An elderly patient with recurrent ICH

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Inter-hospital Geriatric Meeting

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Case presentation

- Mr. Lau
- M/70.
- Ex-smoker, ND
- Live with daughter, walk unaided.

Past history

- Hx of thyrotoxicosis in 1980 with antithyroid drugs treatment and two course of RAI in China in 1987.
- post RAI hypothyroidism, on replacement.
- Hx of old PTB with right pleural effusion in teenage.
- Hx of COAD, bronchietasis in RML and RLL.

- Herniorrhaphy for right reducible inguinal hernia done 08/2001.
- Lumber and cervical spondylosis.
- Eczema.
- Urticaria.

- He admitted to KWH 06/2003 for headache and impaired mobility and left temporal hemianopia for one week.
- MRI done in St Teresa Hospital: right medial parieto-occipital intracerebral hemorrhage.
- Treated as ICH.

- FU KWH neurosurgical OPD.
- Repeat CT brain showed resolving hematoma.
- MRI and MRA(08/2003)done in KWH:1)previous hemorrhage of right occipital lobe. 2)chronic ischemic changes. 3) no abnormal vessel seen.

- Admitted PMH 12/2006 for generalized weakness, preceded by a seizure attack few days before.
- P/E showed left homonymous hemianopia.
- CT brain: new right parieto-occipital hematoma.

- FU CT brain(15/01/2007 PMH): left fronto-parietal-falcine hemorrhage and right fronto-parietal hemorrhage.


Warning: not enough gray scales (32)


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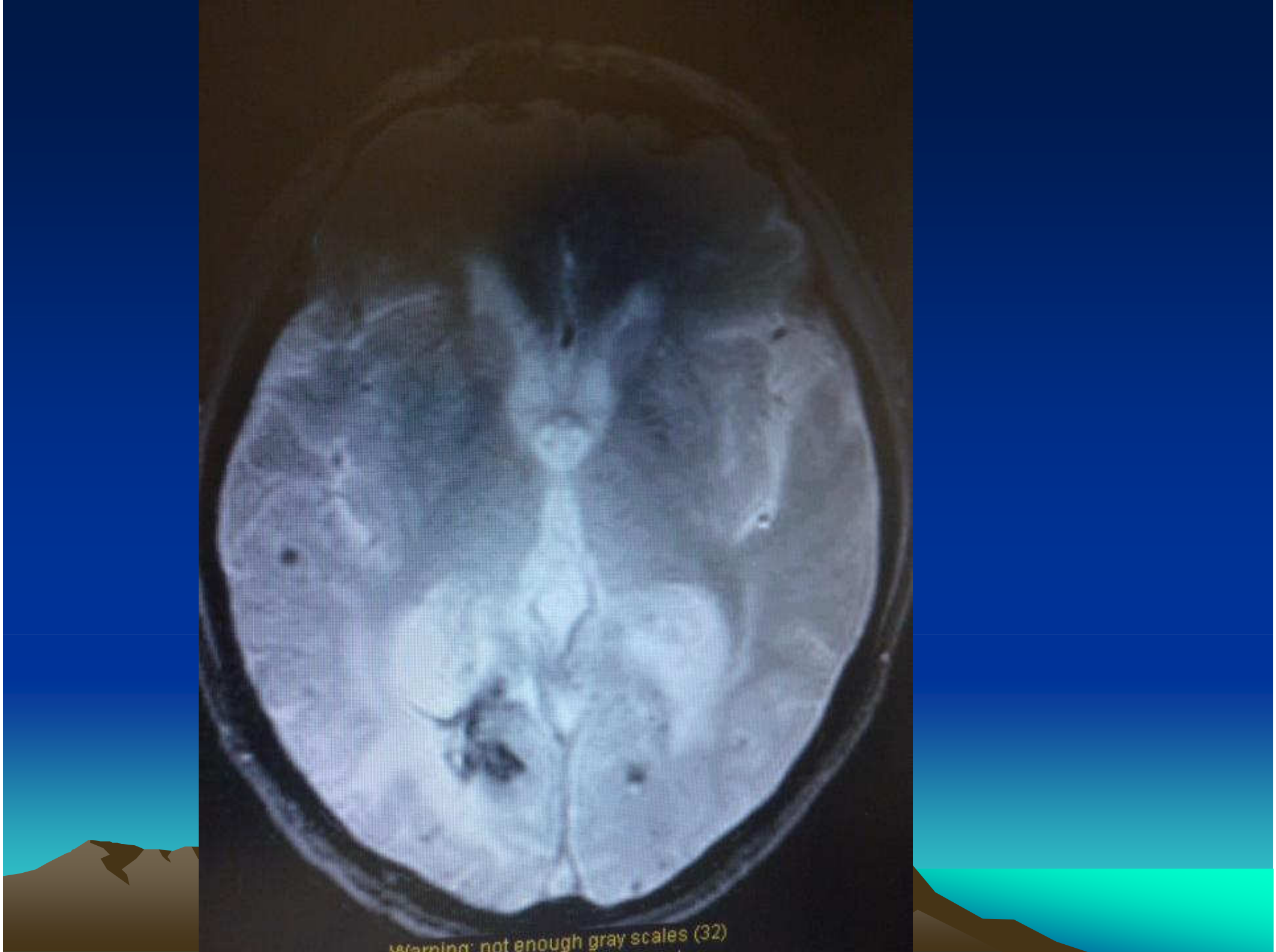
- He Had marked cognitive impairment with low mood. Worthlessness, poor appetite.
- ? Auditory hallucination of hearing voice.
- With delusional idea about unfaith of his wife and always check for wife’s workplace.
- Argue and quarrel with wife everyday.
- Added SSRI.

- Mood slightly better after SSRI.
- MRI(16/08/2007): numerous foci of chronic hemorrhage.—bilateral intracerebral and subarachoid.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- Admitted to QEH 04/2008 for LOC for five minutes.
- Associated with urinary incontinence.
- CT brain: periventricular hypodensities, old infarcts in right parietal and left basal ganglia.
- Diagnosis: Vasovagal attack.

- Admitted ASU CMC 01/2009 for left side weakness.
- Disorientated and confusion.
- Not fully follow commands. on restainer as he climb out of bed.
- CT brain: left intracerebral hemorrhage. Old cerebral infarcts. Ischemic changes.

Investigation

- CBP:HB 13.50 MCV 94
- L/RFT: urea: 8.7 creat: 113 ALP 66 ALT ; 22 glucose: 4.7
- PT:9.9
- APTT:39.1
- TSH: 0.24
- CXR: lung field clear.
- ECG:SR.


AS
Caritas Medic
Req Num:CMC0
LA
M 70
09

- MRMI: 14/40.
- BI 8/100 increased to 34/100.
- Transferred to rehab. ward 05/02/2009.
- Noted convulsion and decreased GC on 09/02/2009.
- CT brain: acute intracerebral hematoma involving right basal ganglion and right corona radiata.

- Noted fluctuating emotion, sometimes aggressive, sometimes calm and cheerful.
- MMSE 1/30.
- Psychiatric assessment: vascular dementia.
- FU CT brain(25/02/2009):1) residual hypodense area in right basal ganglion/corona radiata. 2) left temporal lobe/basal ganglion resolving hematoma.

- ASU team round: poor rehab. potential as limited by poor congnition and vision.
- He was transferred to OLMH on 04/03/2009.

- He was transferred to OLMH on 04/03/2009 for rehabilitation.
- Agitated and uncooperative.
- Four limbs cogwheel rigidity.
- Bilateral plantar response was downgoing.

- Off haloperidol due to marked extrapyramidal side effect.
- changed to Risperidone oral, mood more stable.

- Dysphagia, need dysphagia puree diet. Later changed to minced diet.
- EMS 4/20. mainly chairbound.
- Basic ADL need moderate to much assistance.
- Difficult caring at home. arranged OAH and discharge.

Medication on discharge

- Dilantin 300mg nocte.
- Risperidone 0.5mg daily and 0.5 nocte PRN.
- Thyroxine 100mcg daily.

summary

- 06/2003 KWH right parieto-occipital ICH.
- 12/2006 PMH right parieto-occipital ICH.
- 01/2007 PMH right fronto-parietal ICH and left fronto-parietal-falcine ICH.
- 08/2007 PMH MRI: numerous foci of chronic hemorrhage– bilateral intracerebral and subarachnoid.
- 01/2009 CMC right BG and CR ICH.

- In summary, the patient had recurrent cerebral hemorrhage in 2003, 2006, 2007, 2009.
- Mainly involving lobar region.
- vascular dementia with BPSD.

- The likely diagnosis is cerebral amyloid angiopathy.

Cerebral amyloid angiopathy

- CAA is an important cause of primary lobar intracerebral hemorrhage in the elderly.
- Sporadic disorder, associated with Alzheimer's disease (AD).
- Familial syndromes.

CAA

- CAA is characterized by the deposition of congophilic material in small to medium-sized blood vessels of the brain and leptomenings.
- Mild CAA not associated with clinicial manifestations.
- Severe CAA may cause lobar cerebral hemorrhage and leukoencephalopathy, and dementia.

epidermiology

- The incidence of CAA, is strongly age dependent.
- 2.3% in ages of 65—74.
- 8.0% in age 75—84.
- 12.1% in age over 85.

Pathogenesis

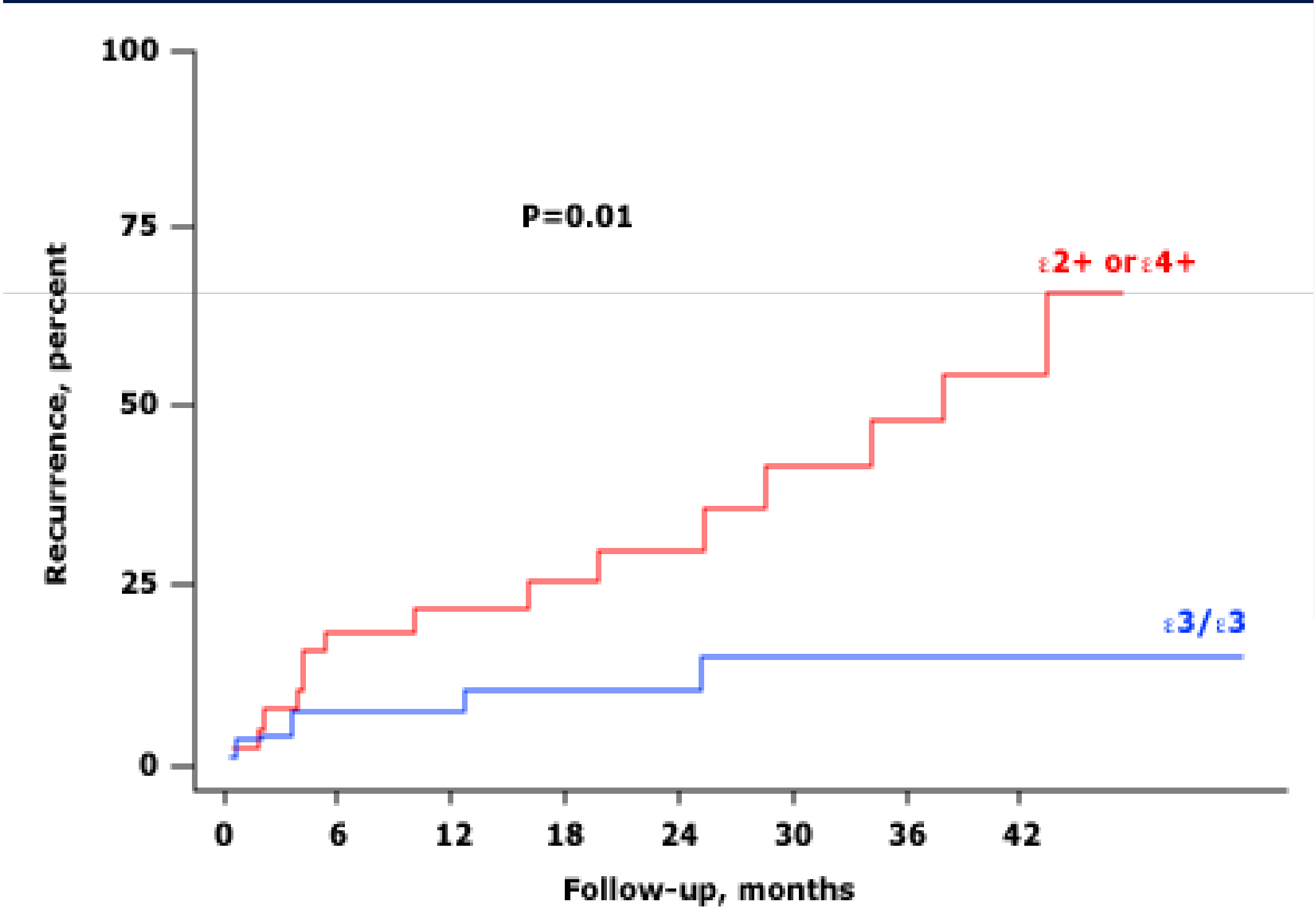
- Vascular amyloid deposits in sporadic CAA are biochemically similar to the material comprising senile plaques in Alzheimer’s disease.
- amyloid Beta-peptide. A 39 to 43 amino acid fragment of the amyloid precursor protein.
-

Mutant amyloid precursor protein

- Mutantions in the gene that encodes the amyloid precursor protein (APP) are responsible for some cases of “presenile” CAA.
- Most of these mutations are associated with at least some of the neuropathologic features of AD.

Apolipoprotein E

- APOE 2(e2) or 4 (e4) alleles appear to be at greater risk for CAA –related hemorrhage than those APOE 3(E3)allele.
- 2/3 patients with CAA have one or two e2 or e4.

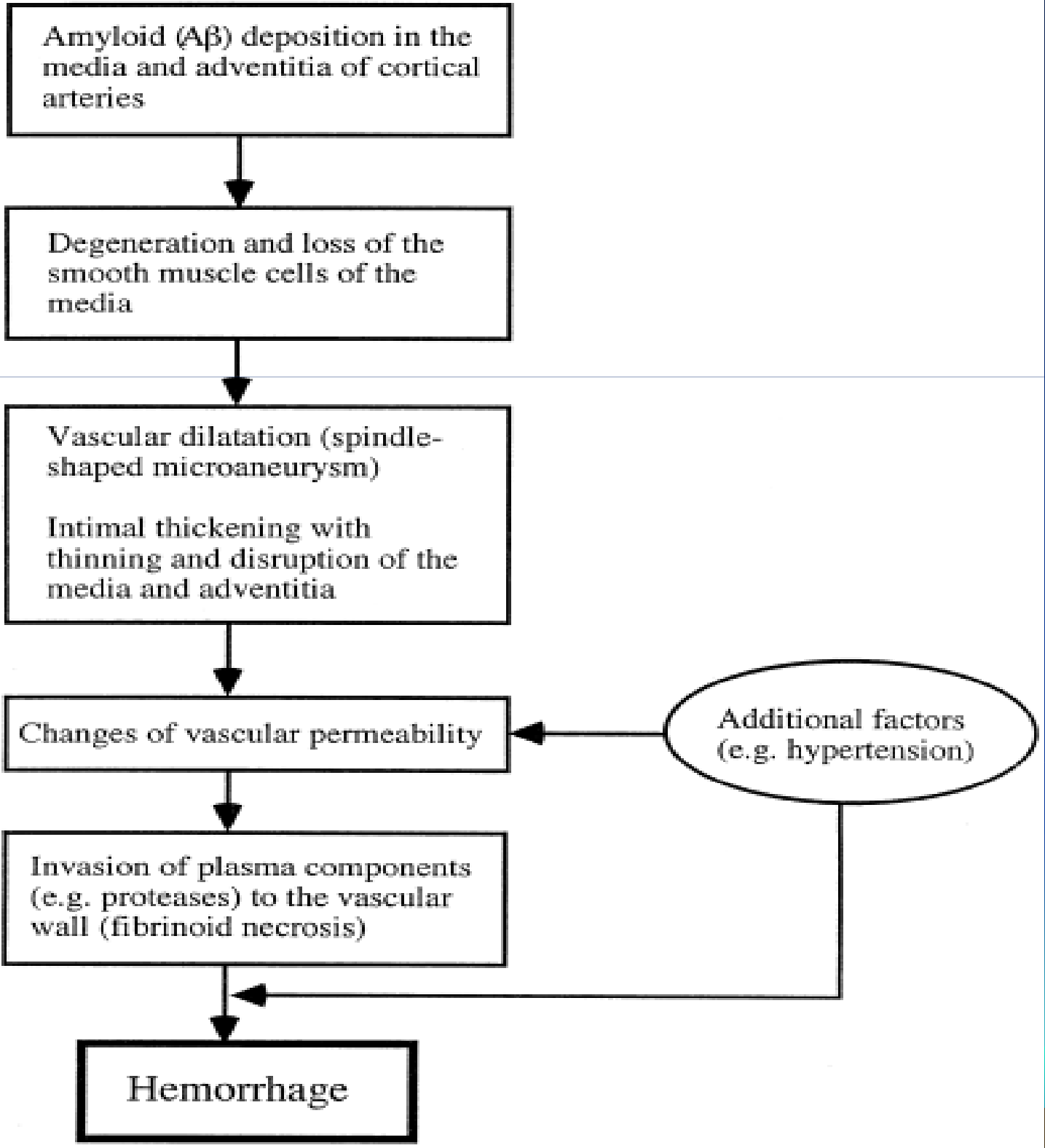

100
75
50
25
0
Recurrence, percent
P=0.01
ε2+ or ε4+
ε3/ε3
0
6
12
18
24
30
36
42
Follow-up, months

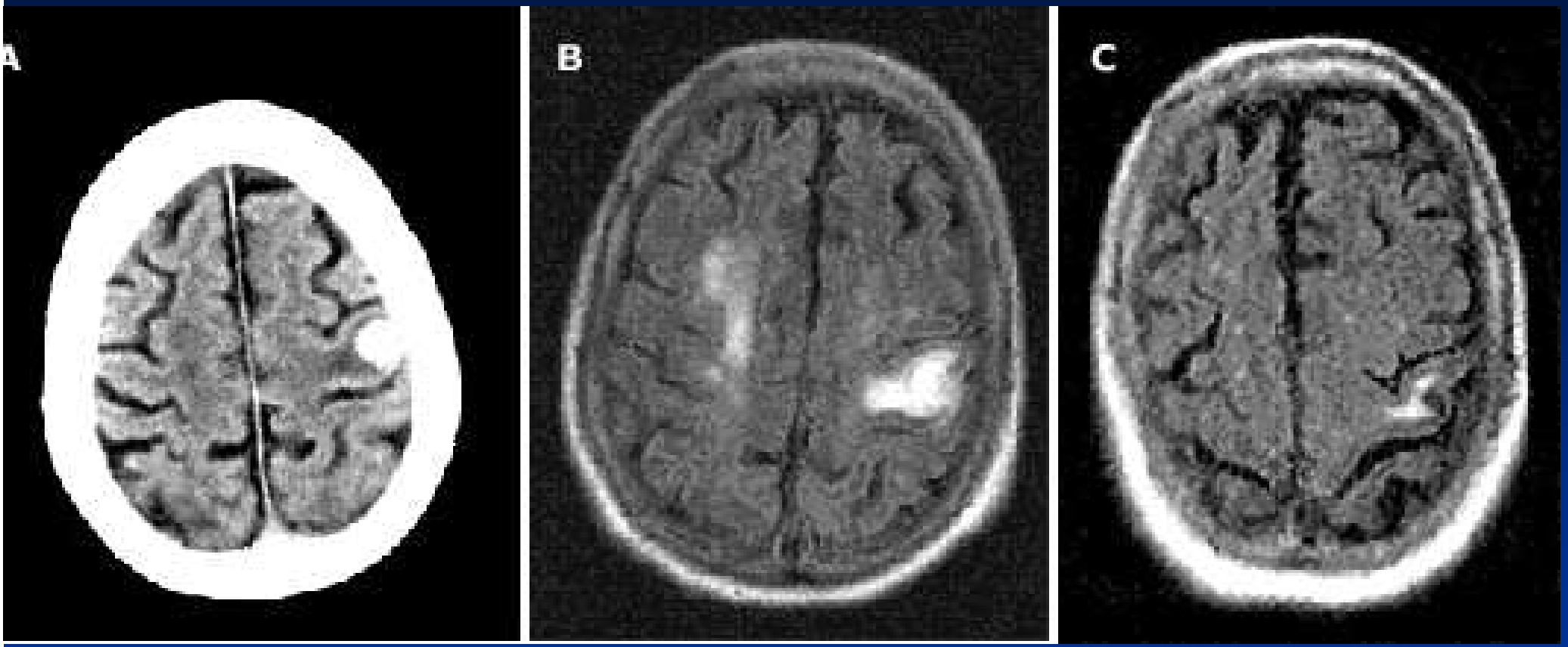
Clinical features

- ICH: the most common clinical presentation of CAA is spontaneous lobar hemorrhage.
- CAA –related hemorrhage often extend into the subarachnoid space, less frequently rupture into ventricle.

ICH

- Predilection to cluster in posterior brain regions.
- Tendency to cluster in same lobe within individual patients.
- More occur in temporal and occipital lobe than frontal and parietal lobes.
- Hemorrhage tend to recur in area of prior hemorrhage.


Amyloid (Aβ) deposition in the media and adventitia of cortical arteries
Degeneration and loss of the smooth muscle cells of the media
Vascular dilatation (spindle-shaped microaneurysm)
Intimal thickening with thinning and disruption of the media and adventitia
Changes of vascular permeability
Additional factors (e.g. hypertension)
Invasion of plasma components (e.g. proteases) to the vascular wall (fibrinoid necrosis)
Hemorrhage


A
B
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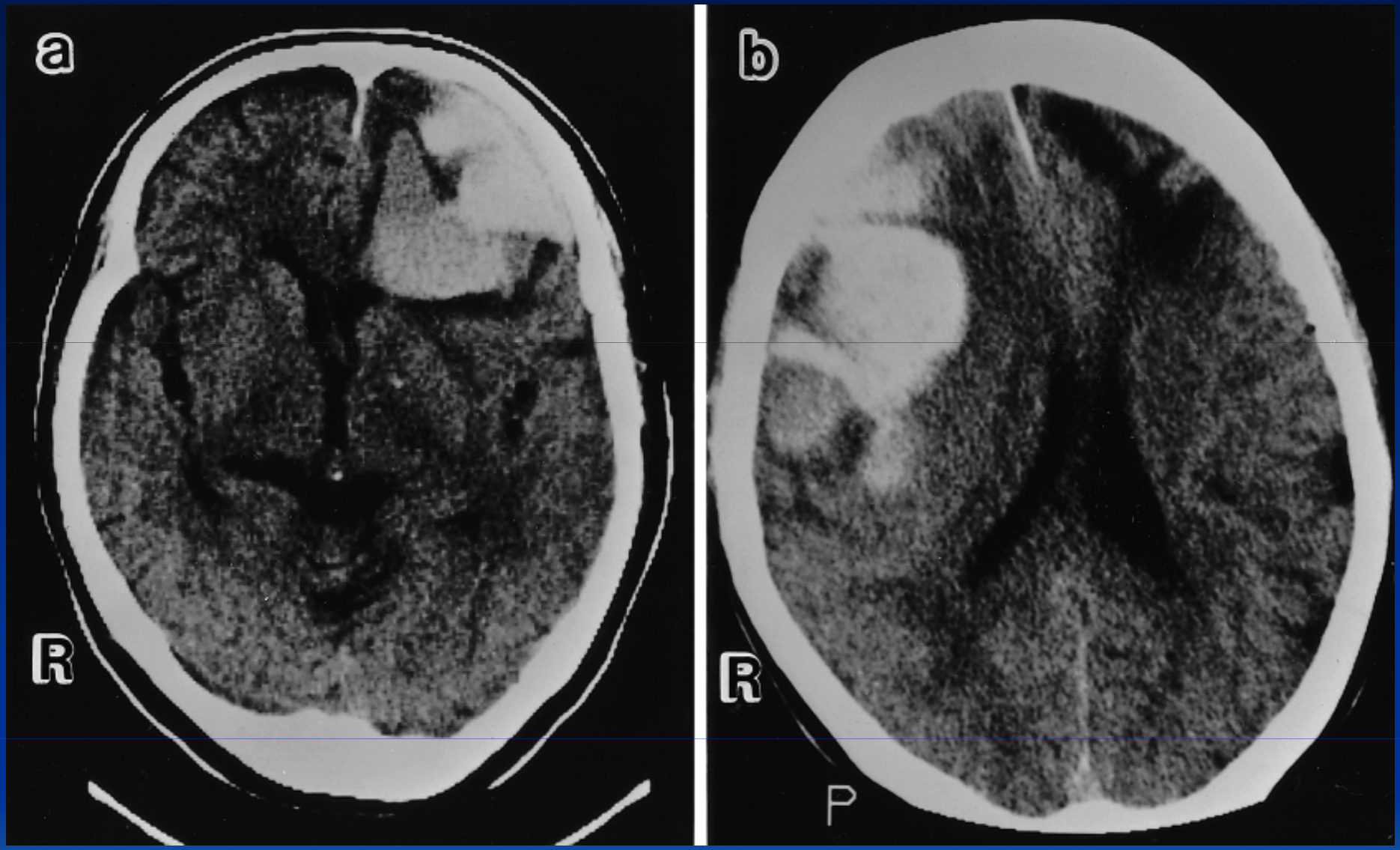
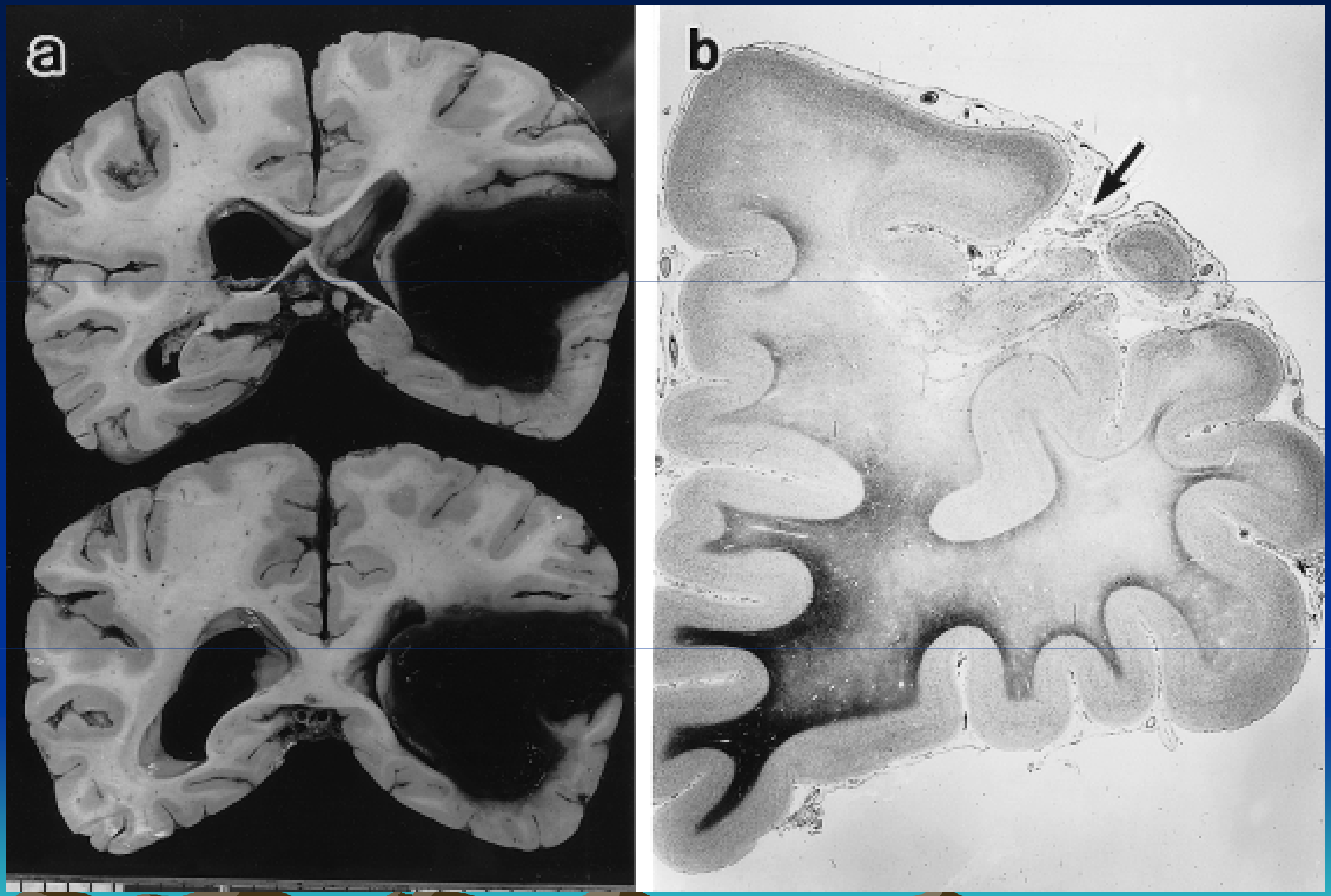
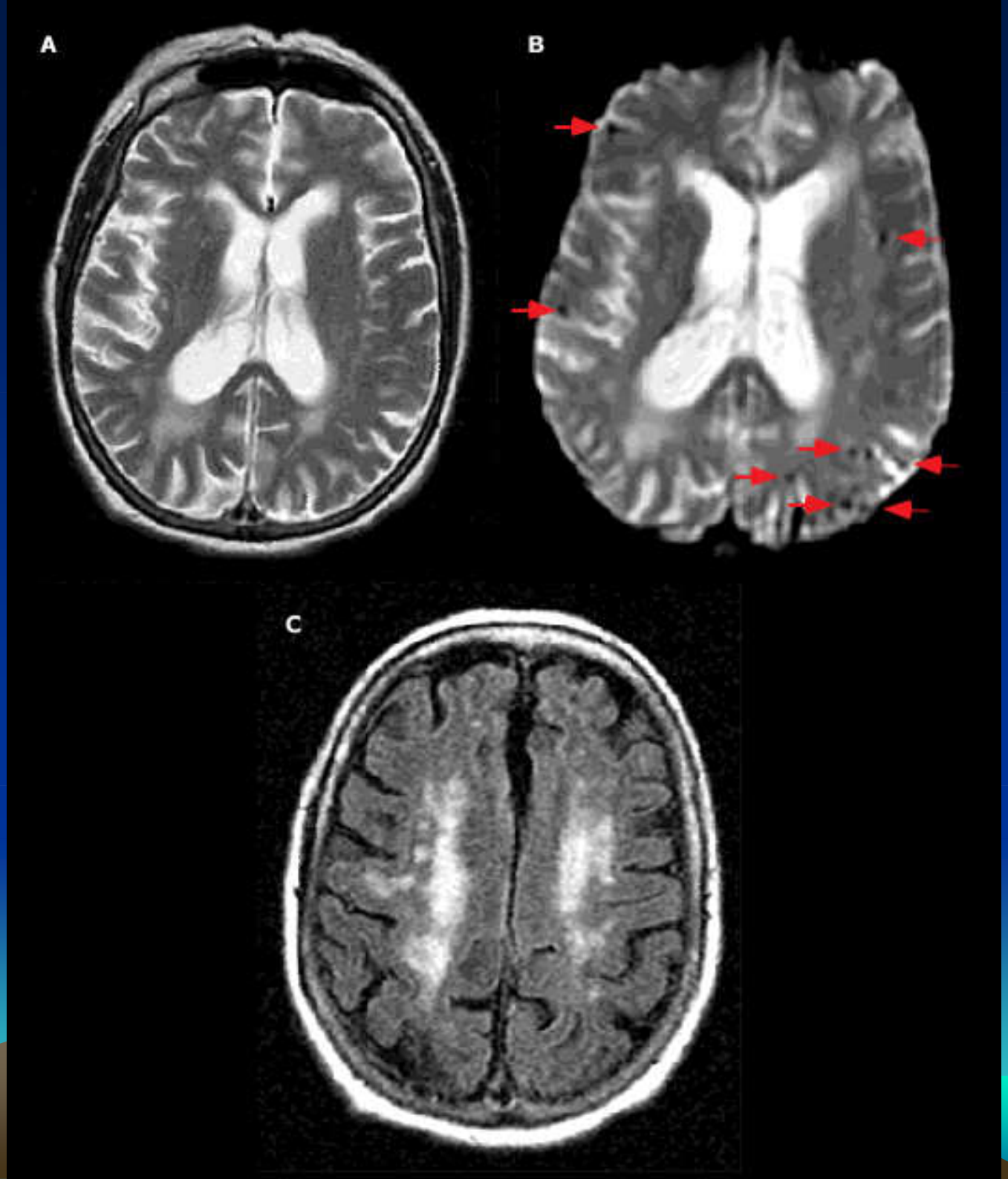

a
R
b
R
P


a
b

Microhemorrhage

- Small subclinical leakage of blood called cerebral microhemorrhages may by relatively common in CAA.
- Gradient Echo or T2 weight MRI can detect these remnants of hemorrhages as 2mm to 5mm focal or multifocal areas of hemosiderin deposition.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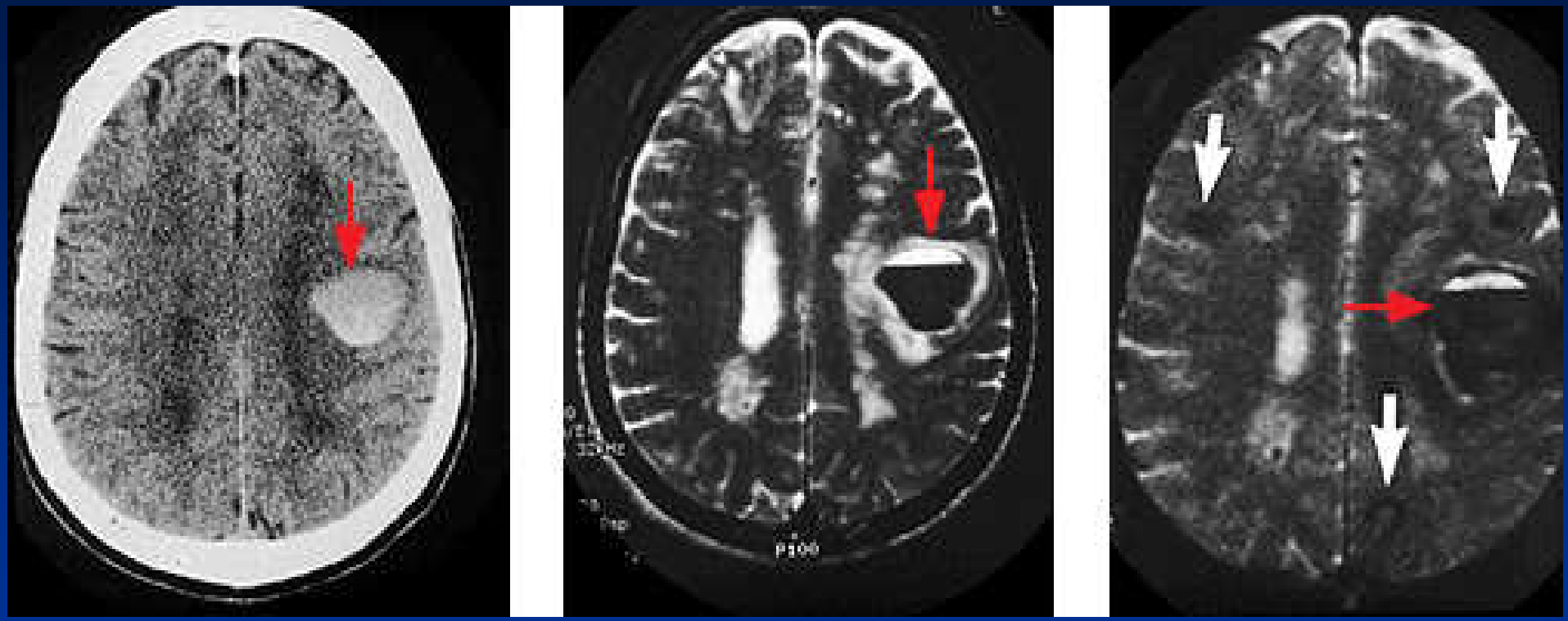
- In the population-based cohort of 472 healthy subjects from the Framingham study, cerebral microhemorrhages were detected by MRI in 4.7% . Nearly three-quarters of the microhemorrhages were found in the cerebral cortex or subcortical white matter, location suggestion amyloid angiopathy rather than hypertensive microangiopathy.

- In another study that analyzed 97 consecutive gradient echo MRI brain scans performed for all clinical indications aged 70 or above. One or more cerebral microhemorrhages interpreted as cerebral amyloid angiopathy were found in 15.5% percent.



Transient neurological symptoms

- Less common.
- Recurrent, brief (minutes), often stereotyped spells of weakness, numbness, parethesis.
- Gradient-Echo MRI: small hemorrhage in cortex.

Perivascular/ vascular inflammation

- A distinct subset of CAA.
- Subacute cognitive decline or seizure rather than hemorrhage.
- MRI: leukoencephalopathy: patchy or confluent white matter hyperintensities.
- Echo MRI: multiple microhemorrhage.

Dementia

- Extensive CAA cause ischemic white matter damage.
- Narrowing of penetrating cortical vessels by amyloid deposits.
- Progressive dementia reminiscent of subcortical arteriosclerotic encephalopathy (Binswanger’s disease).
- CAA also common in conjunction with AD.

- The pathomechanisms underlying the dementia are not uniform.
- Vascular dementia due to CAA.
- Coexistence of AD.
- Mixed dementia of VD and AD.

Features of lobar hemorrhage

- Superficial location and tendency to spare the ventricles.
- Unfavorable outcome: old age and larger hematoma size.
- Overall Mortality 10—30%.
- Best prognosis for patient with smaller hematomas(<50ml) and greater level of consciousness on admission (GCS>8).

- CAA carries a high risk of hemorrhage recurrence.
- One cohort study of 71 cases of lobar hemorrhage had a two years recurrent rate 21%
- All but one of the recurrent hemorrhage were lobar.

Diagnosis

- The presence of CAA should be suspected clinically in patients over the age of 60 who have multiple lobar hemorrhage in the absence of an obvious cause.
- The definitively diagnosis only by full postmortem examination of the brain.

Gradient-echo MRI

- Two or more hemorrhage restricted to those regions typical of CAA (Cortex or grey-white junction).
- Sparing regions typical of hypertensive hemorrhage (basal ganglia, thalamus, or pons).

Examination of tissue

- Evacuated hematoma specimens should be examined with Congo red stain for CAA.

The Boston cerebral amyloid angiopathy guideline

- Definite CAA: full postmortem examination reveale lobar, cortical, or corticosubcortical hemorrhage and evidence of severe CAA.
- Probable CAA with supporting pathological evidence: the clinical data and pathological tissue demonstrate a hemorrhage with the aforementioned characteristics and some degree of vascular amyloid deposition.
- Probable CAA: clinical data and MRI findings demonstrate multiple hematomas in a patient older than 60 years.

- Possible CAA: patient is older than 60 years, and clinical and MRI data reveal a single lobar, cortical, or corticosubcortical hemorrhage without another cause, multiple hemorrhages with a possible but not a definite cause, or some hemorrhage in an atypical location.

Differential diagnosis

- Lobar extensive of a putamental hemorrhage.
- Hemorrhagic transformation of ischemic stroke.
- Arteriovenous malformation (AVM).
- Hemorrhagic tumor.

Treatment

- CAA hemorrhage treated like other acute intracerebral hemorrhage.
- Attention to intracranial pressure.
- Loose control of blood pressure.
- Short term empirical use of anticonvulsants.

surgery

- Surgical hematoma resection appears to carry little or no additional risk in CAA compared with other types of ICH.

Avoidance of anticoagulants and antiplatelet agents

- Because of the high recurrence rate, CAA cases is to avoid anticoagulant and antiplatelet agents.