Symposium Neuroradiologicum

Cerebral Amyloid Angiopathy-related inflammation: an emerging disease

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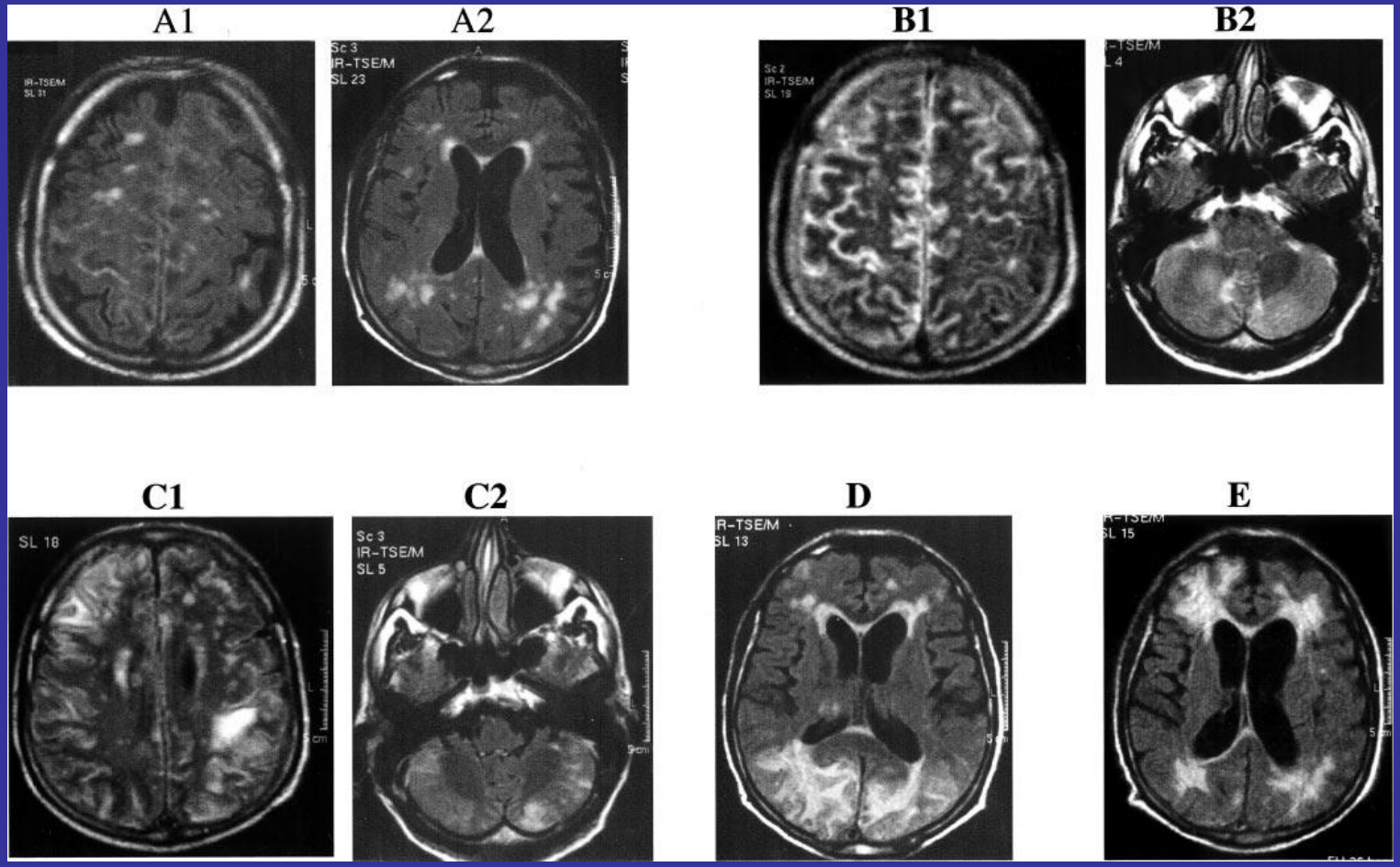
Background

Orgogozo JM et al. Subacute meningoencephalitis in a subset of patients with AD after Aβ42 immunization
Neurology 2003;61:46

- 372 AD patients were randomized: active immunization with amyloid (AN1792) or placebo
- Stop after 4 meningoencephalitides (ME)
- ME in 18/298 (6%) of immunized patients vs. 0/74 in pts with placebo

Orgogozo JM et al. Subacute meningoencephalitis in a subset of patients with AD after Aβ42 immunization. Neurology 2003;61:46



Eng JA et al. Clinical manifestation of cerebral amyloid angiopathy-related inflammation Ann Neurol 2004;55:250

- of 42 pts with definite CAA, 7 had signs of inflammation, clinically manifested by cognitive impairment and epilepsy
- on imaging studies, they had white matter abnormalities
- apolipoprotein E genotype: ε4/ε4 in 71% (vs. 4%)
- good response to immunosuppressive treatment

Pt 1
History

A 76-year-old man, always in good health, with mildly elevated blood pressure, on Aspirin, comes to our outpatient clinic complaining of fatigue and "confusion in his head".

Patient's wife reports that he has some memory loss for the past few months.

Pt is a dental technician, still active at work, without problems

- Normal Neurological examination

- Funduscopy: mild arterial narrowing and sclerosis
- BP 160/80

- MMSE: 27/30 – (25.3/30 corrected for age and education, with some selective failure on memory tasks)

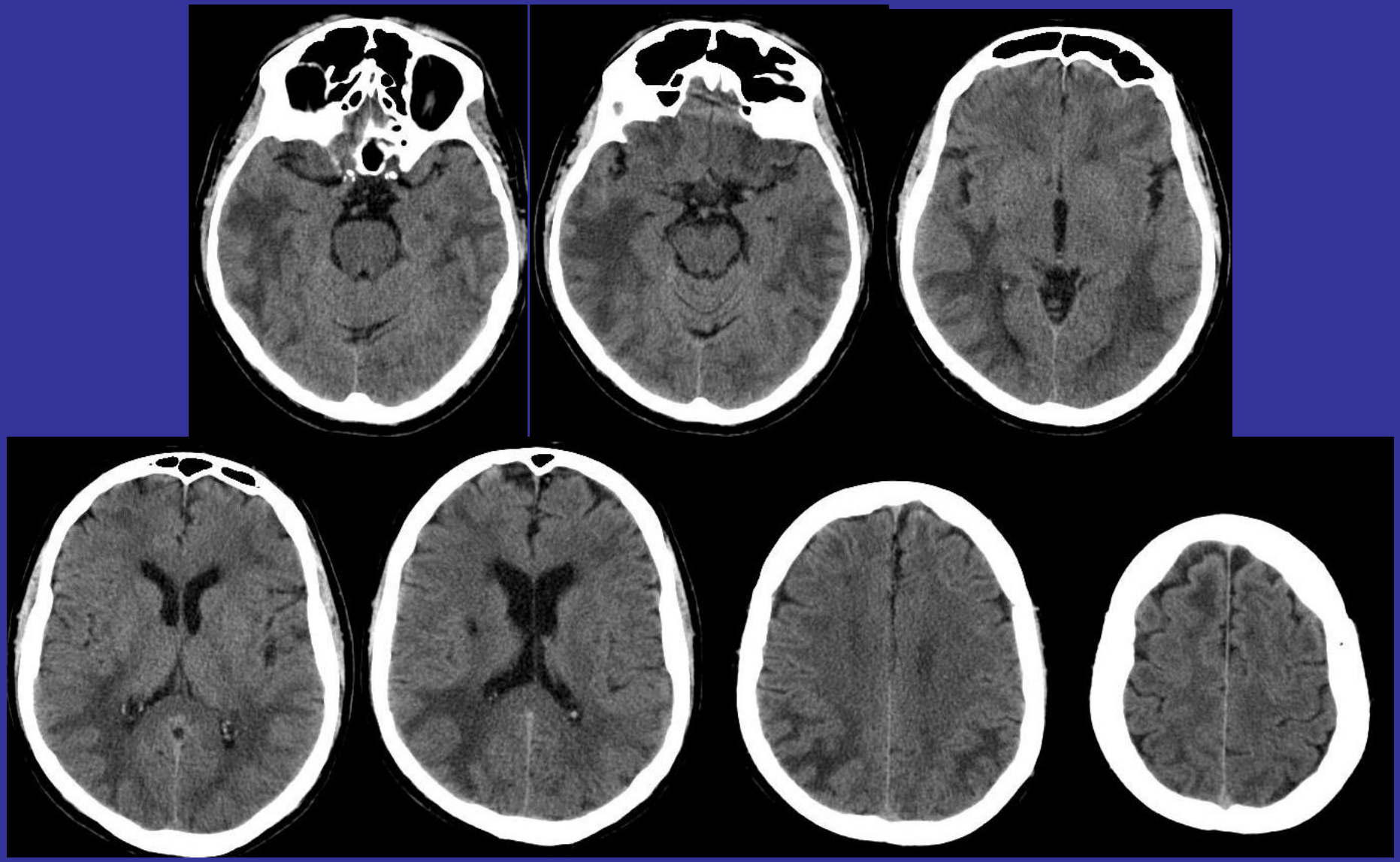
- Blood tests normal, including panel of antibodies, coagulation, inflammation

DIAGNOSIS

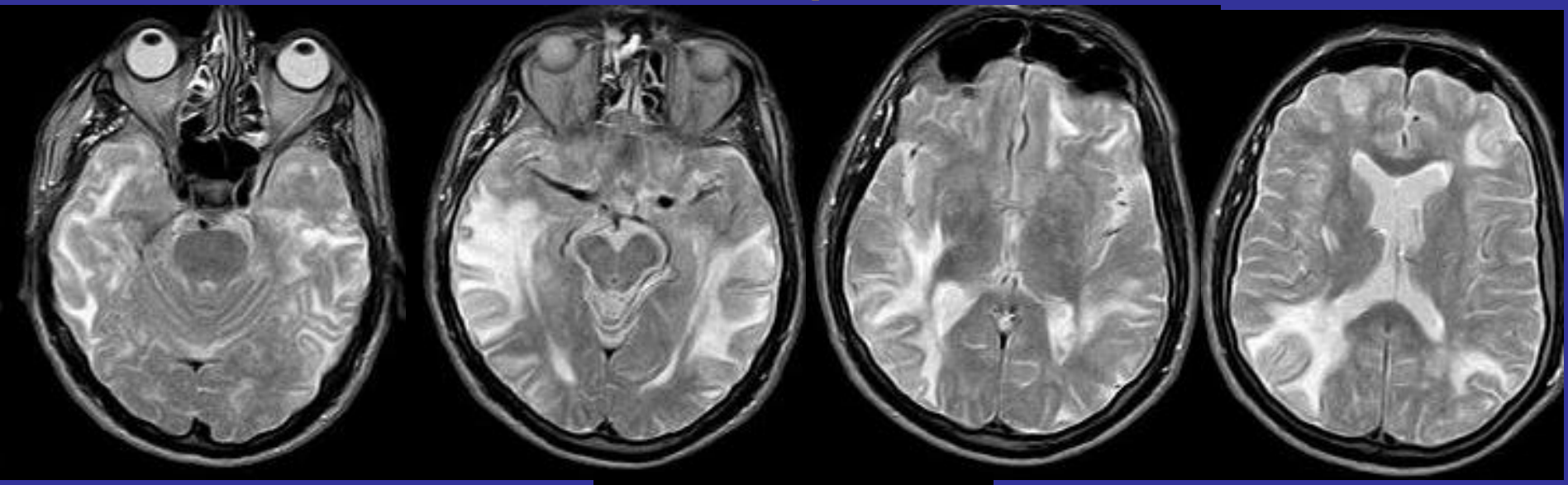
MILD COGNITIVE IMPAIRMENT

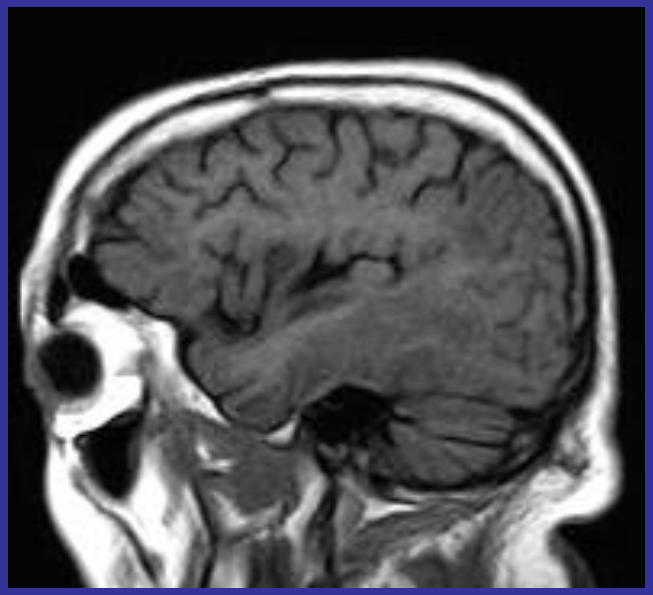
AMNESTIC MCI

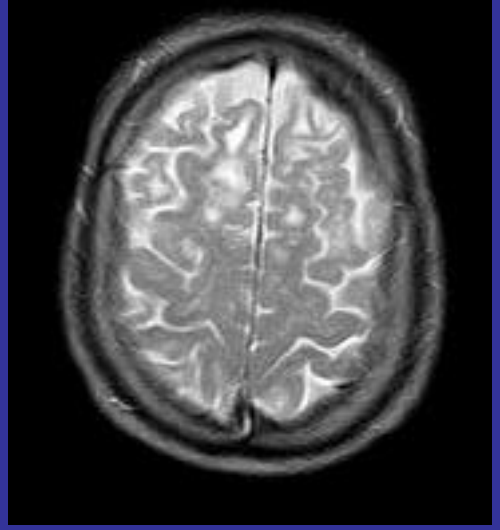
CT Sept. 10, 2008

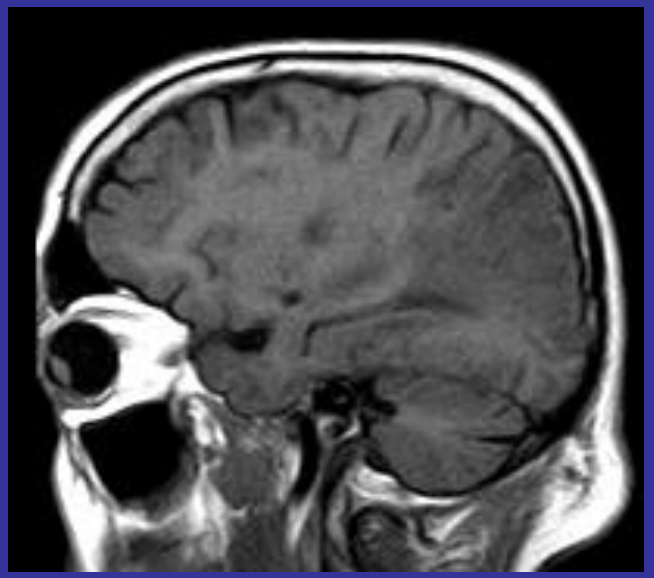


MR 0.5T Sept.11, 2008

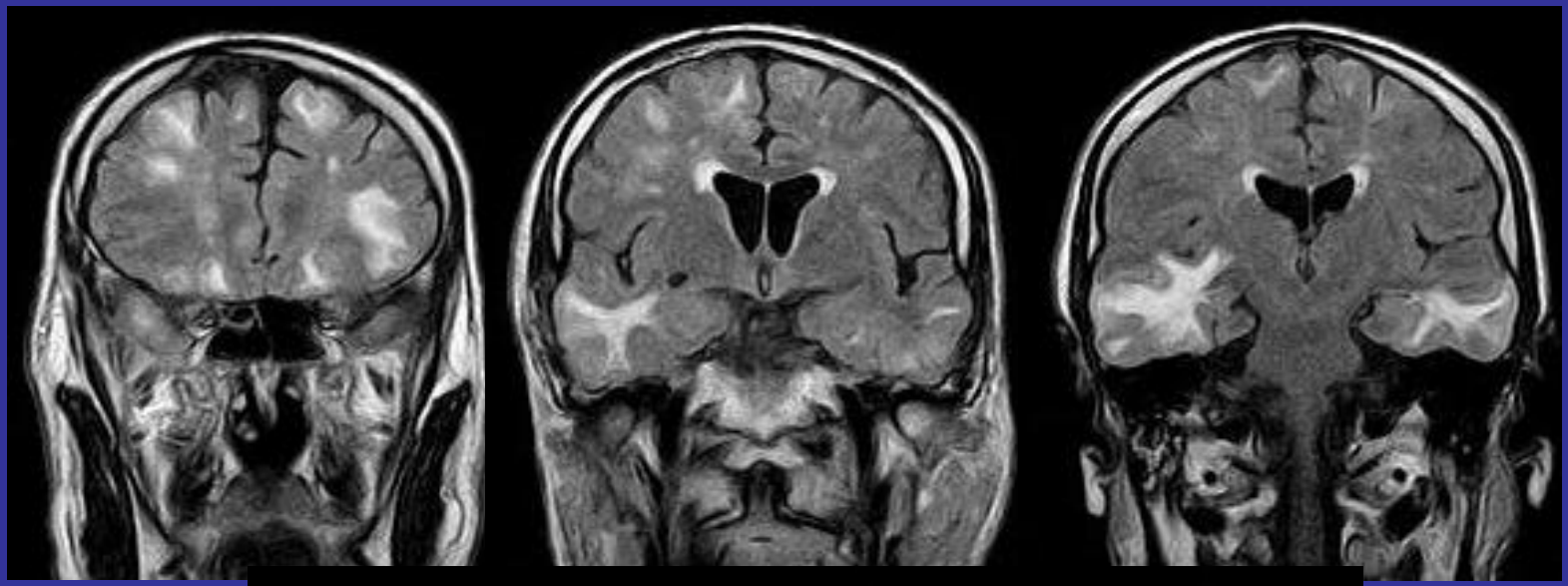


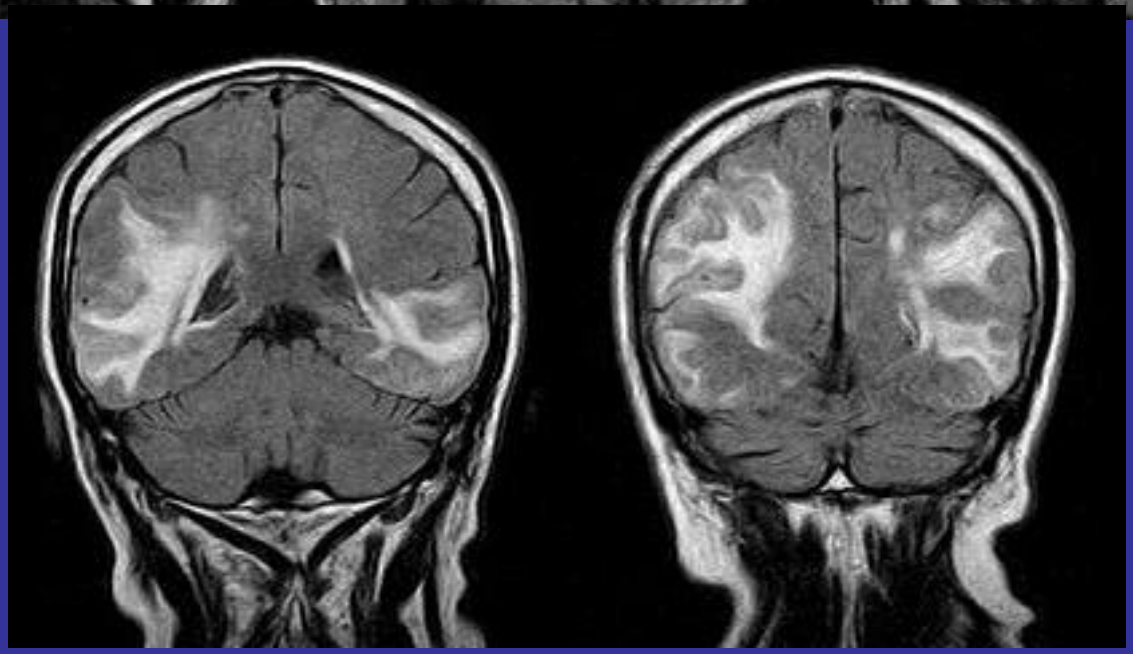


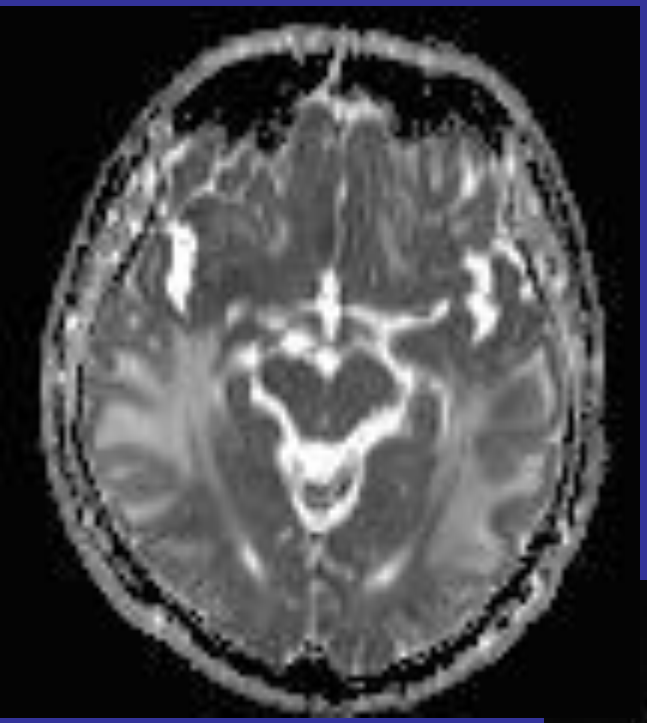




MR - FLAIR

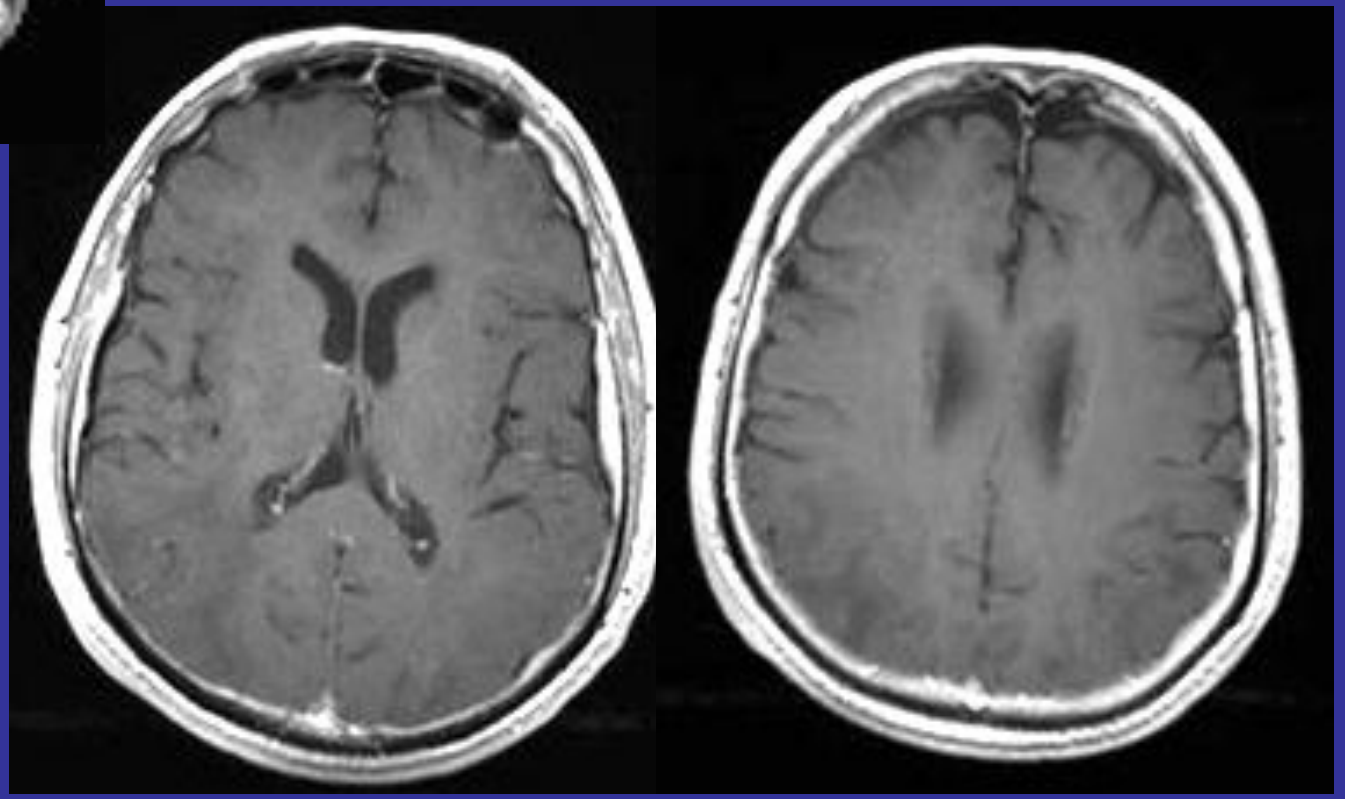




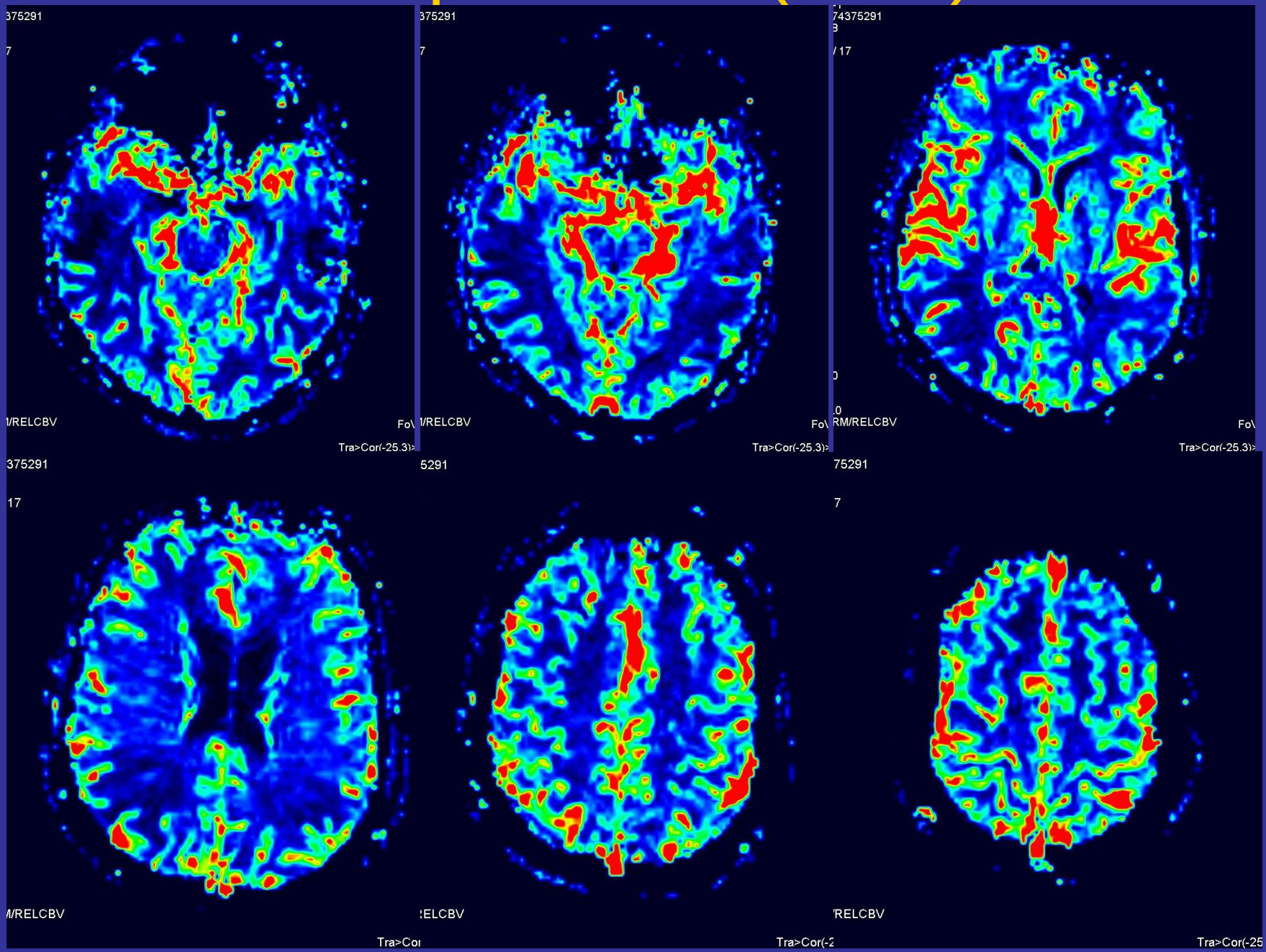


MR 1.5T Sept.11,2008
DWI (ADC)

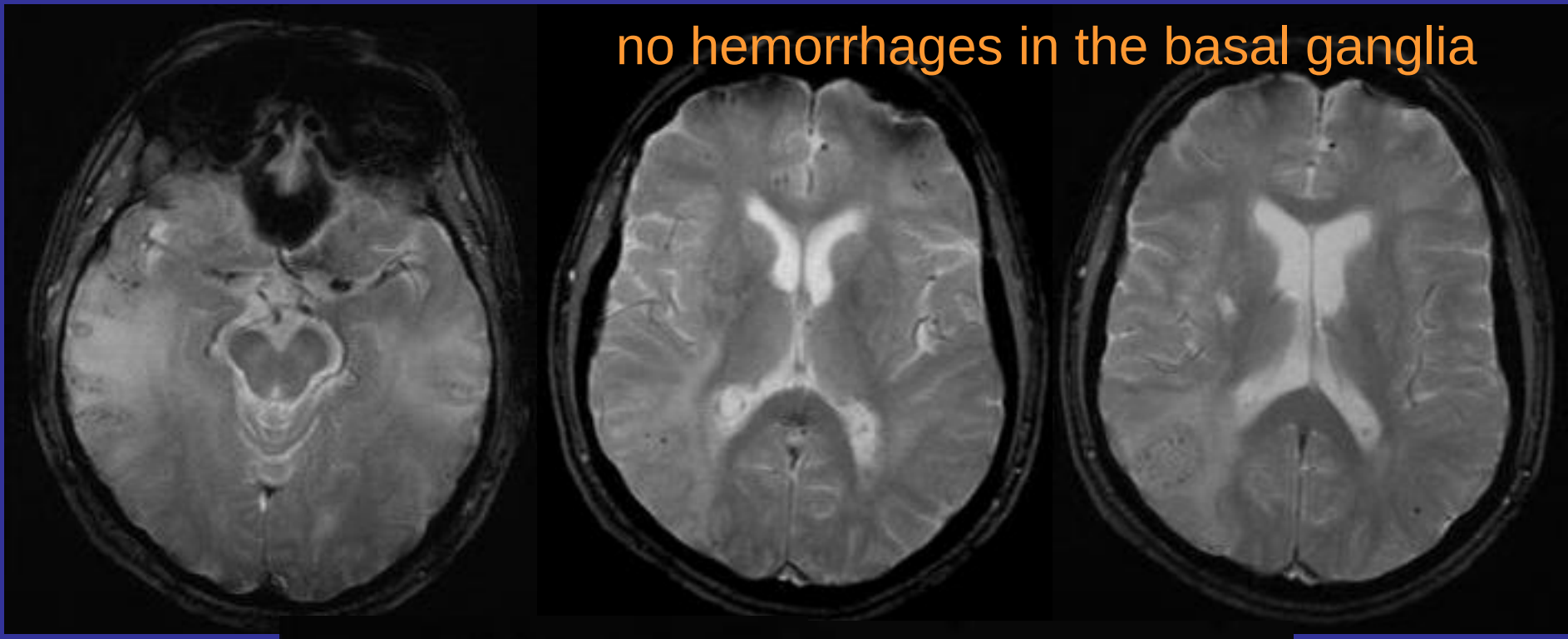
Post-contrast



MR perfusion (CBV)

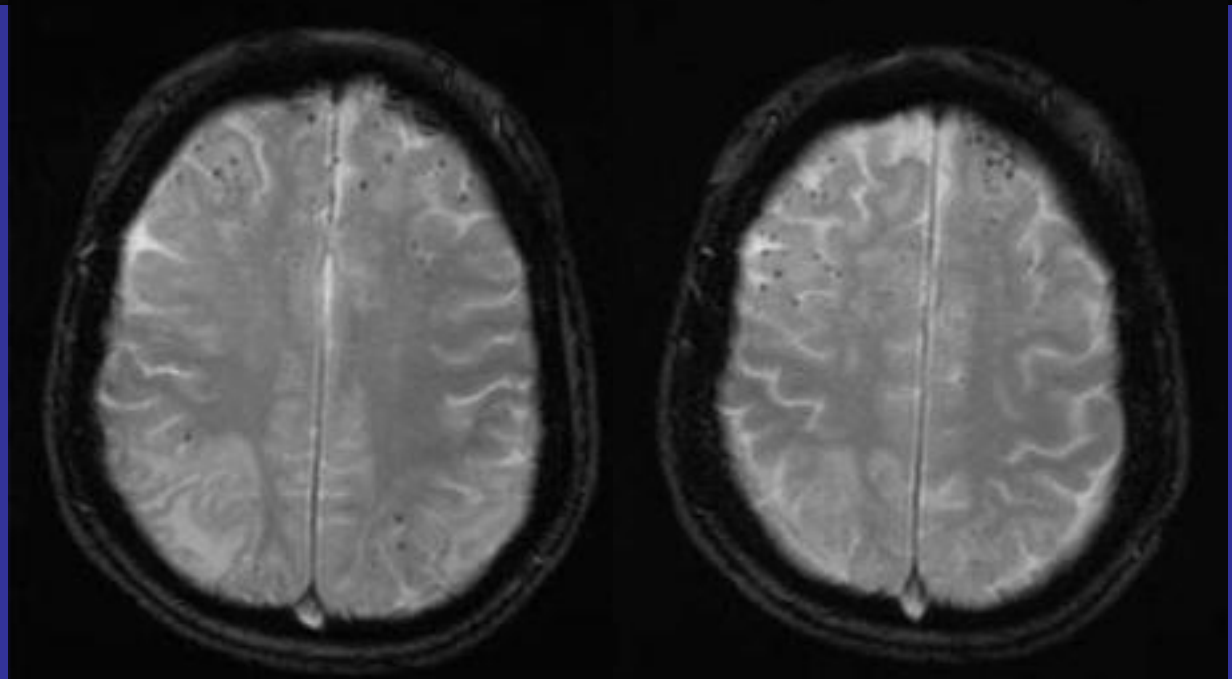


A diagnostic examination was performed.



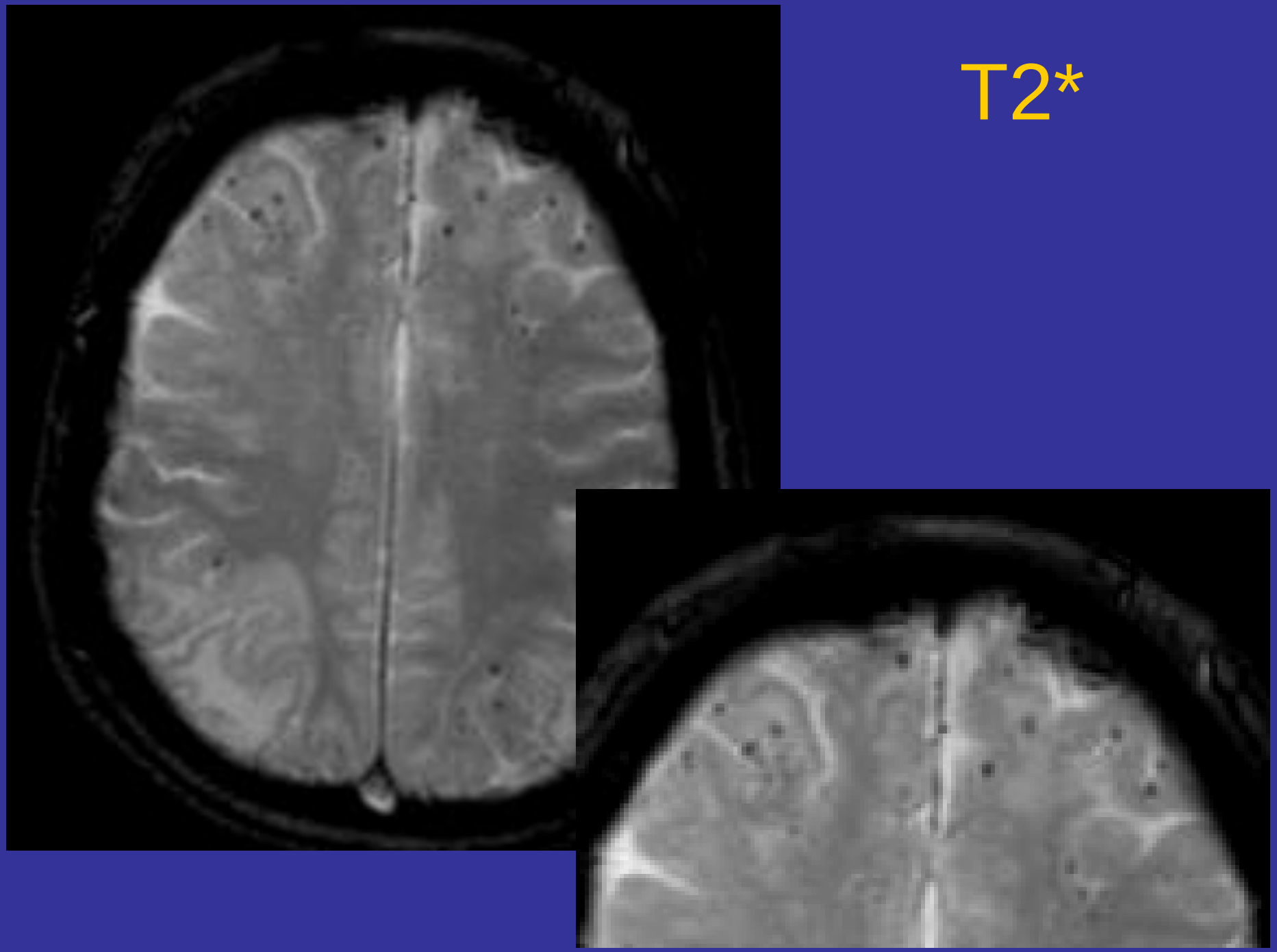
1.5T

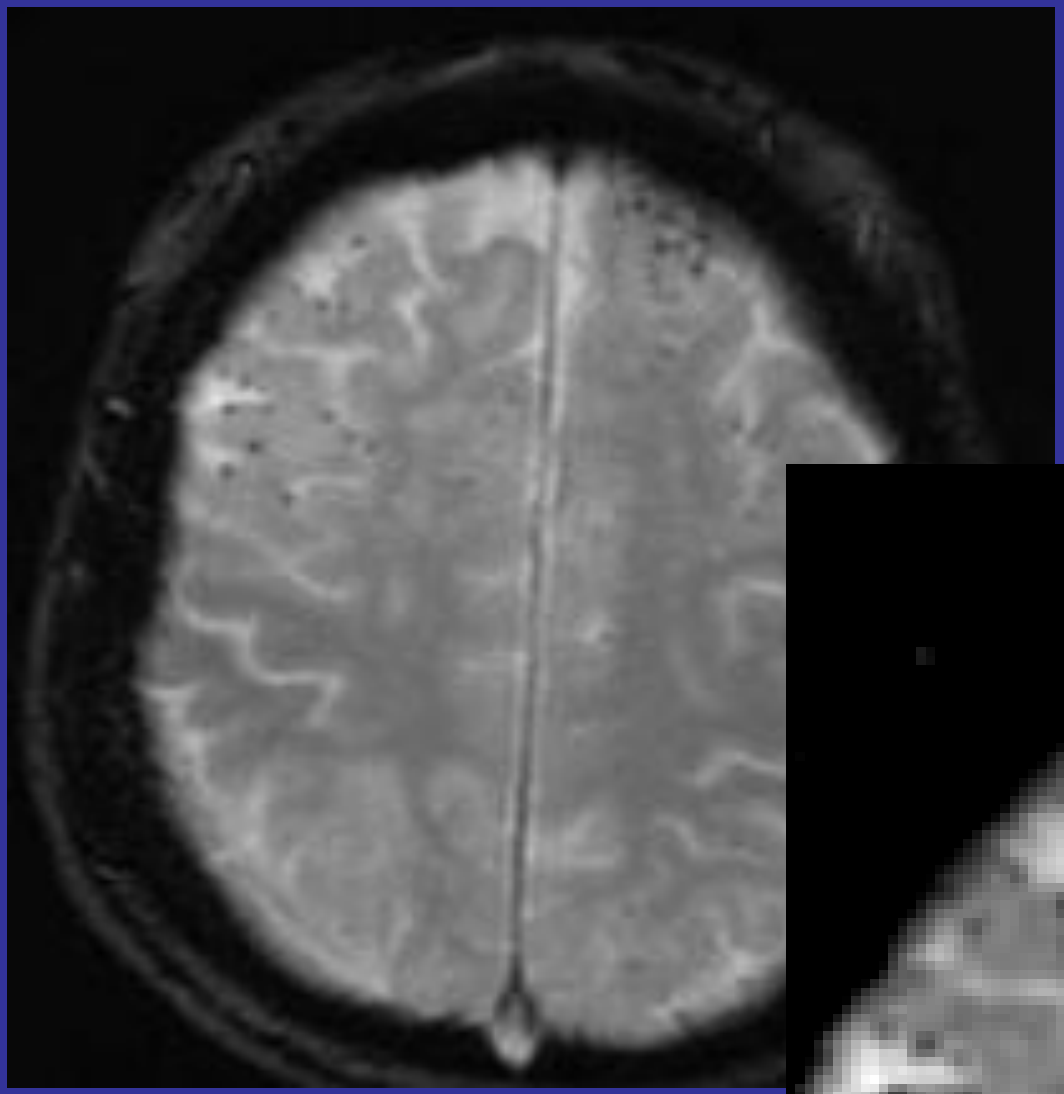
11/9/08

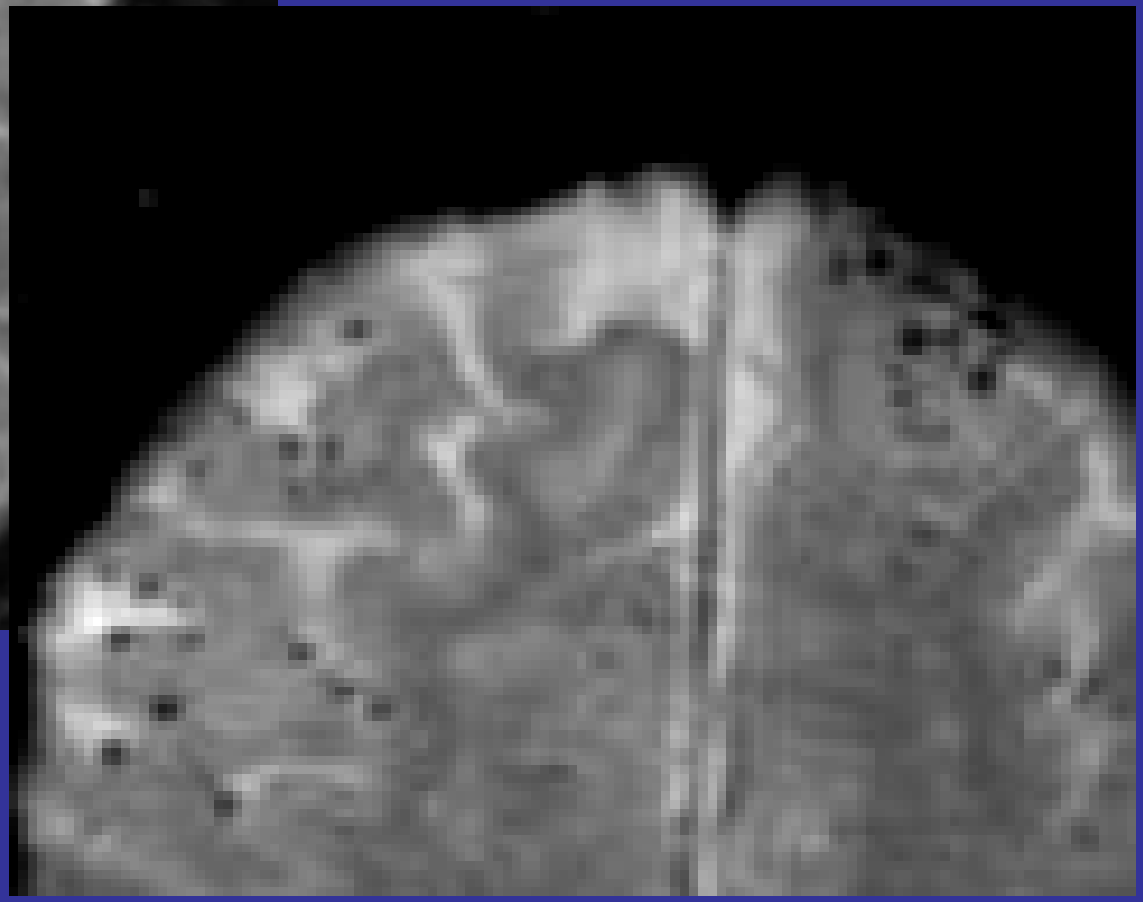


GE

T2*


T2*





T2*

Boston Criteria for the clinical diagnosis of CAA

Knudsen KA et al. Neurology 2001,56:537-539

- Definite (post-mortem or biopsy)
- Probable with pathologic support (biopsy)

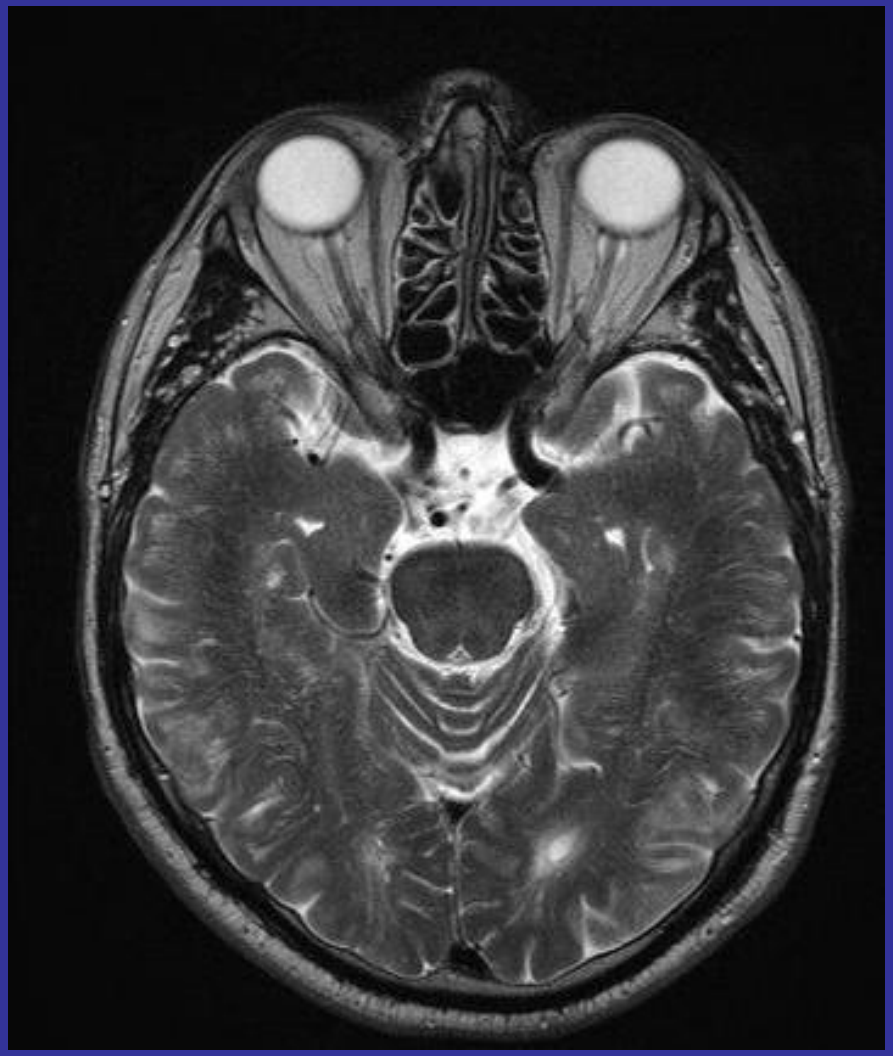
- Probable: clinical data + MRI or CT with
  - multiple lobar hemorrhages, cortical or cortico-subcortical
  - age ≥ 55 years
  - no other causes for hemorrhages
- Possible: same criteria, but single hemorrhage

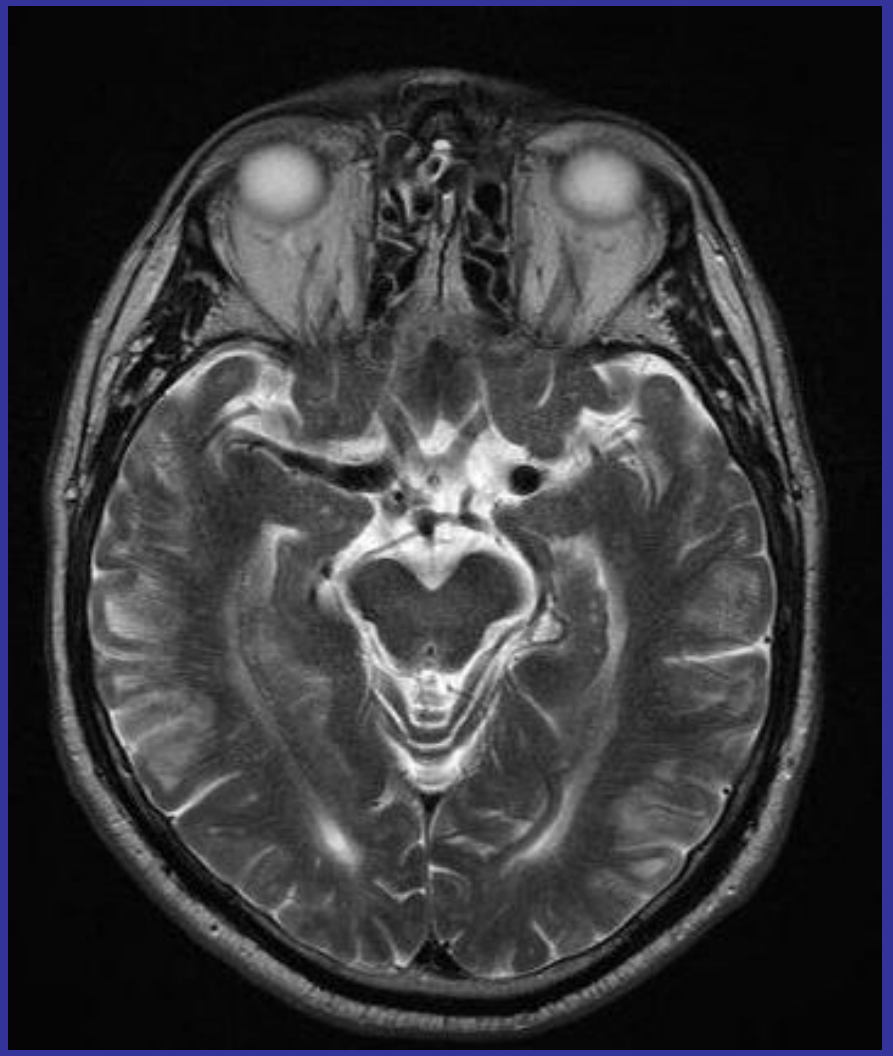
Diagnosis: CAA-related inflammation

Steroid therapy was promptly instituted:

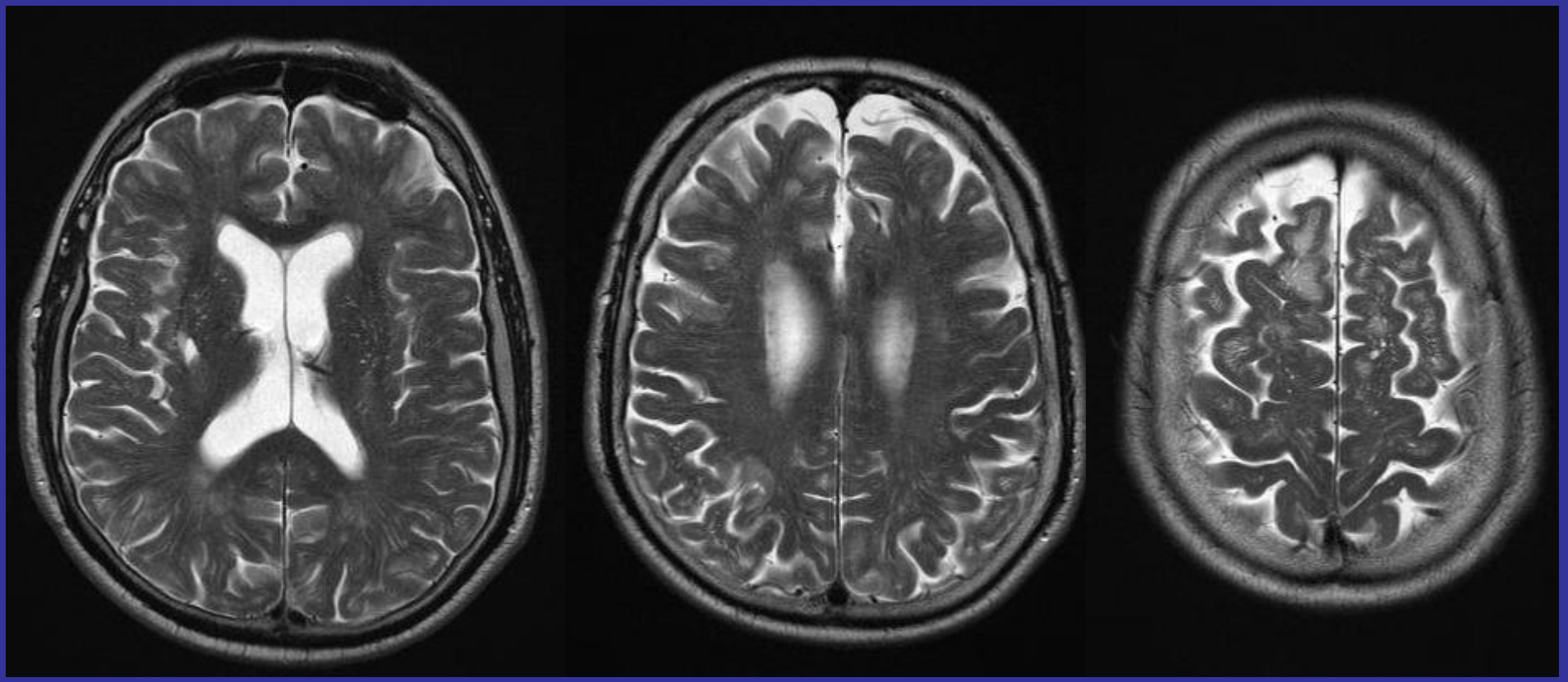
Dexamethasone 8 mg/d i.m. for 1 wk, 4 mg/d in the 2nd wk, then tapering with oral prednisone

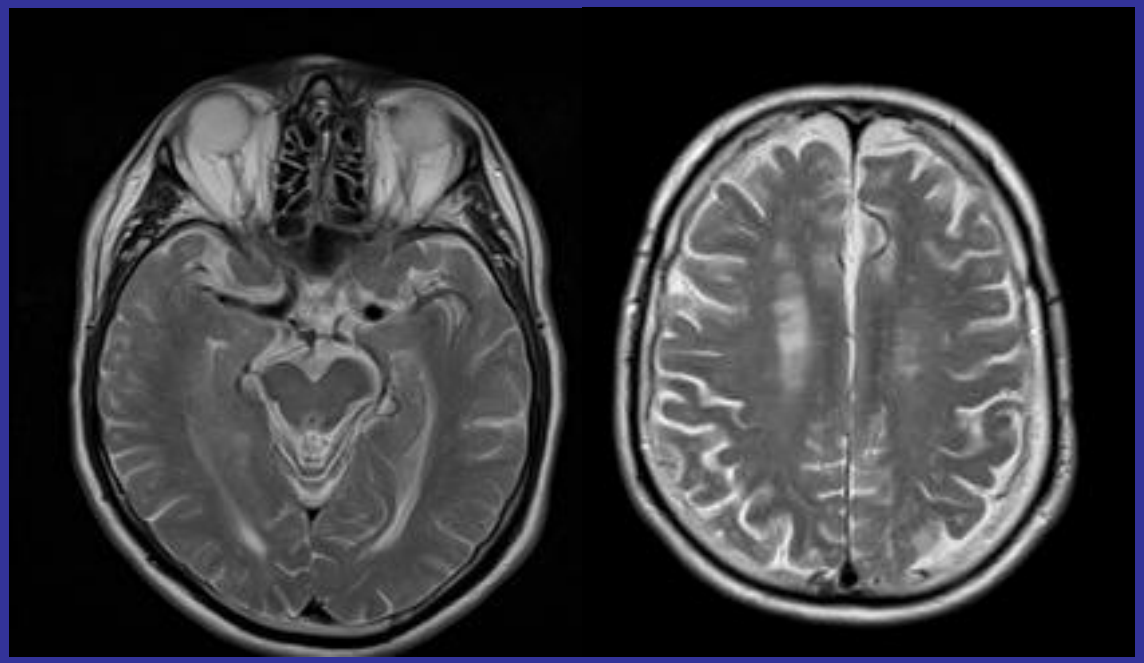
Control MRI after 35 days (Oct 16, 2008)





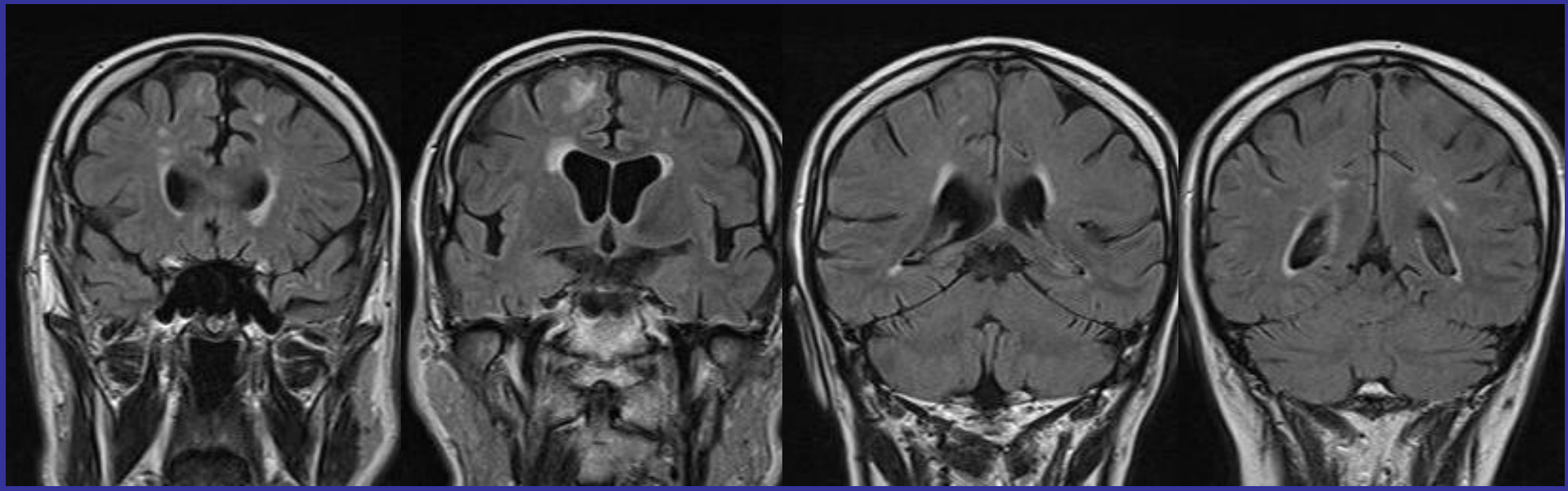
Oct 16, 2008



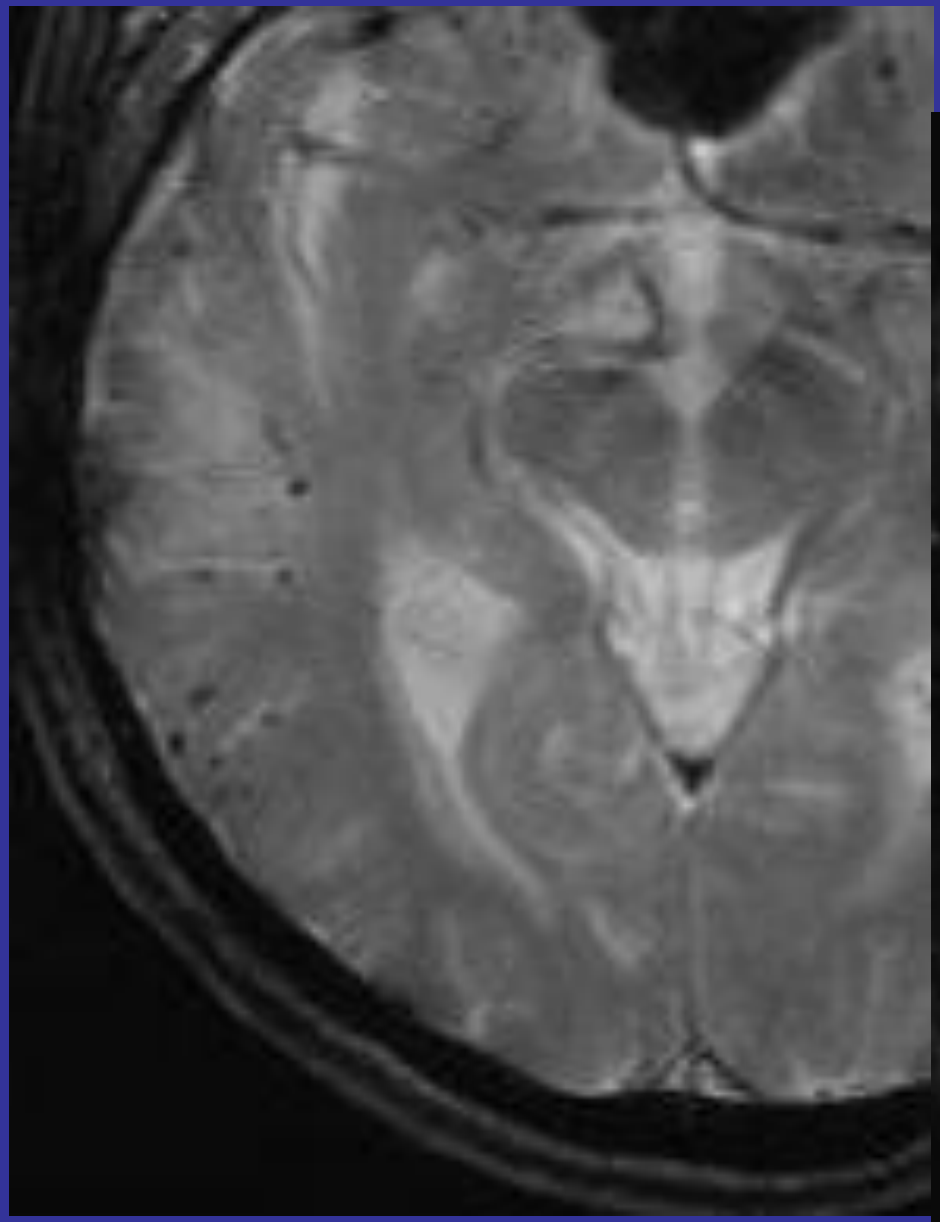


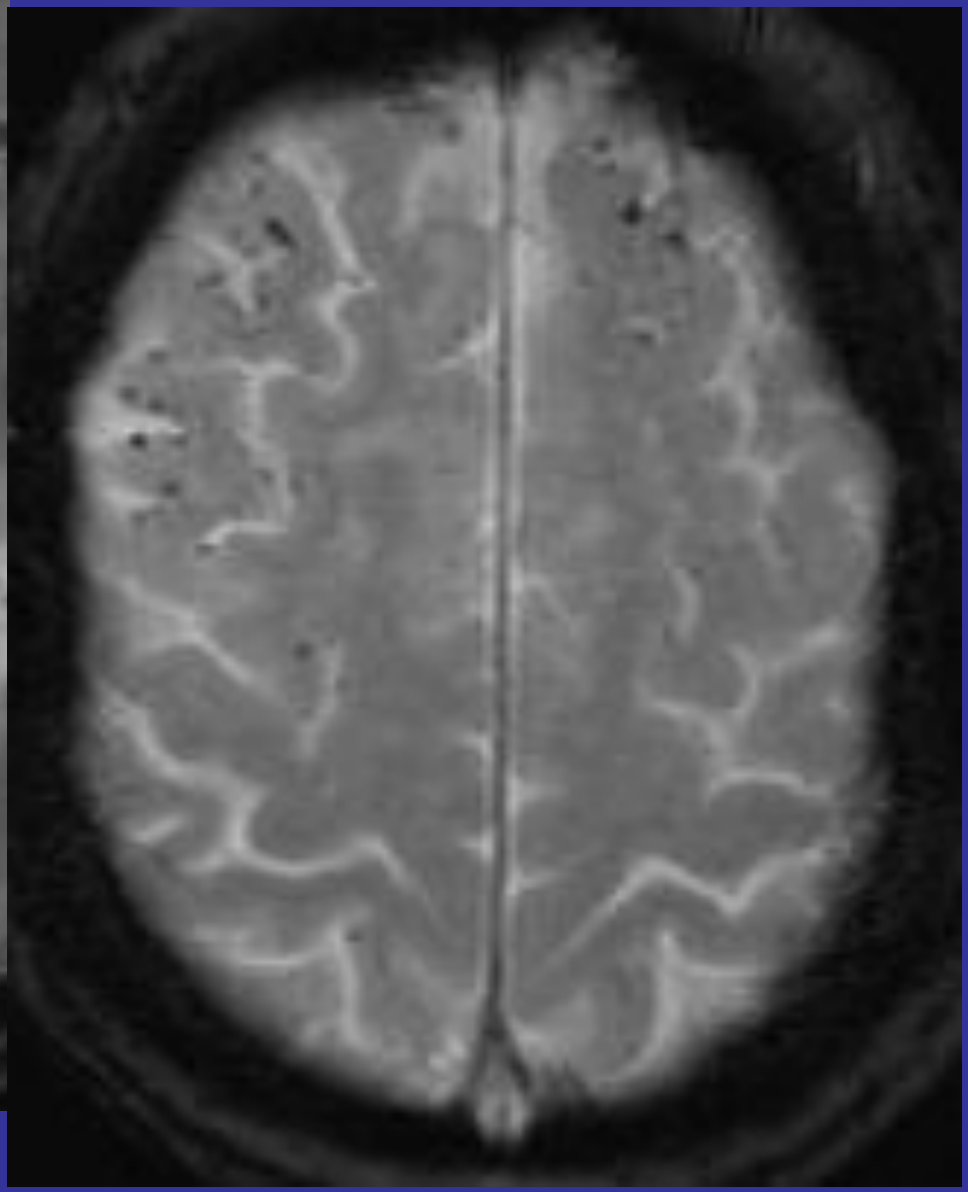
Control MRI
4 months later

(Feb 16, 2009)



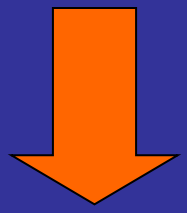
T2*





- Normal neurological examination
- Normal cognitive profile
- MMSE 30/30
- APOE genotype: ε4-ε4

CAA + good response to steroid and ε4-ε4 genotype



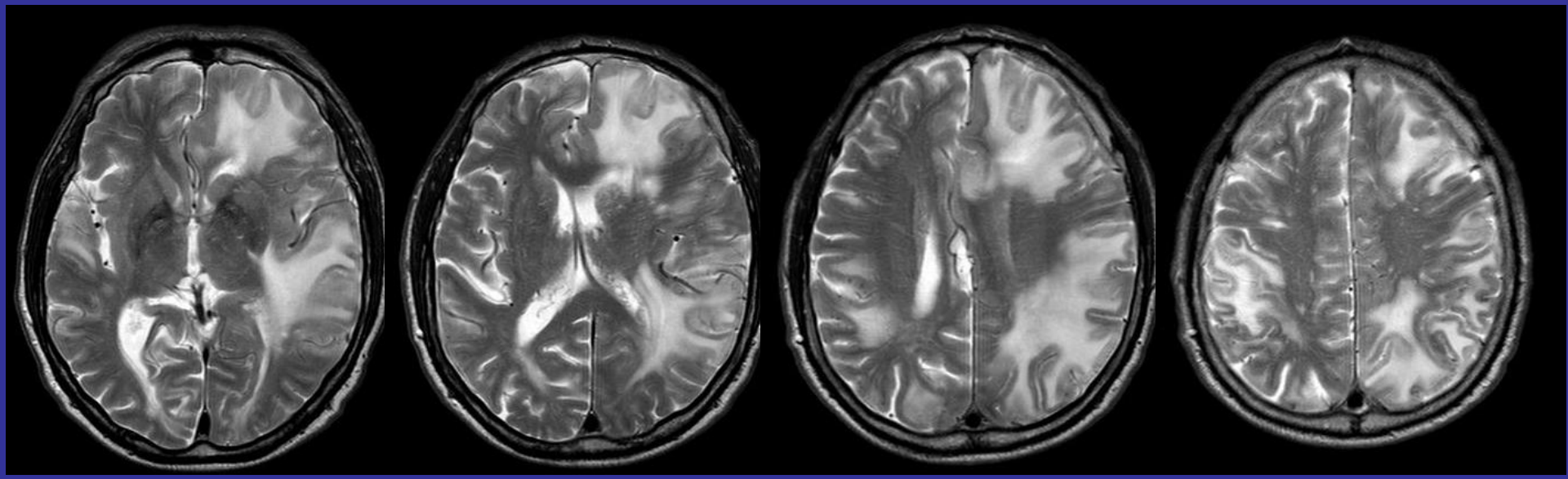
CAA-ri

Patient 2

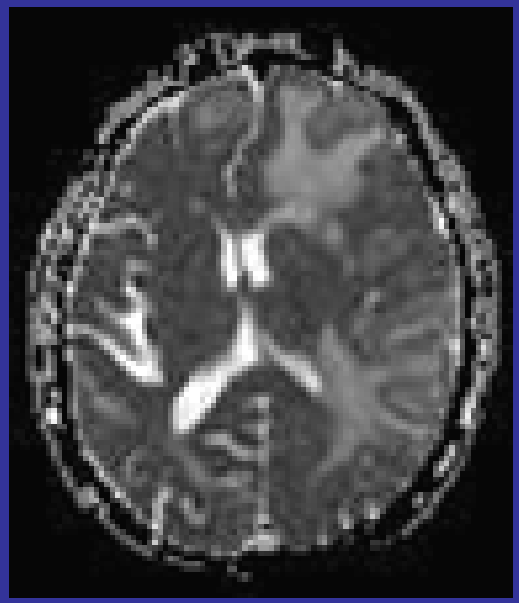
- A 67-years-old man with progressive, severe neurologic involvement, with memory and attention deficit and mood disorder. No focal signs

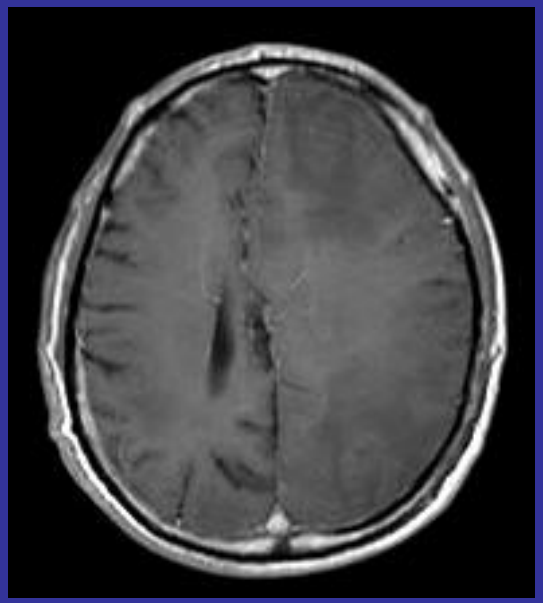
- Normal laboratory findings

Pt. 2 MRI at presentation



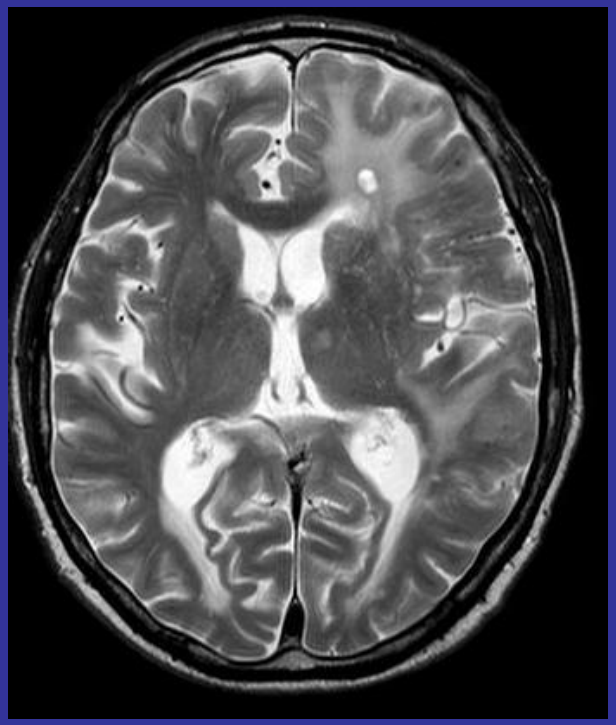
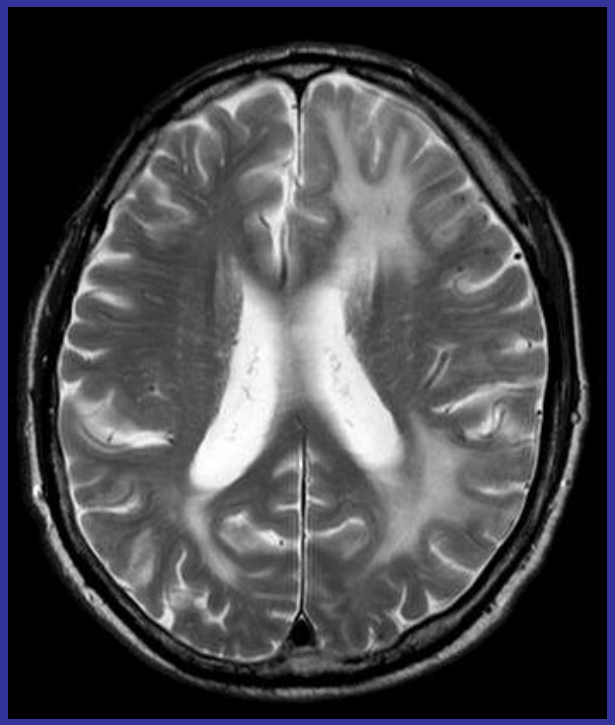
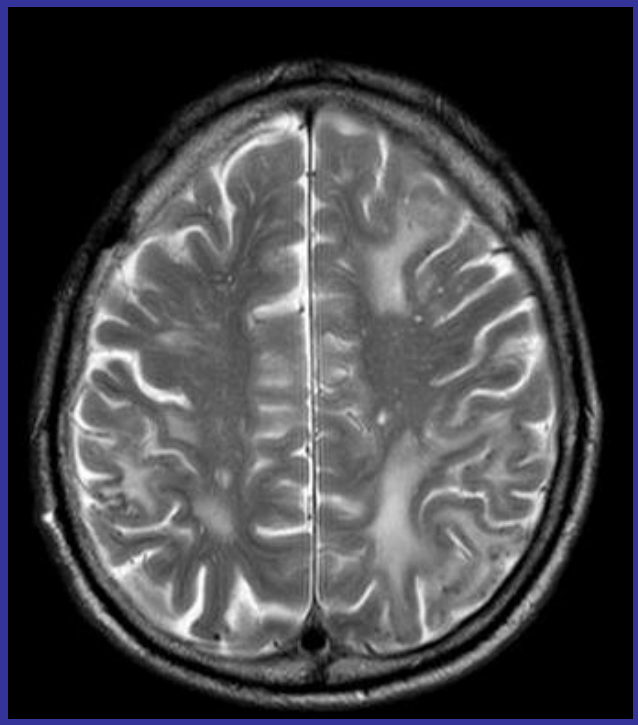
ADC





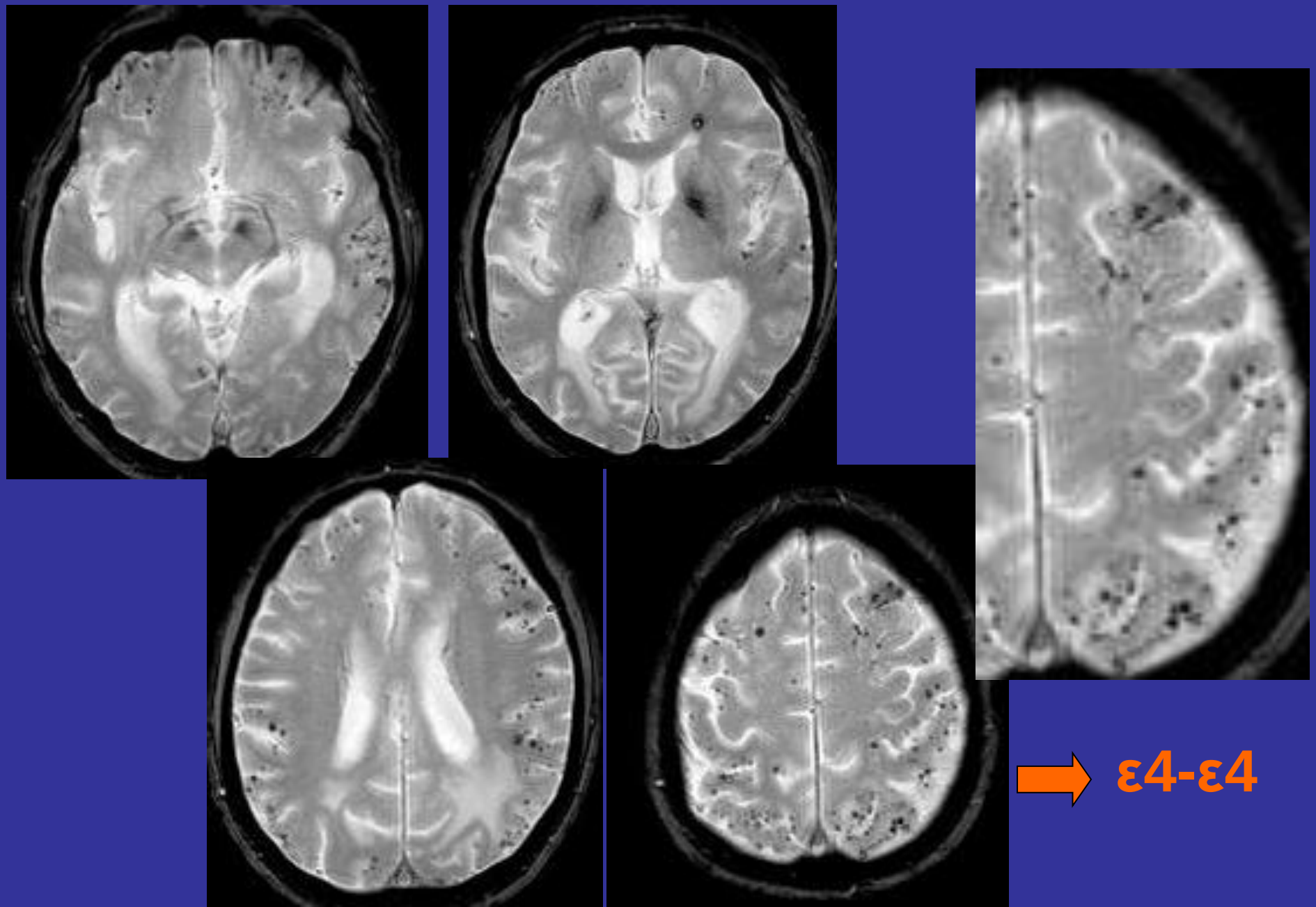
Post contrast

Pt. 2 MRI post left frontal biopsy and steroid treatment

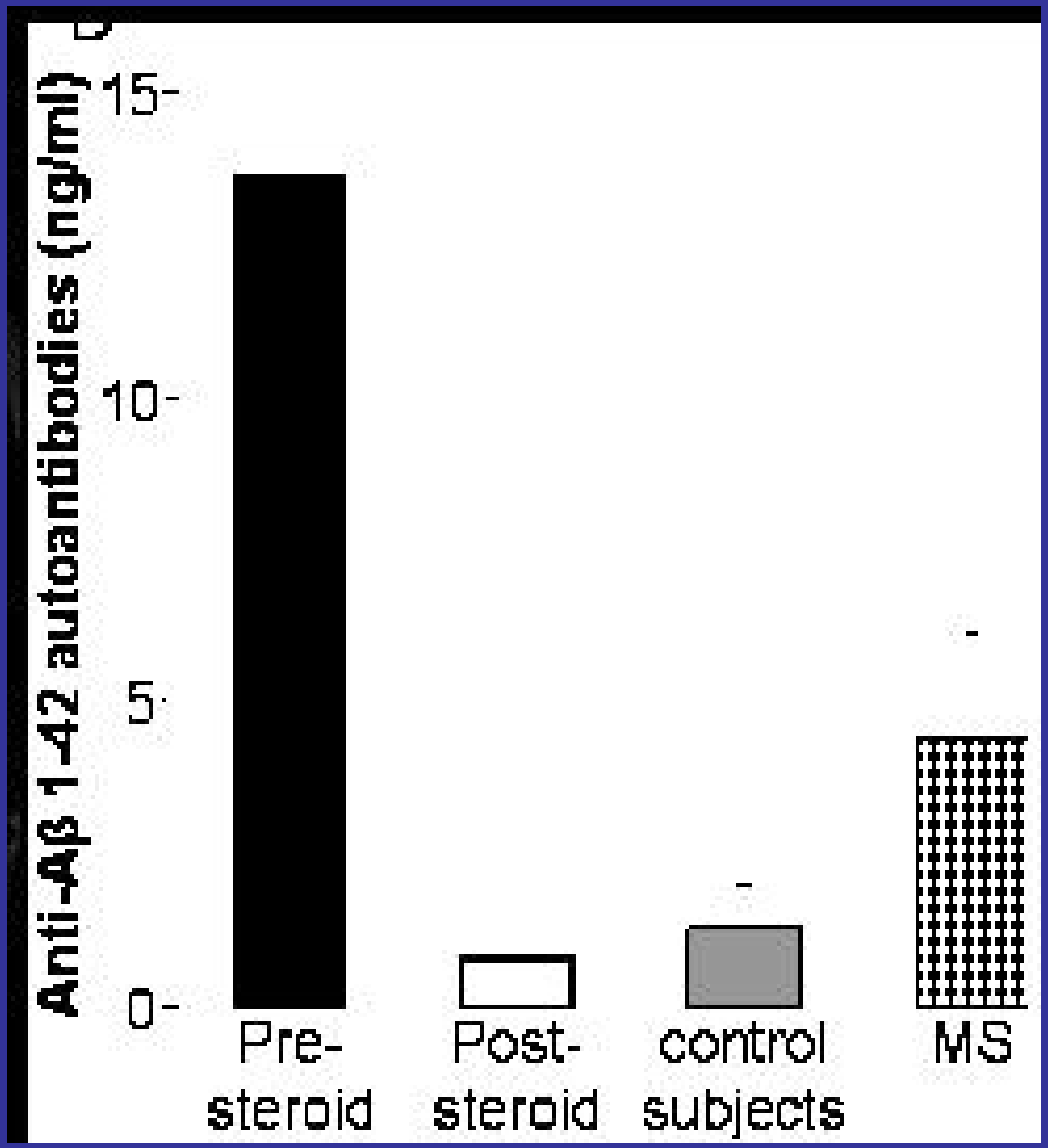




- Brain biopsy: unremarkable
- Good response to steroids

GE sequences solve the diagnostic problem



ε4-ε4



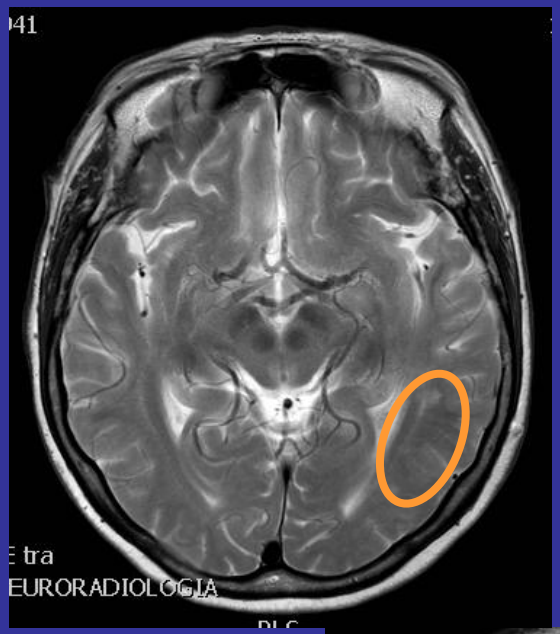
Anti-Aβ 1-40 and 1-42 autoantibodies in CSF may become the biomarker of CAA-ri

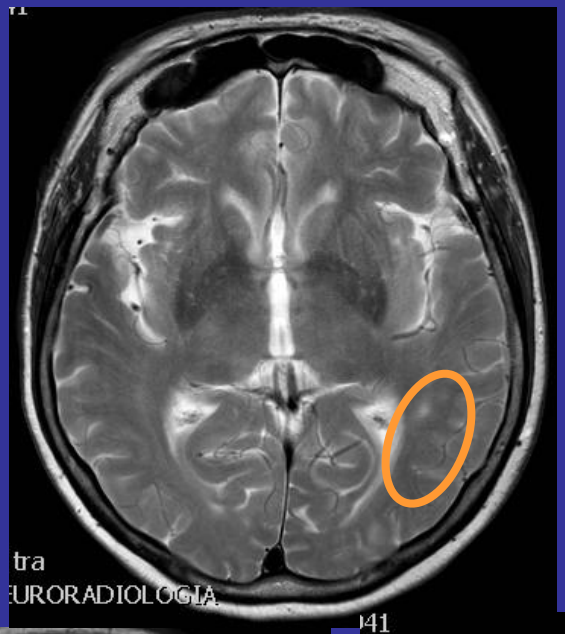
Di Francesco JC et al. Neurology, in press

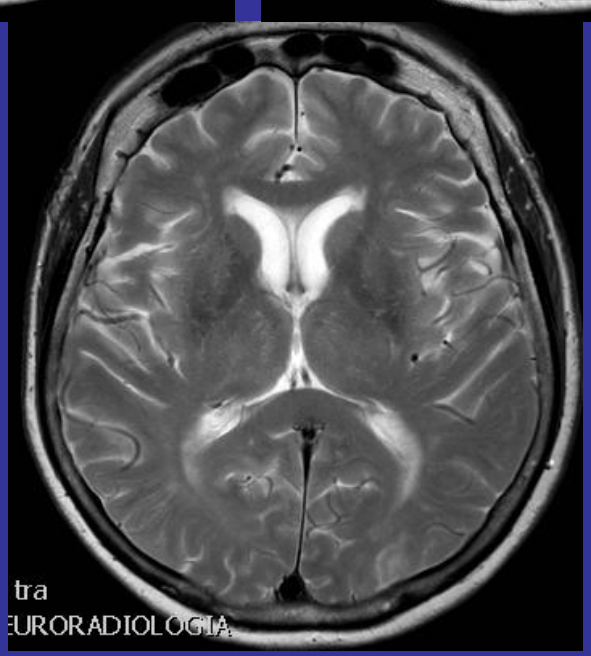
Patient 3

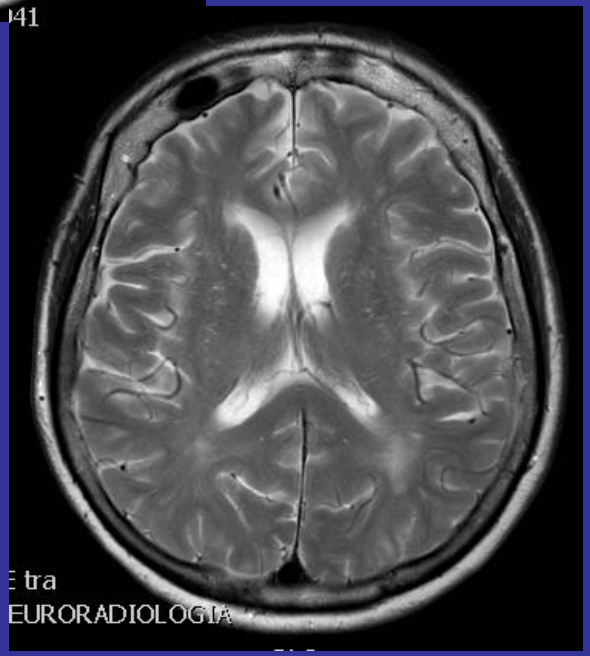
- A 68-year-old woman with acute onset of speech difficulties and right hemiparesis was found to have a single left posterior temporal lesion. Extensive workup was negative. Biopsy refused. Disappearance of lesion after steroid therapy

Pt 3





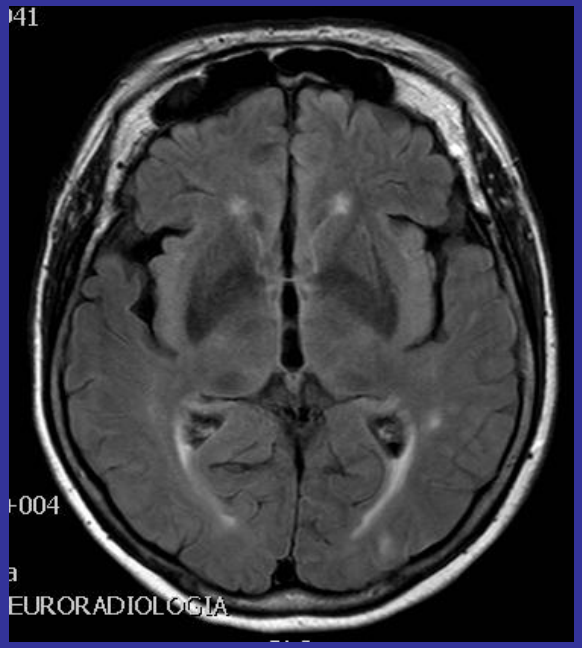


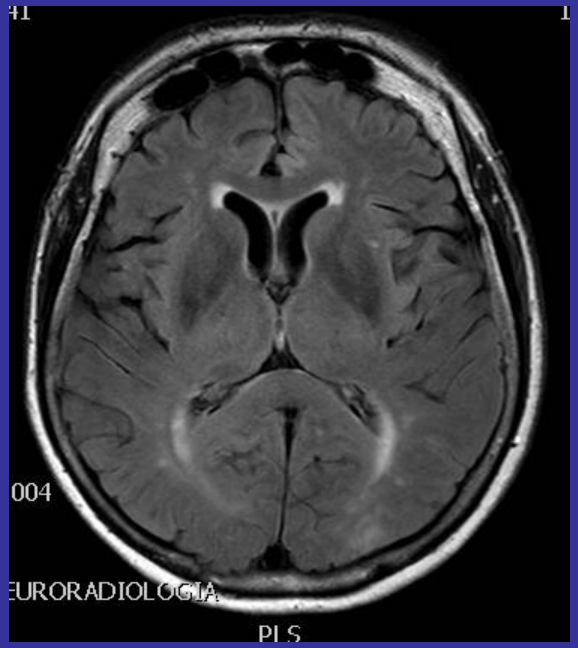


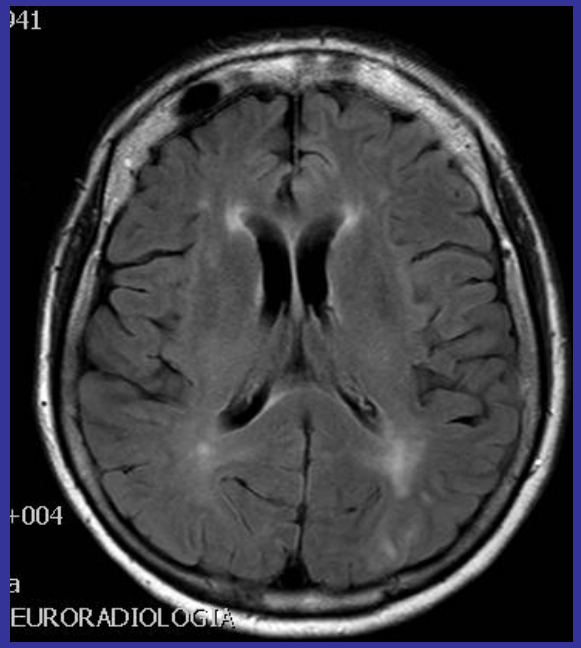
T2-wi

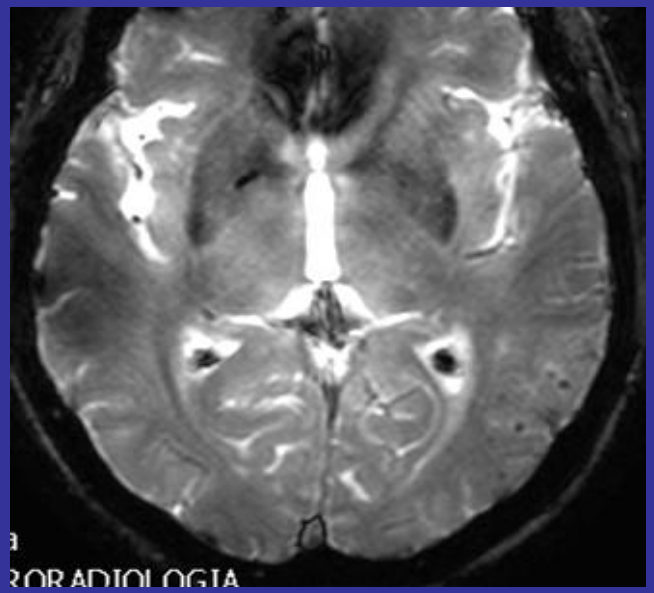
Post-steroid therapy

FLAIR



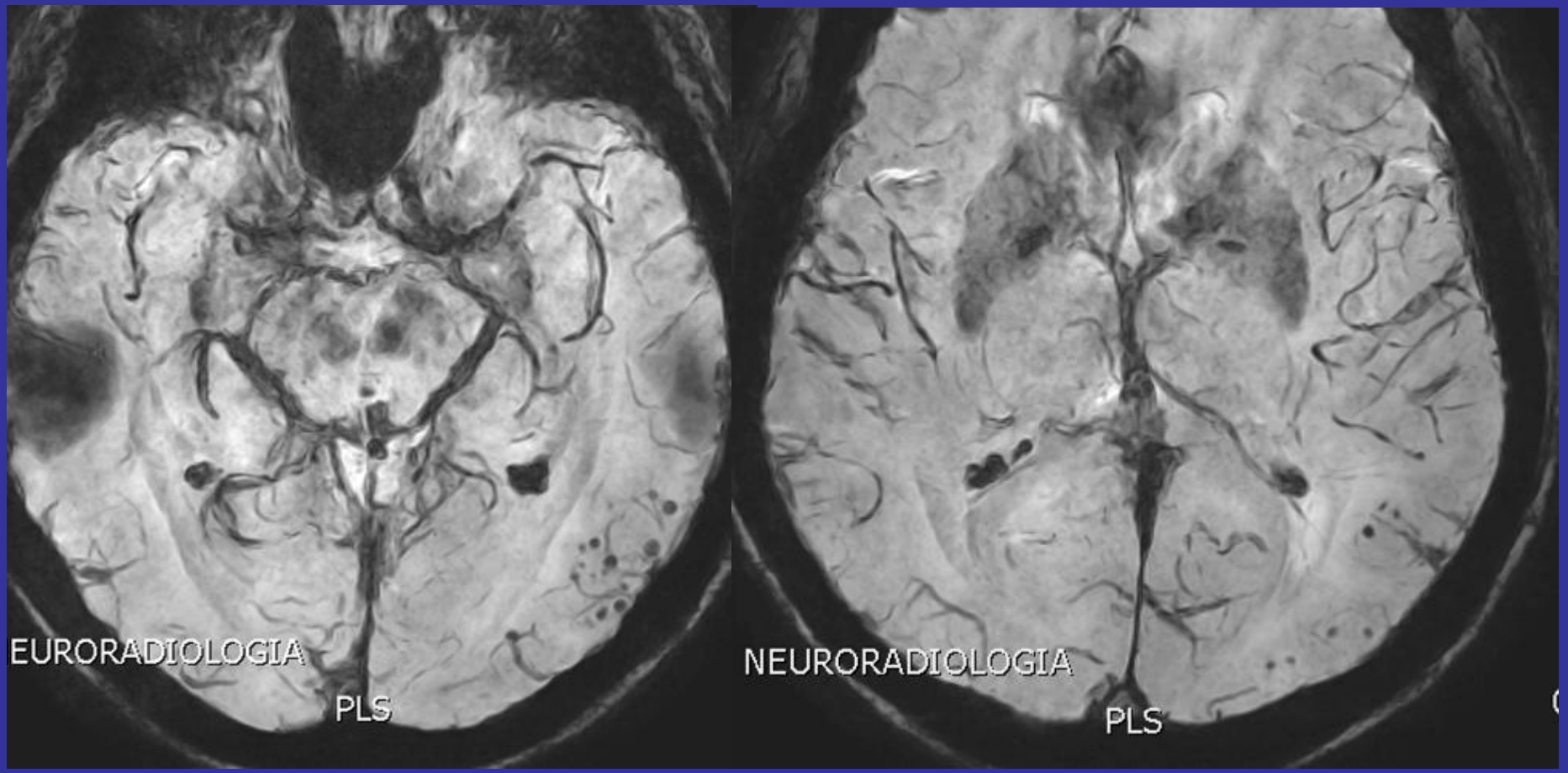






GE T2*

SWI



Two aspects:

1. Multifocal Leucoencephalopathy consistent with an autoimmune/inflammatory reaction

and

2. Cortico-subcortical Microhemorrhages compatible with cerebral amyloid angiopathy

Take-home message:

- GE T2* or SWI are essential to diagnose CAA
- Response to steroid therapy and
- APOE ε4/ε4 genotype support diagnosis of CAA-related inflammation
- Anti-Aβ autoantibodies in CSF may become the biomarker of the disease

There is a spectrum extending from

Cerebral amyloid angiopathy (CAA)-related inflammation

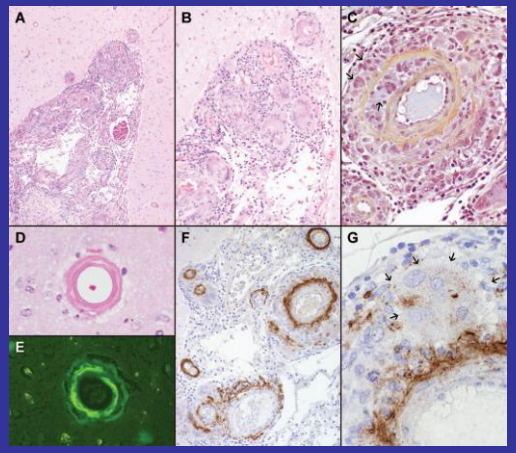
to

CAA-related angiitis

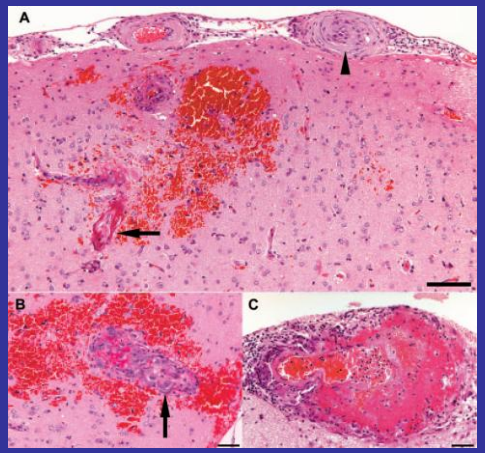
Amyloid β-related inflammation

Aβ-related angiitis (ABRA)

Greenberg SM et al. Neurology 2007;68:782



Scolding NJ et al. Brain 2005;128:500



Thank you for your attention!