Hôpital général juif
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An encephalopathic woman with hearing loss

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8e Colloque neurovasculaire SSVQ
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SSVQ
Société des sciences vasculaires du Québec

Montreal General Hospital (2009)

- ID: 34 yo RHD female, employed by insurance company
- PmHx: migraines, immunocompetent
- Rx: Yasmin
- HPI:
  - Transfer from Lasalle hospital
    - **New confusion, tinnitus, encephalopathy, vertigo**
      - CT head (+ and - contrast): normal
  - 5 d PTA, mental status changes
    - **Forgetting** phone numbers, passwords on the computer
    - **Apathic**, **withdrawn** at work
    - ***Decreased hearing bilaterally*** and **tinnitus**
    - Severe **headaches**
      - **Visual obscurations**, scotomas

- Afebrile, distressed
- Dramatic fluctuating level of arousal
    - When alert; coherent, but somewhat illogical speech – no language impairment
    - When drowsy; very somnolent, not responding to questions or family's interjections
- Obese, but non-toxic with supple neck, no meningismus
- Neurological exam limited by encephalopathy
  - Disoriented to person, place, date, day, year
    - Can't recall own address or phone #
  - "I can't hear"
  - Unexpectedly begins laughing, then rapidly falls asleep
  - Cranial Nerves:
    - Normal fundi
    - Decreased hearing bilat
  - Power normal, limited by poor cooperation, tone
  - Remainder of exam non-focal or limited

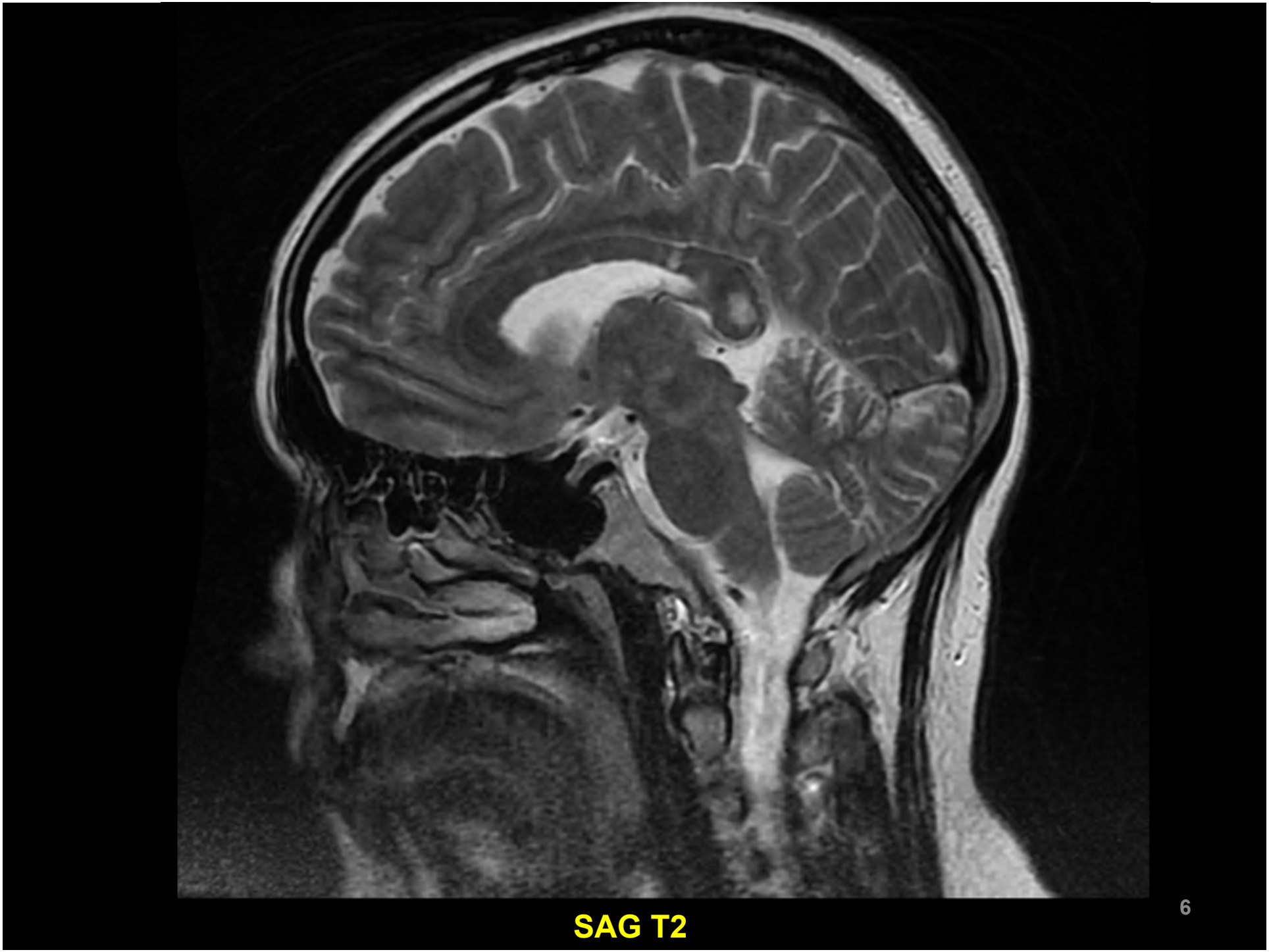
Initial differential

1. **Meningo-encephalitis** (e.g. HSV)
   - LP (urgent)
   - Started on Acyclovir and Ceftriaxone
2. **Cerebral venous sinus thrombosis** (deep)
   - given obesity, OCP, headache, tinnitus, neuropsychiatric symptoms – waxing and waning LOC with vomiting, suggesting increased ICP
     - MRI/MRV
     - Check D-dimer

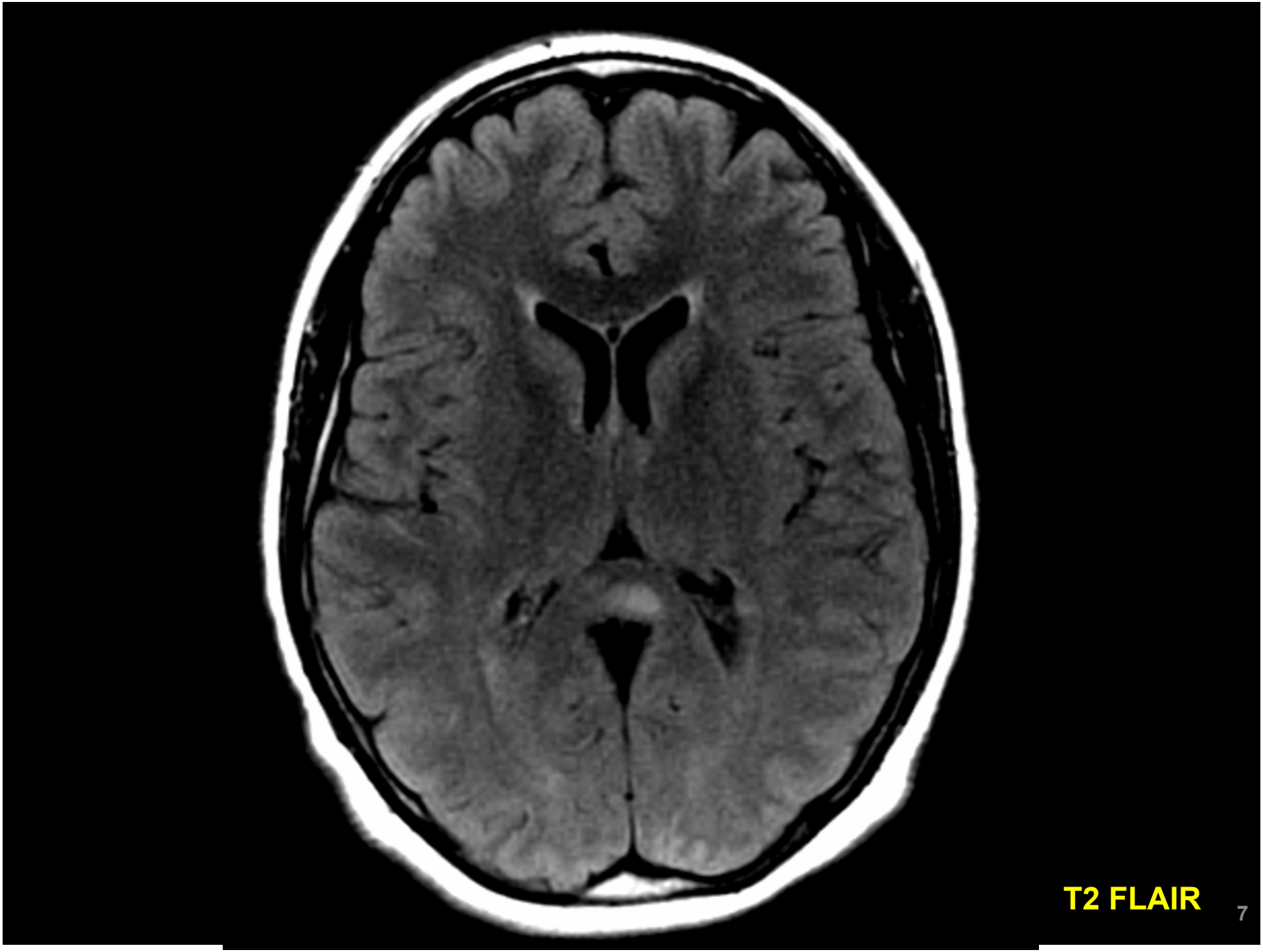
Evolution

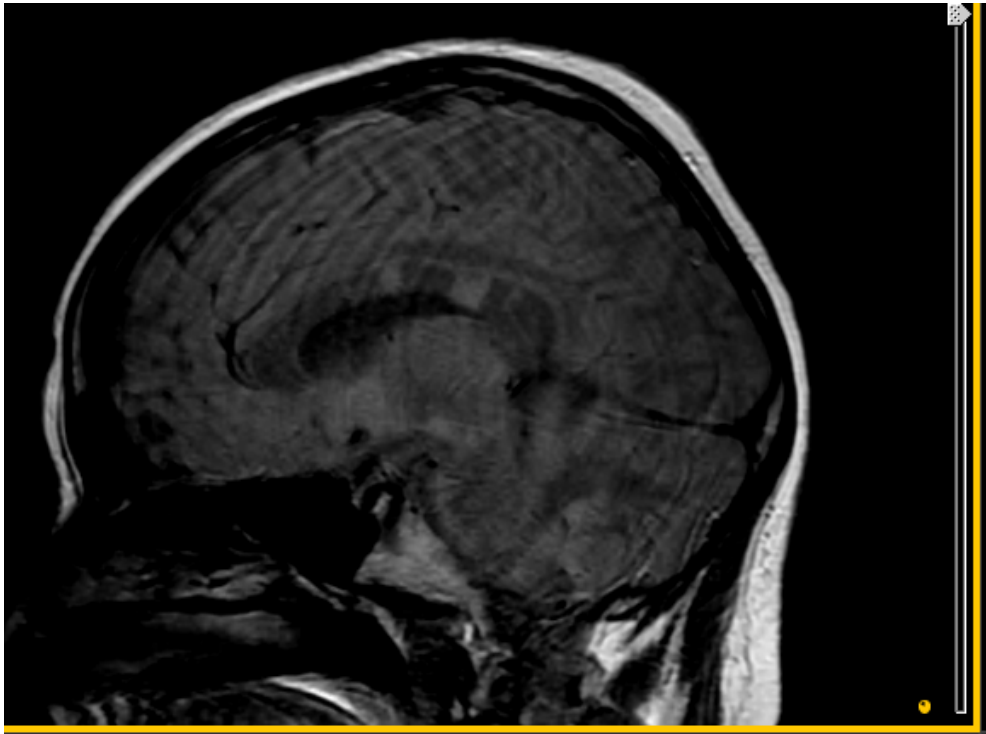
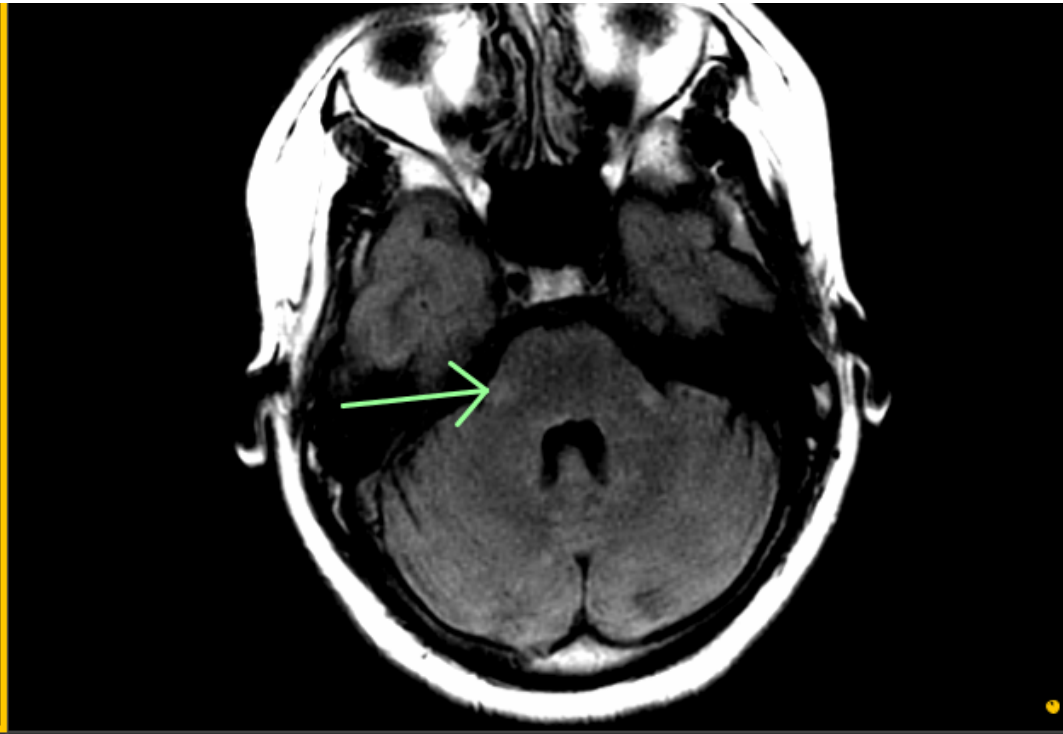
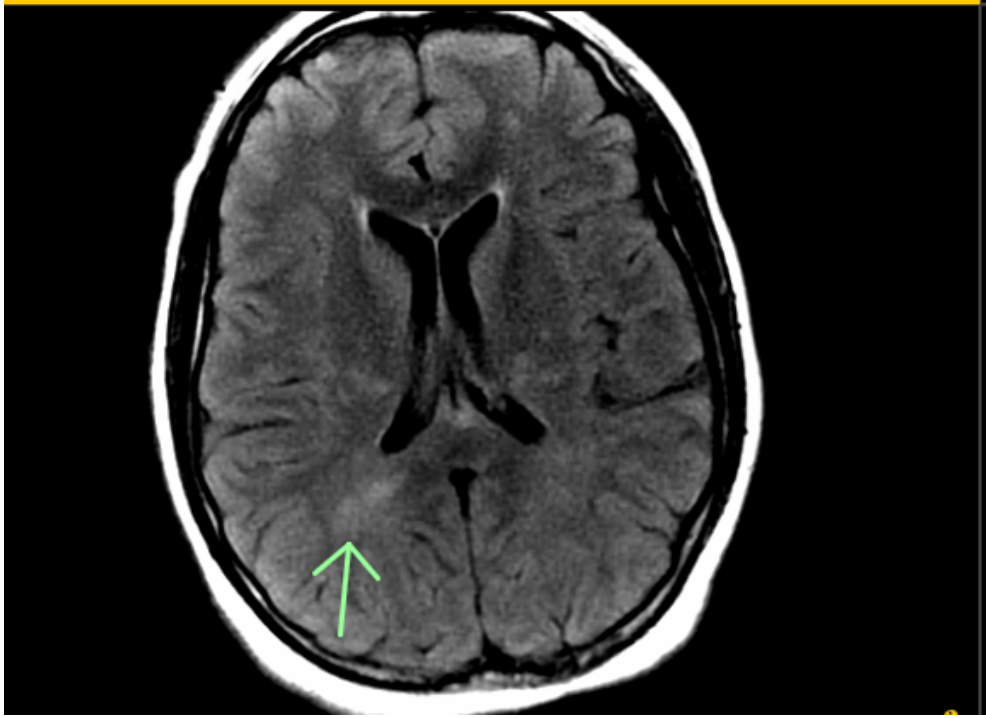
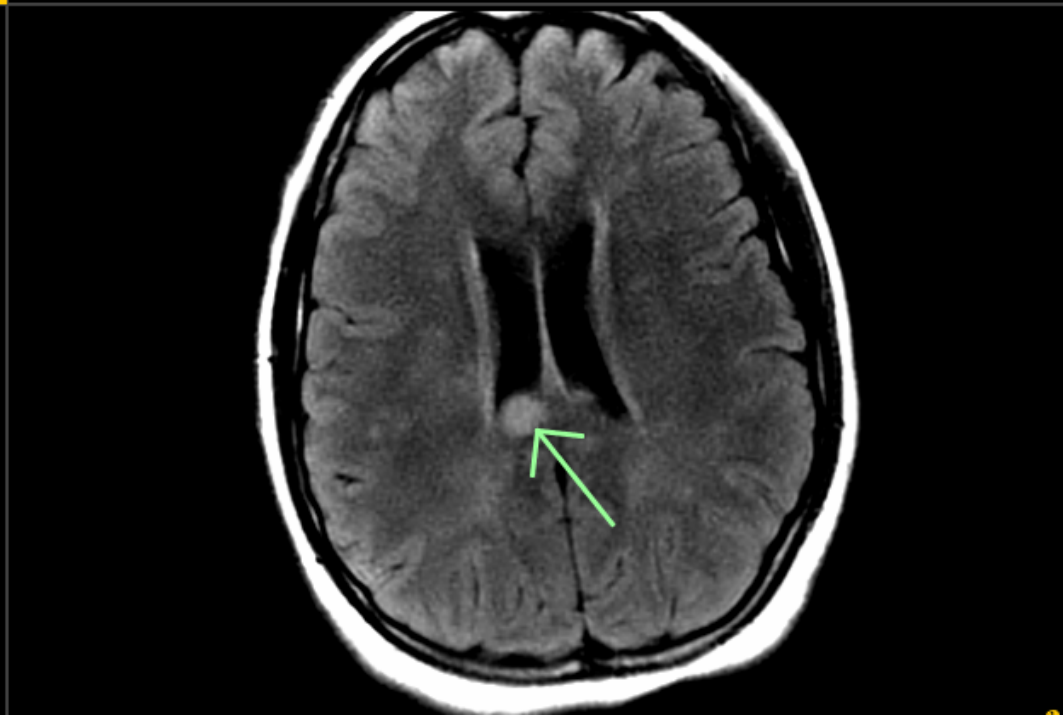
- **Lumbar Puncture**
  - Opening pressure *26cm H_20*, clear and colorless
    - Clear and colorless
    - Total cells:12 || WBC:**10** || RBC:2
      - SEGMENTED NEUTROPHILS: 2%
      - LYMPHOCYTES: **94 %**
      - MONOCYTES:2%
    - CSF PROTEIN **2.58 (H)**
    - CSF GLUCOSE 3.6 CSF LACTATE : 1.70
    - CSF OLIGOCLONAL BAND: absent
    - CSF: IgG INDEX : normal
    - CSF CULTURES and Viral PCR: Neg

- **MRI & MRV brain**
  - No signs of CVST, but…



SAG T2


T2 FLAIR

MS with ***hearing loss***?

Ddx

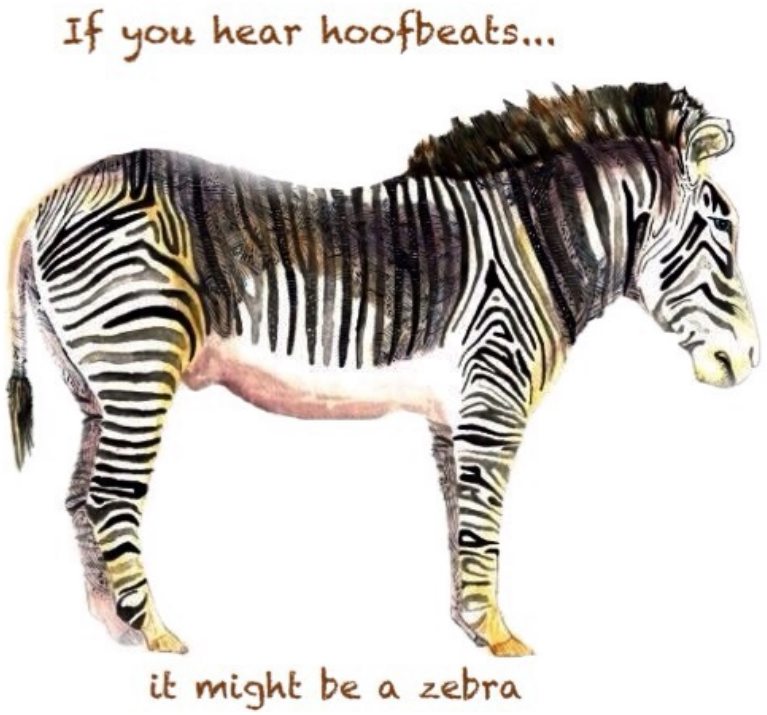
- ***Radiology conclusion:***
  - ***Demyelinating disease***
    - Atypical MS?
    - **ADEM**?

Clinical differential

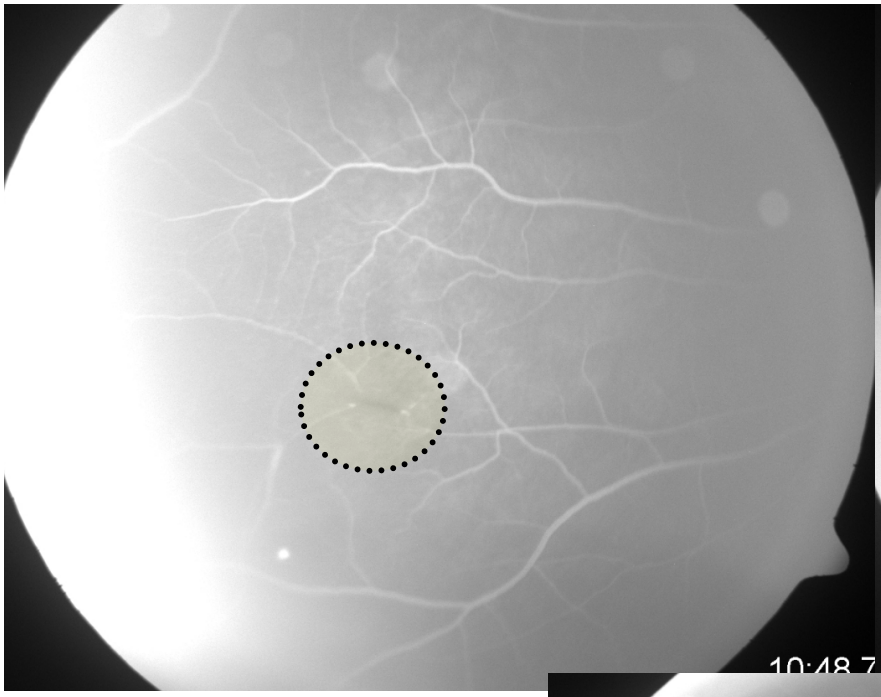
- CNS vasculitis
- Other inflammatory / auto-immune rheumatologic pathologies with CNS involvement
  - SLE? Anti-phospholipid antibody syndrome?

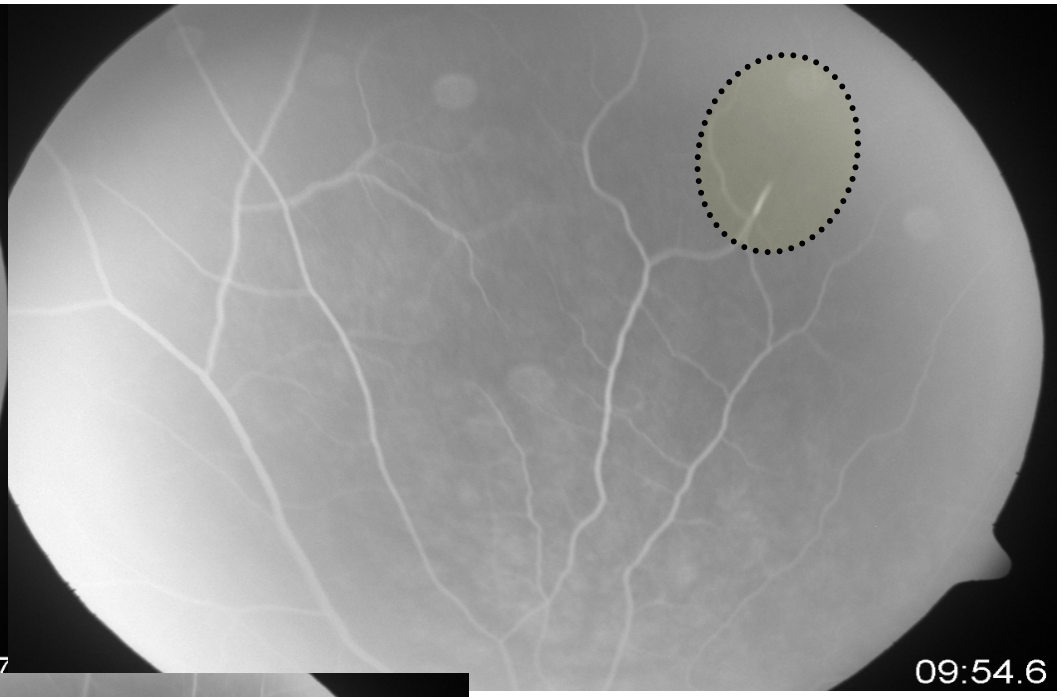
Differential Dx

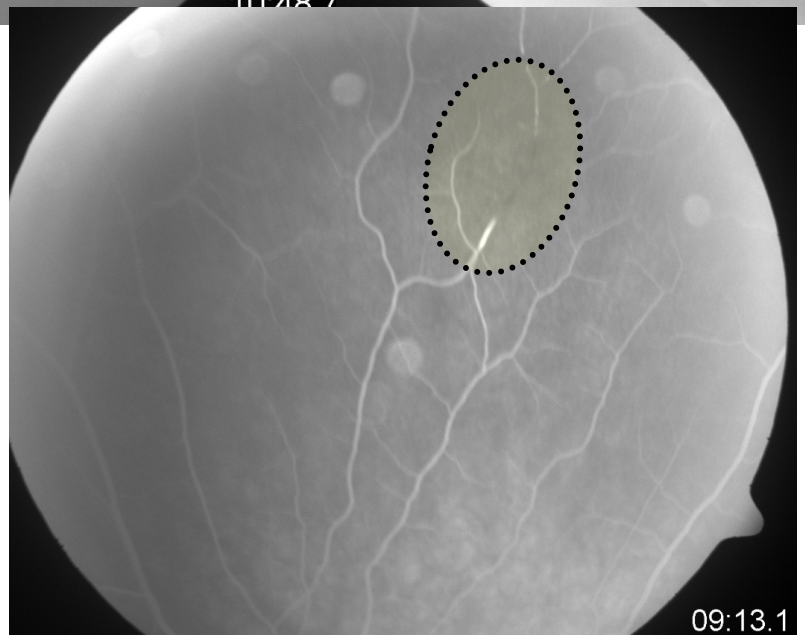
- Susac's Syndrome
  - Requires *ophthalmologic* examination
    - Normal routine fundoscopy
      - Special request for fluorescein angiography
  - *Audiometry*



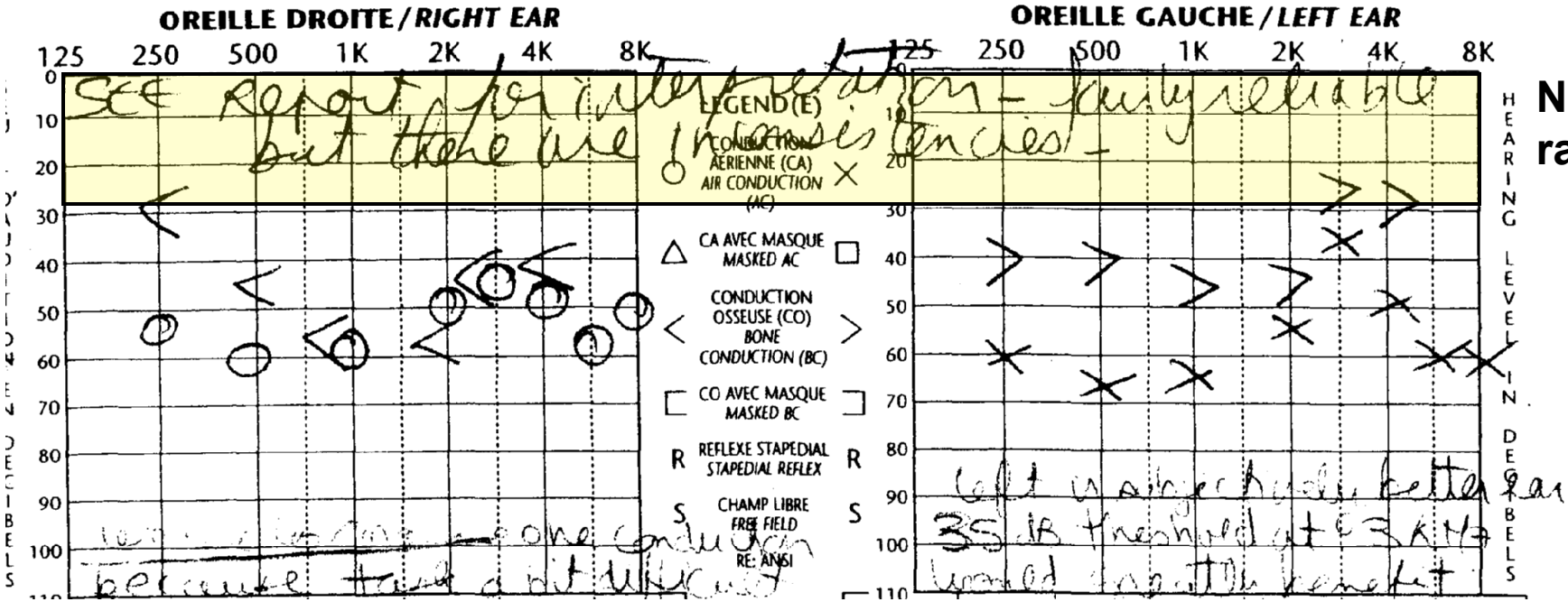
Branch Retinal Artery Occlusions (BRAO)







Audiometry



Normal range

Susac's syndrome

J.Susac

- Clinical **triad** of consisting of *encephalopathy*, branch retinal artery occlusions and sensorineural hearing loss
  - Defined as an **endotheliopathy** or **microangiopathy (<100 μm)** of unknown aetiology involving brain, retina and cochlea.
- 3:1 (F:M)
- 8-59 yo

"Most patients do not exhibit the classic clinical triad at the time of onset…"

13% do

Current Opinion in Neurology 2005, 18:311–314

Susac's syndrome

- Approximately 300 cases identified in the literature, although probably under-recognized and under-diagnosed
  - First reported in 1977 by John Susac
- Pathophysiology:
  - Cause of arteriolar occlusions unknown
    - Most current thinking is: auto-immune
  - Hypotheses include:
    - Anti-endothelial cell antibodies
      - Also found in SLE, RA, Sjogren's, sarcoid, thus ?epiphenomena
    - In-situ thrombus formation
    - Microemboli
    - Vasospasm
    - Micro-vasculitis
- Distribution is enigmatic
    - Selective vulnerability due to ?common embryologic origin

Neurology 1985;35:1113-1121
Current Opinion in Neurology 2005, 18:311–314
Journal of the Neurological Sciences 257 (2007) 270–272

The size of callosal lesions is usually 3–7 mm
Occlusion of small **precapillary arterioles** smaller than **100 *μ*m**

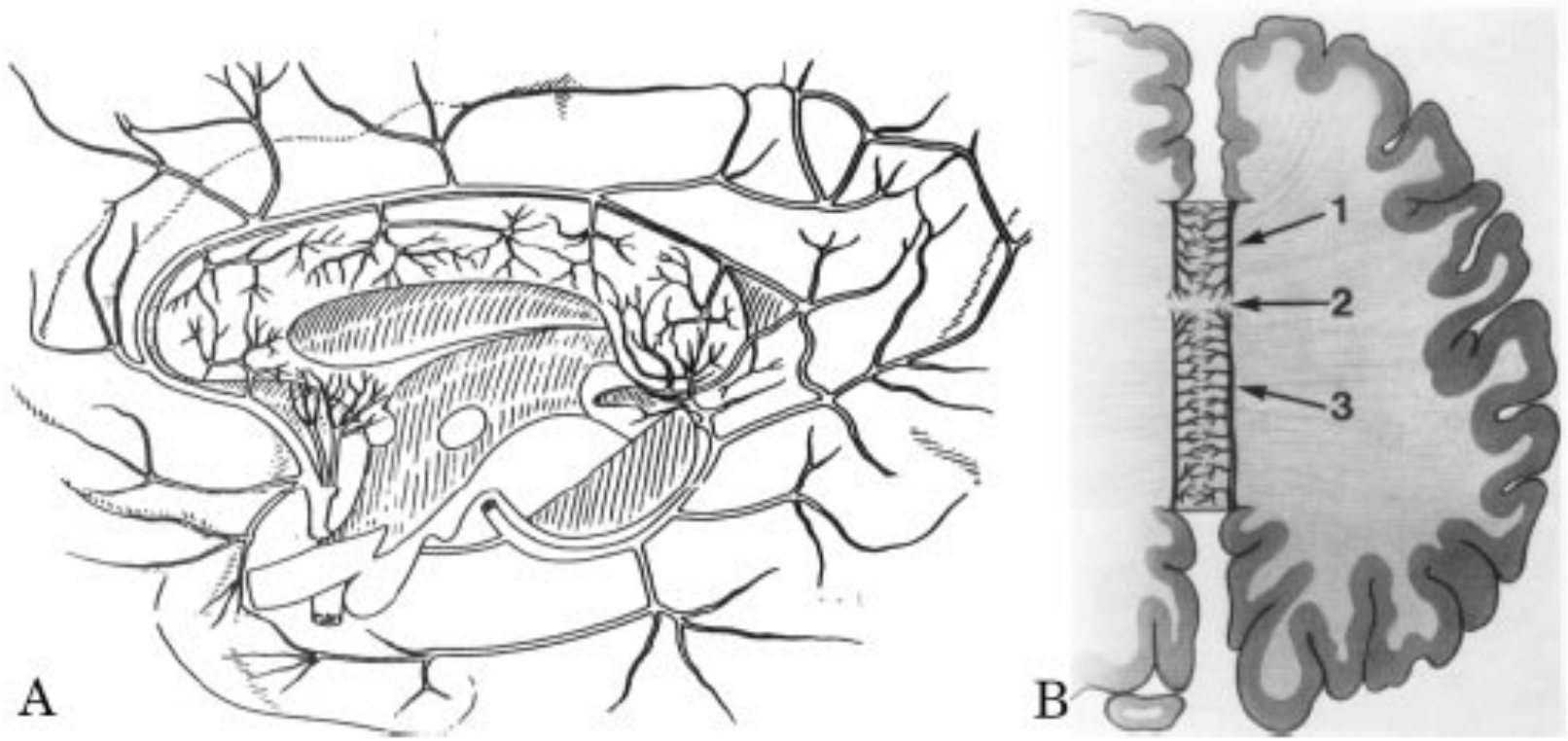


Figure 5. Vascular supply of the corpus callosum, reprinted from Gean et al.[44] with permission.

NEUROLOGY 2003;61:1783–1787

End-organ / System	Clinical Presentation	Mechanism
CNS	Migraine, encephalopathy / *neuro-psychiatric* manifestations, seizures, myoclonus, pyramidal syndrome or ataxia	Microinfarction of CNS white and grey matter
Opthalmologic	Profound visual loss (macula) Posterior pole occlusion Minimal complaint or asymptomatic Peripheral occlusion	Multiple bilateral BRAO's and infarcts
Vestibulocochlear organs	1. Acute, Bilateral, Asymmetric, Sensorineural type as demonstrated by pure-tone audiometry – Low and medium frequencies with poor speech discrimination 2. Vertigo, ataxia, nystagmus, gait impairment – Peripheral end-organ or brainstem	Microinfarcts of the *apical* cochlea Microinfarction of *membranous labyrinth*
Systemic	Myalgias, Arthralgias	

Paraclinical

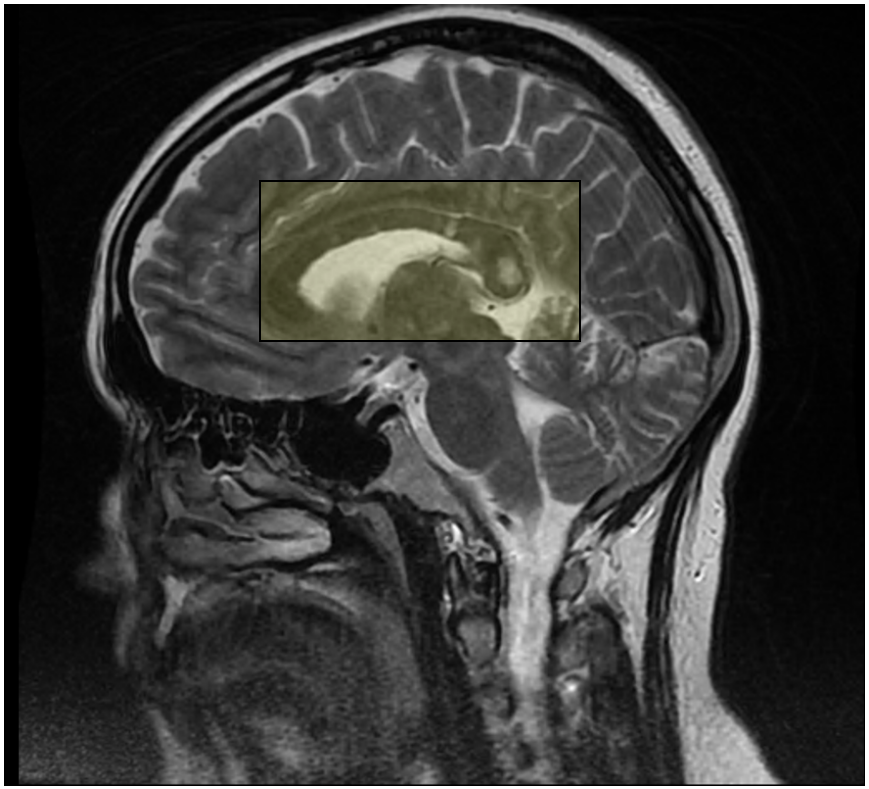
- Labs
  - Serum:
    - ***No*** evidence for infectious, autoimmune or connective tissue disorder
    - ***No*** evidence for thrombophilic state
      - Case reports with elevate IgM & IgG ACL
    - *Some patients have mildly + ANA or RF, ESR,CRP*
      - ***Not more than general population***
    - *Elevated factor VIII & von Willebrand Factor Antigen*
      - endothelial damage
  - CSF:
    - *Elevated protein, lymphocytic pleocytosis (<20)*
    - Absent OCB

Journal of the Neurological Sciences 257 (2007) 270–272

Neuroimaging

- **Location of lesions:**
  1. ***Corpus Callosum***
     - *Central portion* with relative sparing of the periphery
       - MS and ADEM callosal lesions extend to the undersurface at septal interface
     - ***'Callosal holes'*** (T1) are pathognomonic
  2. Multiple small hyperintense foci on T2WI in **white** and **grey** matter of both supratentorial and infratentorial structures (W>G)
     - Often misinterpreted as MS or ADEM
     - Contrast enhancement acute lesions and leptomeninges* (1/3)

Typical MRI of SS



Acute phase

Sag T2: Patient H

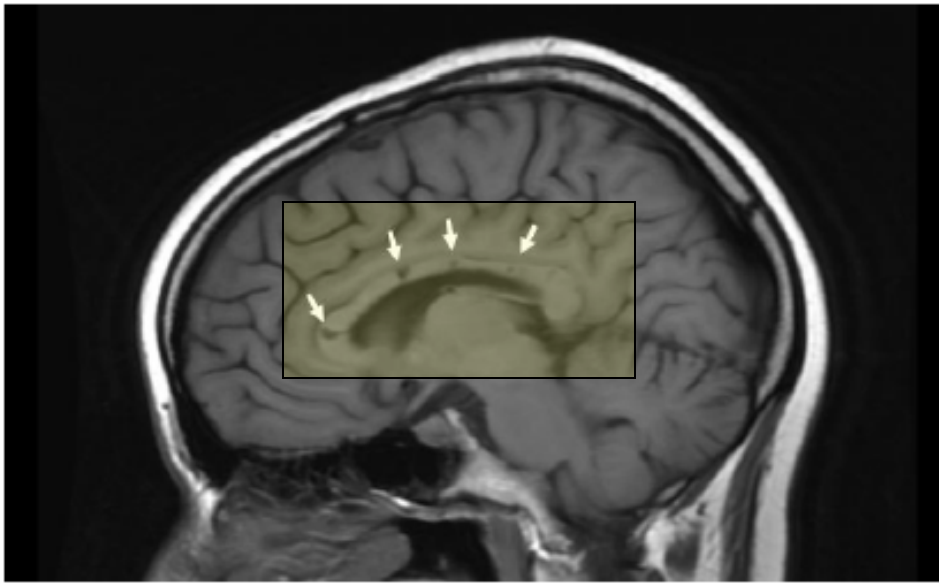


Figure 4
MRI brain. Sagittal T1 image showing the pathognomonic central callosal "holes" (microinfarcts) of SS. These residual "holes" (and sometimes, "spokes") develop as the acute callosal changes resolve.

Convalescent phase

Pediatric Rheumatology 2008, **6**:3

Treatment

- **No** gold standard (expert consensus)
- Immunosuppression based on histological similarity to dermatomyositis and proposed ***anti-endothelial Ab***
  - Steroids* (IV pulse x 3-5 d, followed by prolonged oral taper)
  - IVIG*
  - Cyclophosphamide*
  - Cellcept
  - PLEX
  - Rituxan (aberrant B cell behaviour producing Ab) in refractory cases
- ASA +/- CCB (nimodipine)
- AC *not* recommended
- Cochlear implants [long term]

Journal of the Neurological Sciences 257 (2007) 215–220

Course in hospital & F/U

- Encephalopathy gradually improved and resolved after 5 days of admission.
  - Residual tinnitus and very mild unsteadiness of gait.
  - Hearing loss improved later (before discharge).
  - Visual disturbance resolved.
  - Excellent outcome.

- Tx
  - Had a total of 2, 5d courses of 1 g SoluMedrol
  - 1 course of IVIG over 2 days
  - Started on ASA 81 mg QD
  - Started on Cyclophosphamide, 1x per month IV x 2 yrs

Bottom Line

- Important to recognize this clinical constellation (triad) of findings in otherwise **healthy young females**
- MRI is the gold standard imaging modality
  - *Central* callosal lesions, 'holes'
    - Central lesions are pathognomonic for SS
  - *Leptomeningeal* enhancement
    - Exceptionally unusual for MS
    - Can sometimes be seen in ADEM
      - thalamic lesions
- **Deafness** is rare in MS (6%), never reported in ADEM
- Finding **BRAO** is incompatible with MS, never reported with ADEM
    - MUST insist on fluorescein study (essential), as regular fundoscopy can be normal

Susac's Syndrome = Immune mediated micro-vasculopathy

Overlap syndrome which mandates swift coordination between neurology, immunology, psychiatry, ENT, rhumatology

Thank You

Questions?

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