinating disease  
B. Metastatic disease  
C. Primary brain tumor

**Tumefactive demyelination**
- One or sometimes two large (>2 cm) lesions mimicking a neoplasm
- Incomplete ring or open ring enhancement (on WM side of lesion)
- Little mass effect or vasogenic edema
- Low rCBV may be helpful

**5 months later...**

**Case 10**
- 26 yo F with double vision & headache

- FLAIR
Most likely diagnosis?
A. Demyelinating disease
B. Metastatic disease
C. Primary brain tumor
D. Who knows??

Summary: a few pearls
• Looks like MS but with lesions in middle layers of CC → consider Susac
• Early dementia + temporal pole WM lesions → consider CADASIL
• WM lesions/infarcts in pattern atypical for athero → consider vasculitis
• If CAA, look for inflammatory changes

Summary: a few pearls
• If optic neuritis or transverse myelitis → consider NMO
• DDx for diffuse symmetric WM disease includes HIV encephalopathy, toxic and post-anoxic leukoencephalopathy, and metabolic disorders; history is key
• Tumor with incomplete/open ring enhancement → consider tumefactive demyelination
References

References