Symposium Neuroradiologicum

Cerebral Amyloid Angiopathy-related inflammation: an emerging disease


Fondazione IRCCS Istituto Neurologico C. Besta, San Gerardo Hospital, Monza, University of Milano –Bicocca, University of Milan Medical School, IRCCS Istituto Auxologico Italiano, San Raffaele University and Hospital, Milan, Italy
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 meningoencephalitis (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

- Funduscropy: 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
MR - FLAIR
MR 1.5T Sept. 11, 2008
DWI (ADC)
Post-contrast
MR perfusion (CBV)
A diagnostic examination was performed.
no hemorrhages in the basal ganglia
T2*
Boston Criteria for the clinical diagnosis of CAA


- 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 $\geq$ 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)
Control MRI
4 months later
(Feb 16, 2009)
• 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
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
Two aspects:

1. Multifocal Leuкоencephalopathy 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 (ABRA).

Greenberg SM et al. Neurology 2007;68:782
Thank you for your attention!