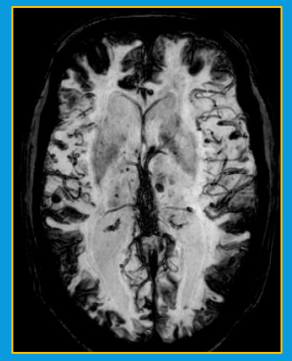
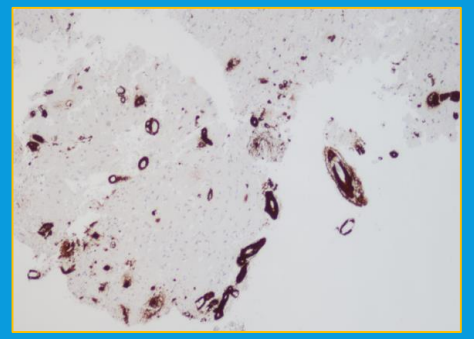
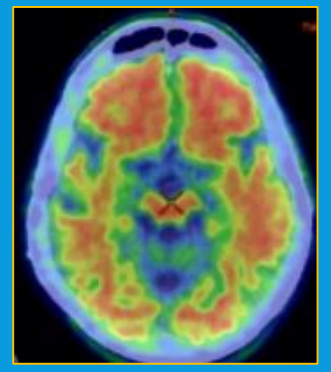
EMERGING CONCEPTS IN SPORADIC CEREBRAL AMYLOID ANGIOPATHY

Francisco Hernández, MD, phD.

Vascular and Interventional Neurology Unit. Albacete University Hospital.

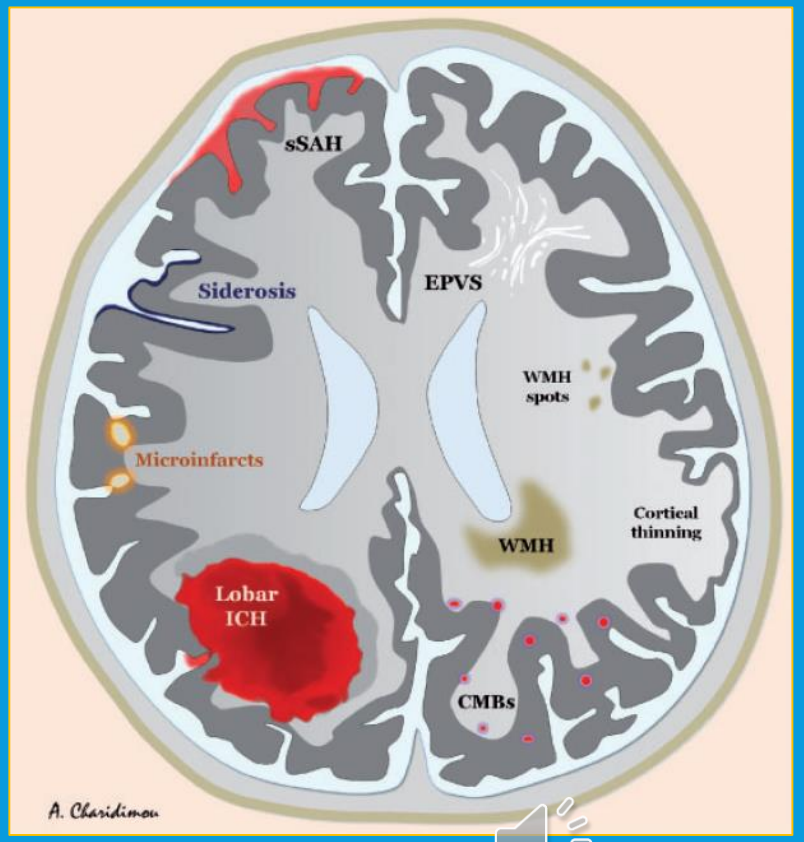






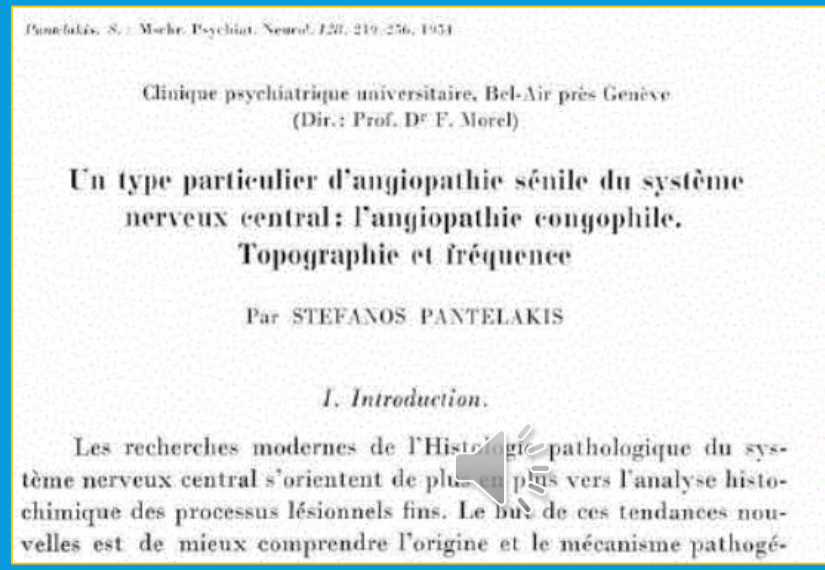
INDEX:

1) Introduction
2) Emerging concepts
3) Iatrogenic CAA (iCAA)
4) Clinical Case Series. Albacete University Hospital
5) Potential ramifications
6) Conclusions



INTRODUCTION

- **First description by Stefanos Pantelakis in 1954** (Geneva Brain Collection)
  1) Raised the hypothesis that vascular amyloid may originate in the brain
  2) Described the pathological hallmarks of CAA:
     (i) preferential involvement of small arterioles and capillaries of the leptomeninges and cortex
     (ii) topographical distribution favouring posterior lobar brain regions (especially the occipital lobes)
     (iii) lack of involvement of white matter small vessels
     (iv) association with increased age and dementia
     (v) lack of association with hypertension and arteriosclerosis
     (vi) lack of any link with systemic amyloidosis
- **1972: invention of CT scanner → post-mortem correlations**
- **1996: Greenberg et al → microbleeds, Boston criteria**



Pantelakis, S.: Archiv. Psychiat. Nervenkr. 120, 219–256, 1954

Clinique psychiatrique universitaire, Bel-Air près Genève
(Dir.: Prof. Dr F. Morel)

Un type particulier d'angiopathie sénile du système nerveux central: l'angiopathie congophile. Topographie et fréquence

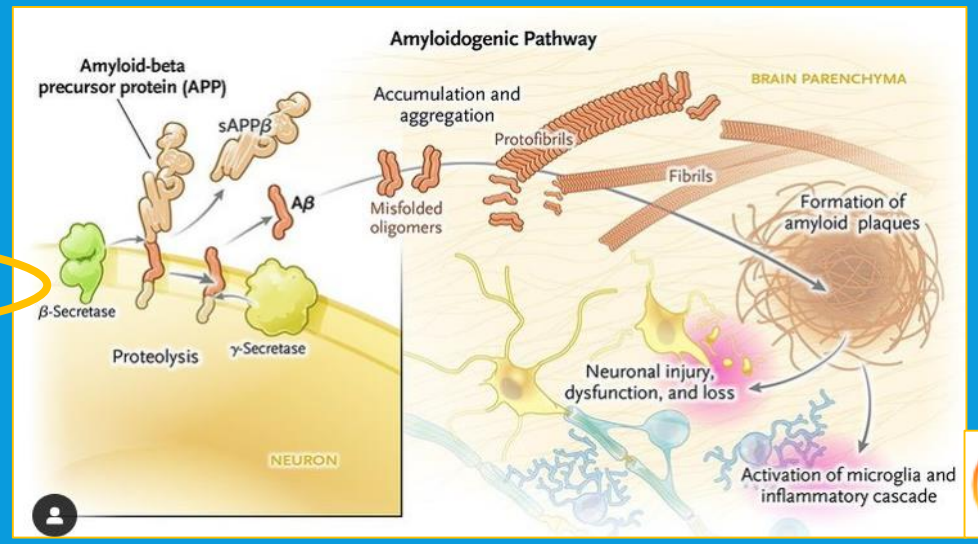
Par STEFANOS PANTELAKIS

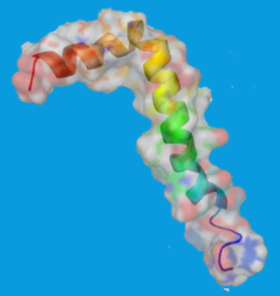
I. Introduction.

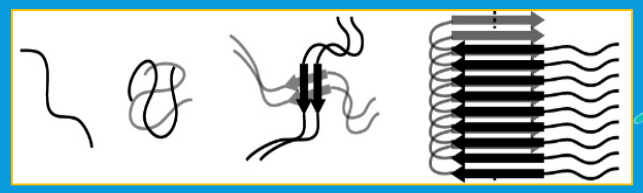
Les recherches modernes de l'Histologie pathologique du système nerveux central s'orientent de plus en plus vers l'analyse histochimique des processus lésionnels fins. Le but de ces tendances nouvelles est de mieux comprendre l'origine et le mécanisme pathogé-

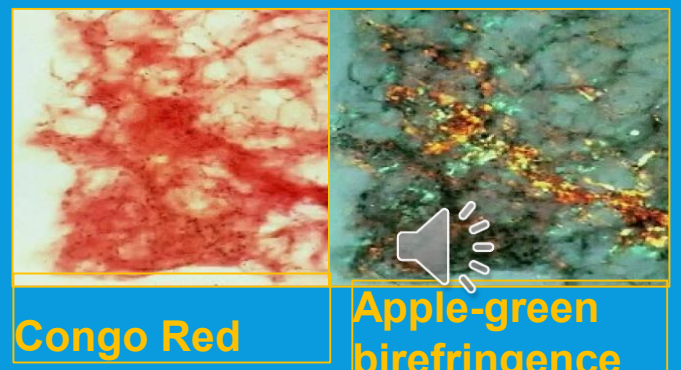
INTRODUCTION: Beta-amyloid peptide

- APP → cleavage by secretases into isoforms. Toxic isoforms Aβ40 y Aβ42:
  - Aβ42, plaques in the parenchyma → Alzheimer Disease
  - Aβ40 > Aβ42, vascular involvement → Cerebral Amyloid Angiopathy (CAA)
- Pathological process of β-folding, aggregation and precipitation, inducing misfolding also to other proteins: dissemination.
- **MISFOLDING**: soluble oligomers → amyloid fibrils → amyloid plaques









EMERGING CONCEPTS

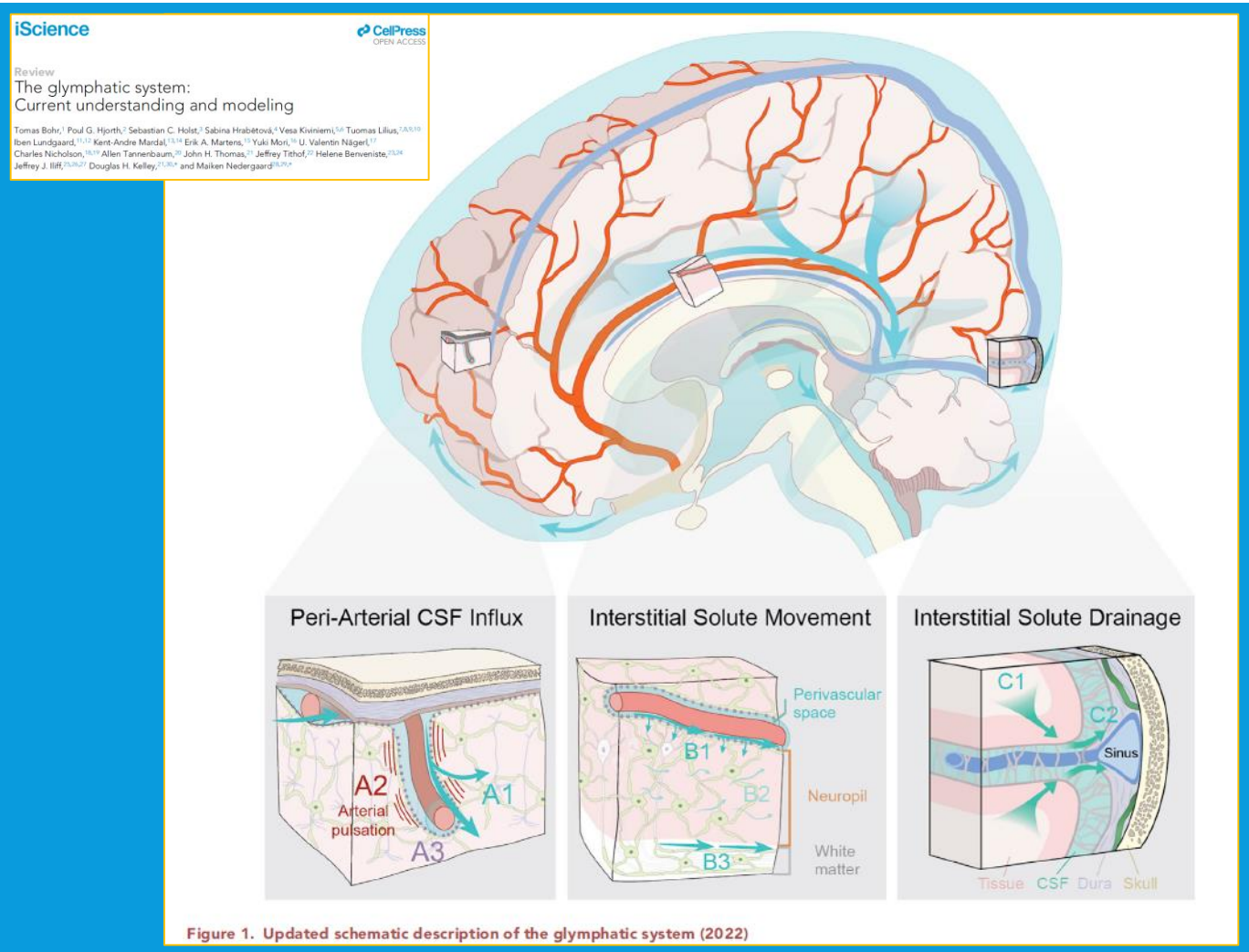
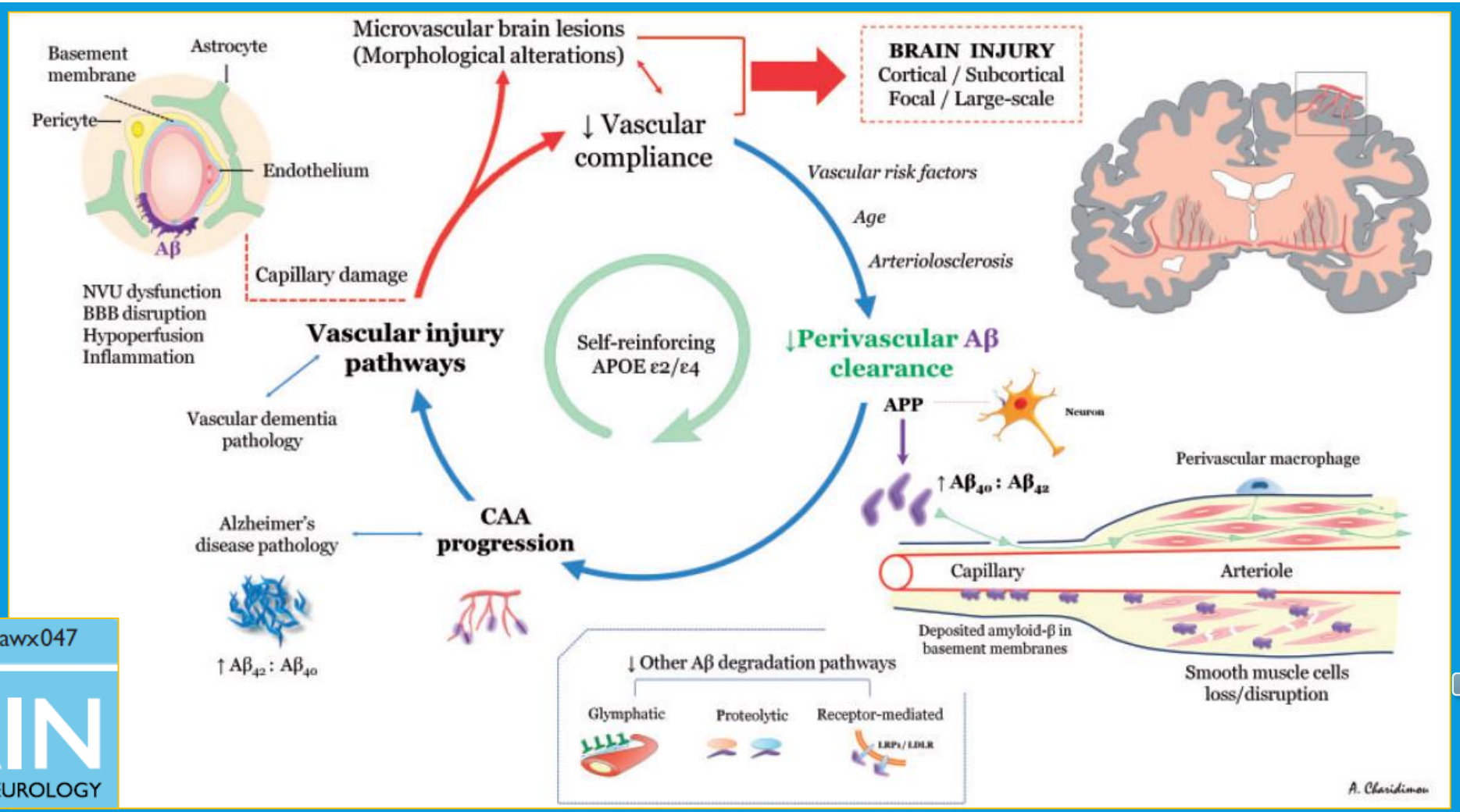


Figure 1. Updated schematic description of the glymphatic system (2022)

- Both perivascular CSF flow and interstitial clearance of solutes, including β-amyloid, depend on astroglial water transport: AQP4
- This hydrodynamic sequence is faster during sleep than in arousal (Xie et al, *Science*,2013)
- Meningeal lymphatics assist drainage

EMERGING CONCEPTS



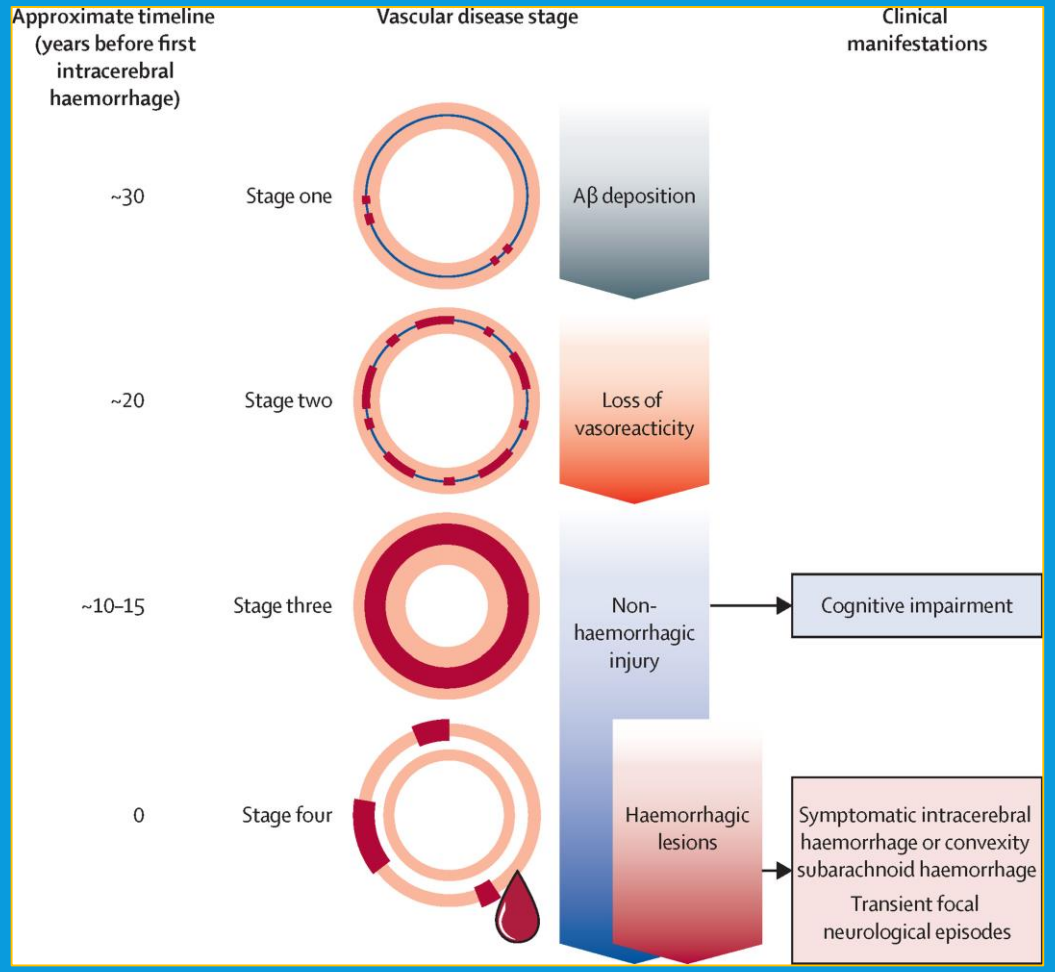
doi:10.1093/brain/awx047
BRAIN
A JOURNAL OF NEUROLOGY

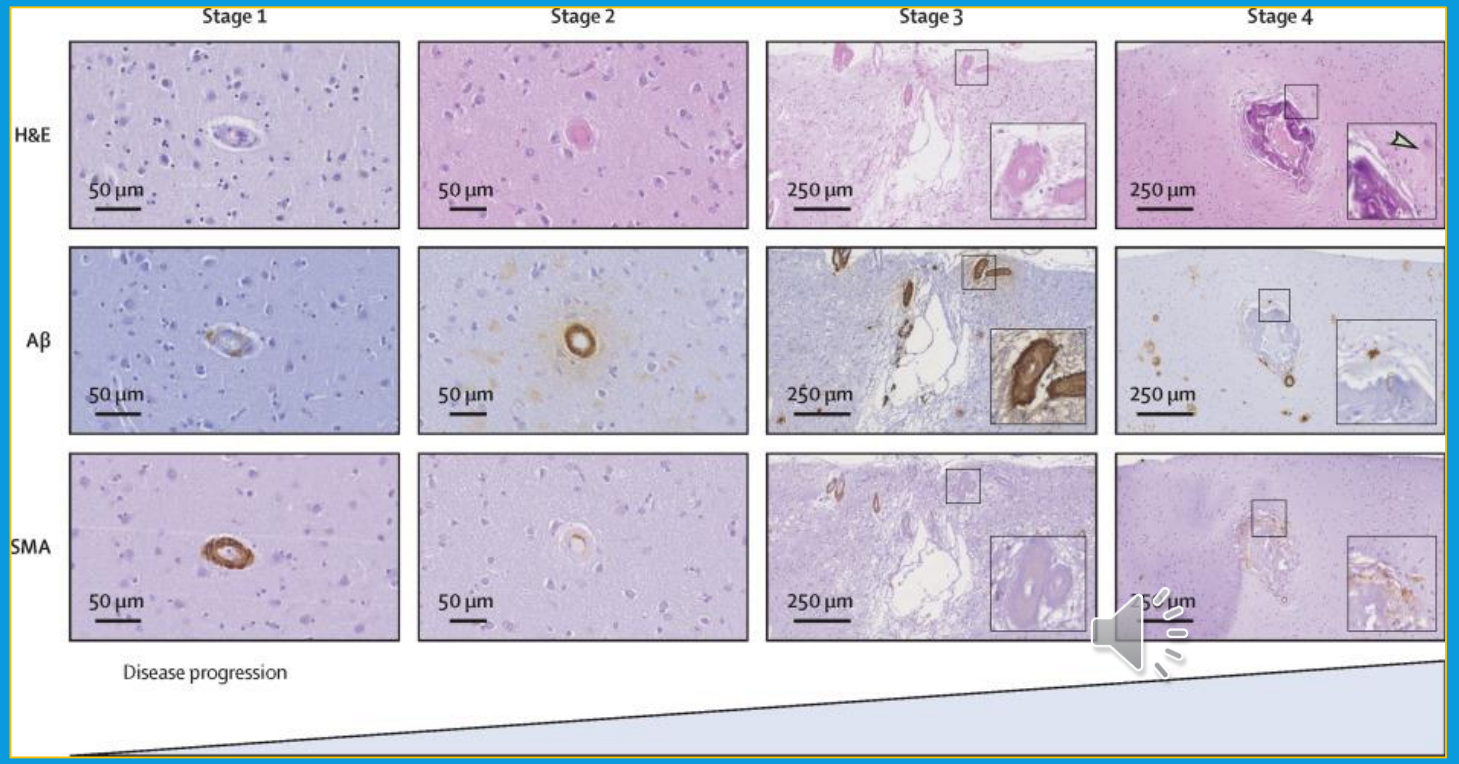
EMERGING CONCEPTS

Review > Lancet Neurol. 2023 Jul;22(7):632-642. doi: 10.1016/S1474-4422(23)00114-X. Epub 2023 May 23.

Progression of cerebral amyloid angiopathy: a pathophysiological framework

Emma A Koemans [1], Jasmeer P Chhatwal [2], Susanne J van Veluw [2], Ellis S van Etten [1], Matthias J P van Osch [1], Marianne A A van Walderveen [1], Hamid R Sohrabi [3], Mariel G Kozberg [2], Zahra Shirzadi [2], Gisela M Terwindt [1], Mark A van Buchem [1], Eric E Smith [4], David J Werring [5], Ralph N Martins [6], Marieke J H Wermer [1], Steven M Greenberg [7]

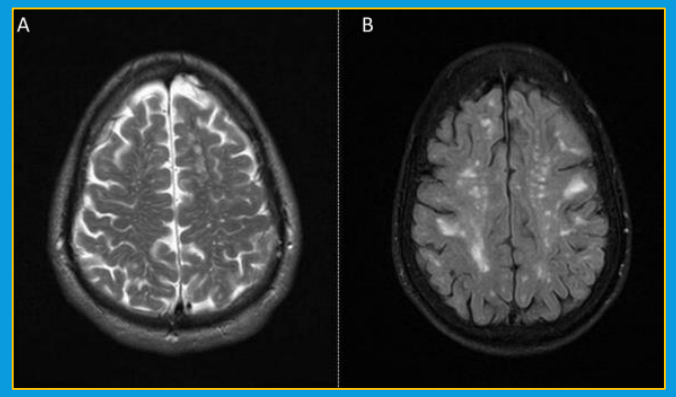




EMERGING CONCEPTS

- BOSTON CRITERIA 2.0 (2022)
  - Age of diagnosis: ≥50 y-o
  - At least two strictly lobar haemorrhagic lesions

    OR
  - One + at least one white matter characteristic
  - Absence of any Deep haemorrhagic lesions



Panel: Boston Criteria v.2.0 for probable cerebral amyloid angiopathy

(Diagnosis can be made when all 5 of the following criteria have been met)

1. Patients aged 50 years and older

2. Clinical presentations with one of the following:
   - Spontaneous intracerebral haemorrhage
   - Transient focal neurological episodes
   - Cognitive impairment or dementia

3. Brain MRI demonstrating:
   - At least two of the following strictly lobar hemorrhagic lesions on T2*-weighted MRI, in any combination or alone:
     - intracerebral haemorrhage
     - cerebral microbleeds
     - cortical superficial siderosis
     - convexity subarachnoid haemorrhage

   OR
   - One stritly lobar haemorrhagic lesion + one white matter feature (severe perivascular spaces in the centrum semiovale or white matter hyperintensities in a multispot pattern)

4. Absence of any deep haemorrhagic lesions (i.e. intracerebral haemorrhage or cerebral microbleeds) on T2*-weighted MRI

5. Reasonable exclusion of other causes of hemorrhagic lesions (see paper)

@a_charidimou

Adapted from Lancet Neurol 2022; 21: 714-25

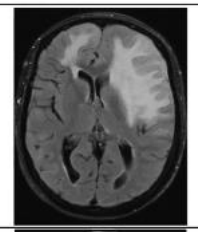
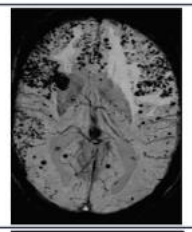
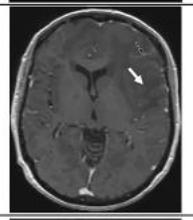
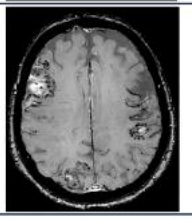
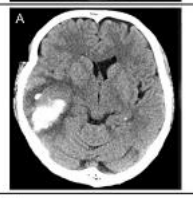
EMERGING CONCEPTS

Stroke

CLINICAL AND POPULATION SCIENCES

Clinical, Neuroimaging, and Genetic Markers in Cerebral Amyloid Angiopathy-Related Inflammation: A Systematic Review and Meta-Analysis

Prevalence of Neuroimaging Markers and Clinical Features among CAA-ri patients.

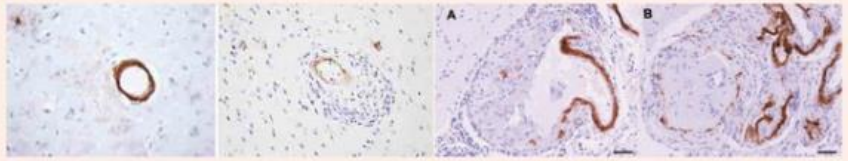
T2/FLAIR Hyperintense white matter Lesions (98%)		CMBs (96%)	
Gd+ Enhancing Lesions (54%)		cSS (51%)	
Lobar Hemorrhage (40%)		1. Cognitive Decline (70%) 2. Focal Neurological Deficits (55%) 3. Encephalopathy (54%)	

FLAIR: Fluid - attenuated inversion recovery
Gd+: Gadolinium

CMBs: Cerebral Microbleeds
cSS: Cortical Superficial Siderosis

Inflammatory Cerebral Amyloid Angiopathies

Inflammatory CAA



Sporadic CAA | CAA-ri | Aβ-related angiitis (ABRA)

1. CAA-relation inflammation (CAA-ri)

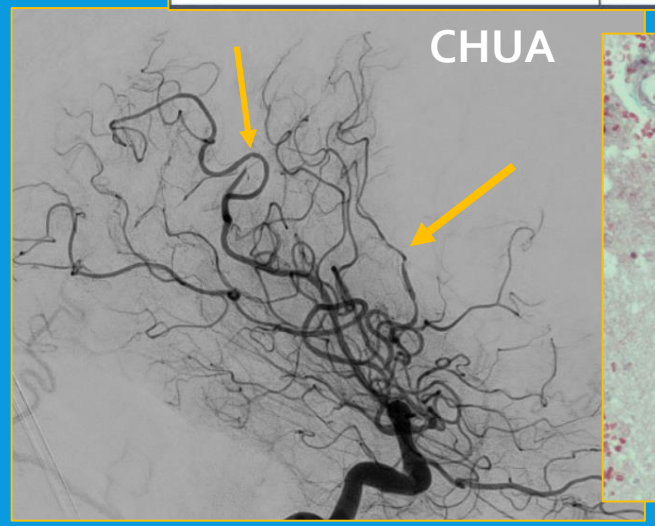
Predominantly perivascular inflammatory infiltrates

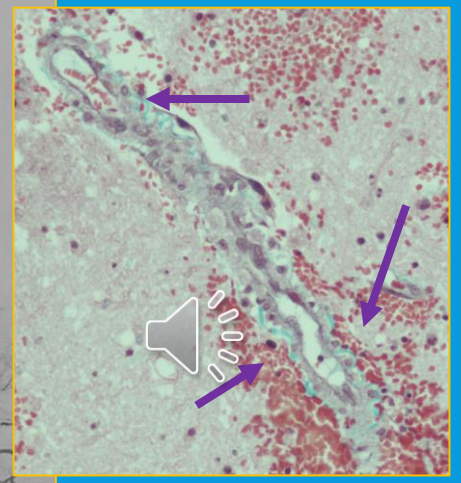
2. Aβ-related angiitis (ABRA)

Transmural vasculitic process, with or without granulomas (angio-destructive inflammation)

3. Amyloid-Related Imaging Abnormalities (ARIA)

Associated with amyloid-modifying therapies





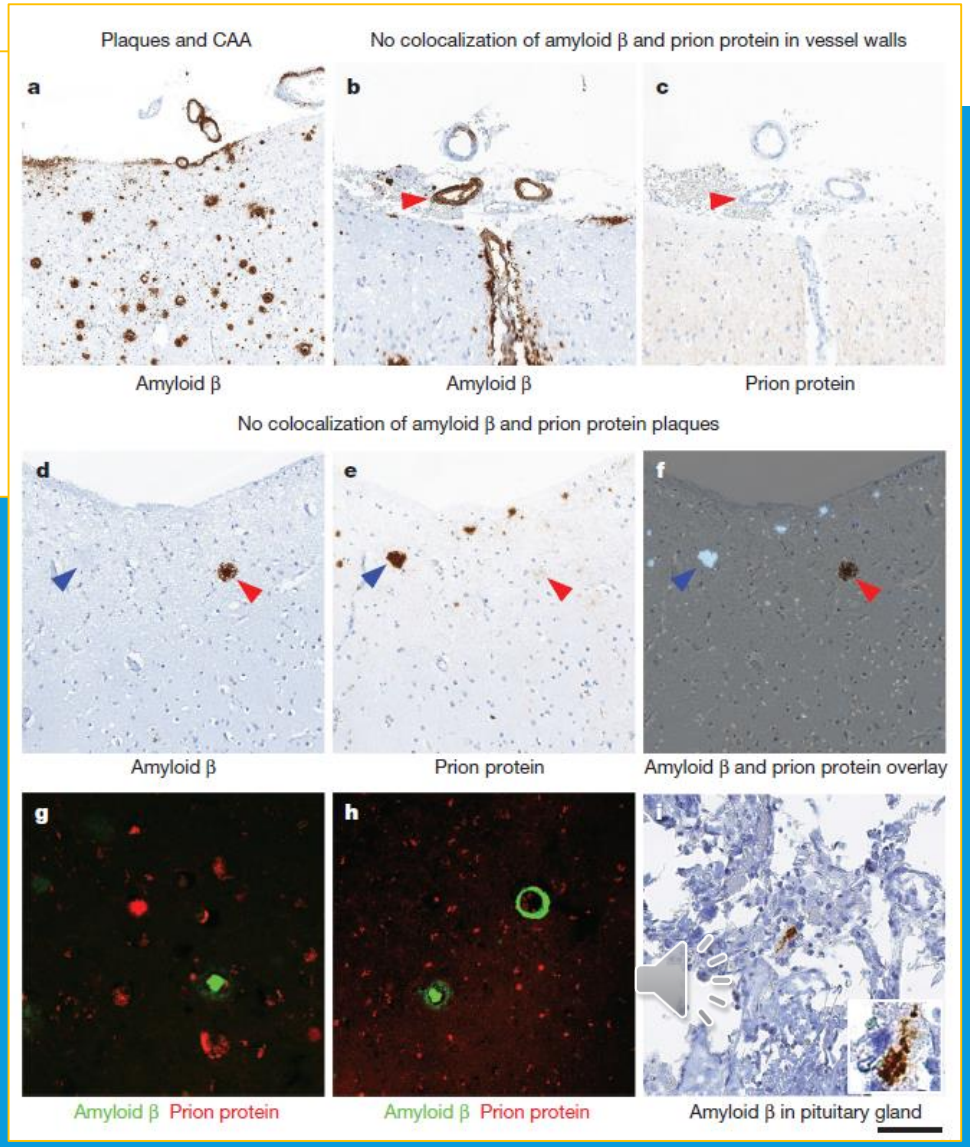
EMERGING CONCEPTS: iatrogenic CAA (iCAA)

LETTER

doi:10.1038/nature15369

Evidence for human transmission of amyloid-β pathology and cerebral amyloid angiopathy

Zane Jaunmuktane[1], Simon Mead[2,3,4], Matthew Ellis[3], Jonathan D. F. Wadsworth[2,3], Andrew J. Nicoll[2,3], Joanna Kenny[2,4], Francesca Launchbury[3], Jacqueline Linehan[2], Angela Richard-Loendt[3], A. Sarah Walker[5], Peter Rudge[2,4], John Collinge[2,3,4] & Sebastian Brandner[1,2,3]



- 1993: First descriptions of amyloidosis described in coexistence with PrP in CJD (Watanabe, 21 cases)
- 2015: First pathological description of transmission in humans. 4/8 young patients with iCJD: amyloid deposition typical of Alzheimer's disease and CAA
- Marked $A\beta$ deposition in parenchyma and vessels in relatively young patients suggests a risk of prion-like transmission of $A\beta$ in humans

iatrogenic CAA (iCAA)

› Nature. 2018 Dec;564(7736):415-419. doi: 10.1038/s41586-018-0790-y. Epub 2018 Dec 13.

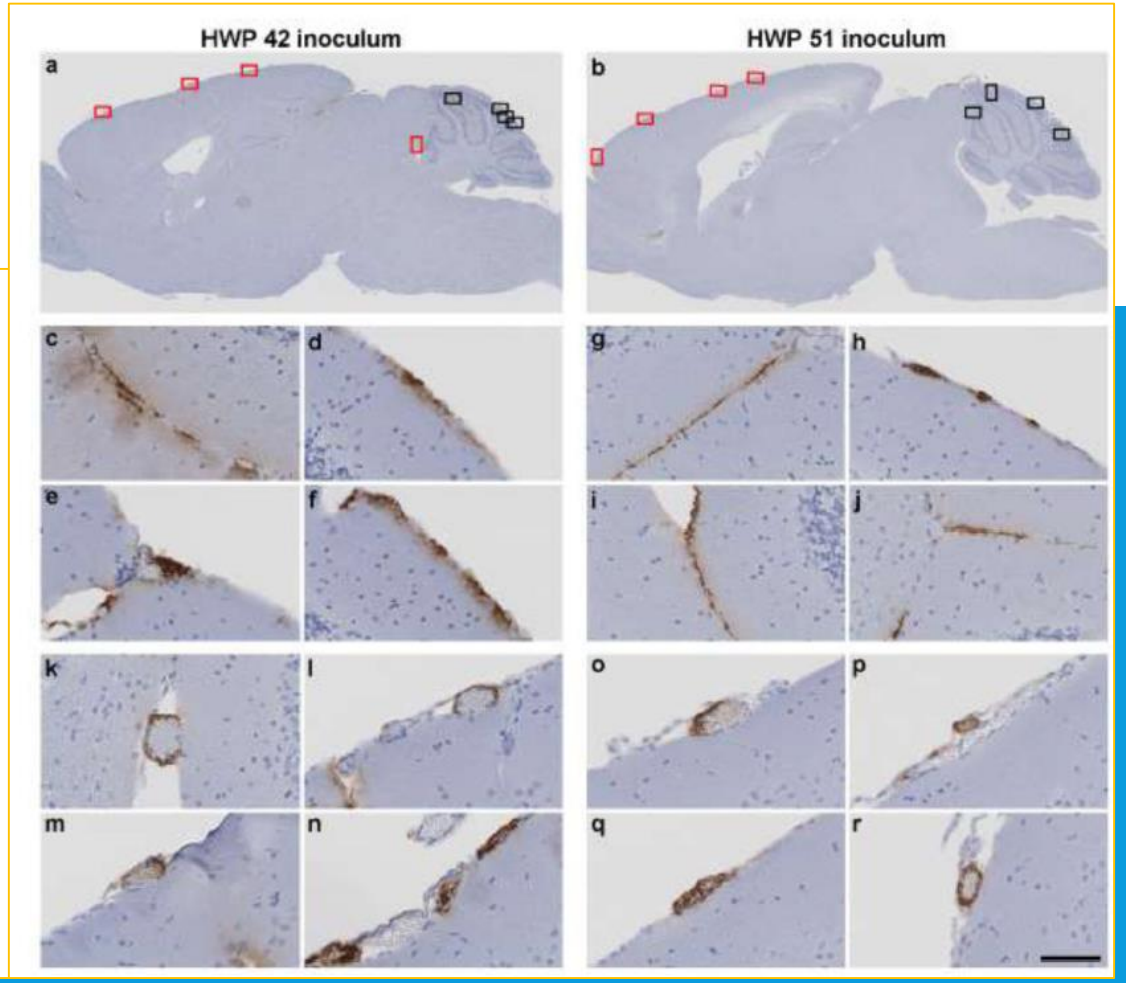
Transmission of amyloid-β protein pathology from cadaveric pituitary growth hormone

Silvia A Purro [1], Mark A Farrow [1], Jacqueline Linehan [1], Tamsin Nazari [1], David X Thomas [1], Zhicheng Chen [2], David Mengel [2], Takashi Saito [3], Takaomi Saido [3], Peter Rudge [1], Sebastian Brandner [1 4], Dominic M Walsh [1 2], John Collinge [5]

Affiliations – collapse

Affiliations

1 MRC Prion Unit at UCL, UCL Institute of Prion Diseases, London, UK.
2 Laboratory for Neurodegenerative Research, Ann Romney Center for Neurologic Diseases, Brigham and Women's Hospital and Harvard Medical School, Boston, MA, USA.
3 Laboratory for Proteolytic Neuroscience, RIKEN Center for Brain Science, 2-1 Hirosawa, Wako, Japan.
4 Division of Neuropathology, National Hospital for Neurology and Neurosurgery, London, UK.
5 MRC Prion Unit at UCL, UCL Institute of Prion Diseases, London, UK. jc@prion.ucl.ac.uk.



- 2018: Experimental confirmation of prion transmission of Aβ with Aβ-contaminated GHh preparations
- Inoculation in mice expressing a humanised form of APP
- Aβ seeds confirming suspected Aβ transmission in humans with these preparations (and/or other medical procedures)

iatrogenic CAA (iCAA)

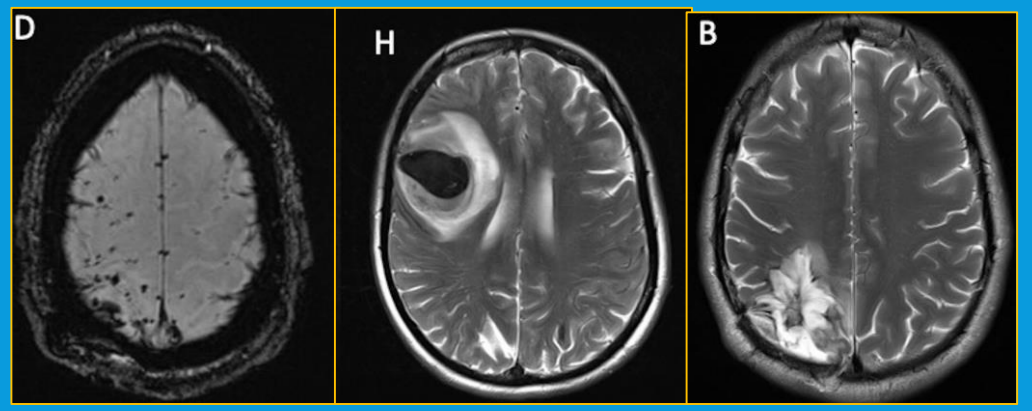
To cite: Banerjee G, Samra K, Adams ME, *et al*. *J Neurol Neurosurg Psychiatry* 2022;**93**:693–700.

Cerebrovascular disease

Review

Iatrogenic cerebral amyloid angiopathy: an emerging clinical phenomenon

Gargi Banerjee [1], Kiran Samra [2], Matthew E Adams,[3] Zane Jaunmuktane,[4,5] Adrian Robert Parry-Jones,[6,7] Joan Grieve,[8] Ahmed K Toma,[8] Simon F Farmer,[9] Richard Sylvester,[9] Henry Houlden [5], Peter Rudge,[1] Simon Mead [1], Sebastian Brandner,[1,2,4] Jonathan M Schott [2], John Collinge,[1] David J Werring [10]



- Newly described form of CAA (2015) and experimentally confirmed (2018)
- Cases with iCJD excluded
- Patients in the 3rd-5th decade of life with ICH and other symptoms (Epilepsy, cognitive impairment)
- Latency period 2-4 decades
- **History Remote neurosurgical history, GHh, cadaver embolisation material**
- JNNP (2022). Number of cases increasingly recognised - 3 cases (48, 39, 34 years) and review of cases described up to that date (n=20)

iCAA

Cerebrovascular disease

Review

Iatrogenic cerebral amyloid angiopathy: an emerging clinical phenomenon

Gargi Banerjee ,[1] Kiran Samra ,[2] Matthew E Adams,[3] Zane Jaunmuktane,[4,5] Adrian Robert Parry-Jones,[6,7] Joan Grieve,[8] Ahmed K Toma,[8] Simon F Farmer,[9] Richard Sylvester,[9] Henry Houlden ,[5] Peter Rudge,[1] Simon Mead ,[1] Sebastian Brandner,[1,2,4] Jonathan M Schott ,[2] John Collinge,[1] David J Werring [10]

Box 1 Proposed diagnostic criteria for iatrogenic cerebral amyloid angiopathy (CAA)

1. Age of onset

⇒ Symptom onset before age of 55 years (ie, below the age threshold for 'probable' or 'possible' CAA within the modified Boston criteria[9]); *strongly suggestive (although note ascertainment bias)*

⇒ *Note: diagnosis cannot be excluded based on age alone, and should be considered in people aged 55 years or above, should they meet the other criteria (detailed below)*

2. History of potential exposure; *one or more of the following*:

⇒ Procedure or treatment using cadaveric human CNS tissues (ie, brain, meninges, pituitary-derived hormones); *strongly suggestive*

⇒ Relevant neurosurgical procedure (ie, those involving the brain, spinal cord, posterior eye)

⇒ *Note: diagnosis can be considered if history of alternative potential exposure and all other criteria are met*

3. Clinical and radiological features consistent with a diagnosis of CAA:

Clinical:

⇒ Evidence of at least one of the following features, either at presentation or during disease course:
- ⇒ Intracerebral haemorrhage or convexity subarachnoid haemorrhage (single or multiple)
- ⇒ Transient focal neurological episodes ('amyloid spells')
- ⇒ Focal seizures (with or without secondary generalisation)
- ⇒ Cognitive impairment not attributable to another cause (including acute stroke)

Radiological; at least one of the following:

⇒ CT:
- ⇒ Lobar intracerebral haemorrhage
- ⇒ Convexity subarachnoid haemorrhage

⇒ MRI (blood sensitive sequences; T2*-GRE, SWI)
- ⇒ Cerebral microbleeds with predominantly lobar distribution, distant from sites of parenchymal intracerebral haemorrhage
- ⇒ Cortical superficial siderosis (focal or disseminated) on MR blood sensitive sequences

4. Evidence of amyloid-beta (Aβ) accumulation in the CNS:

⇒ Positive amyloid-PET scan (note this is not specific for vascular Aβ deposition)

⇒ Supportive CSF features (reductions of Aβ–42, Aβ–40)

⇒ Brain biopsy demonstrating vascular Aβ deposition, in the absence of significant inflammation

⇒ *Notes raised:*
- ⇒ *A positive amyloid-PET scan in isolation might not necessarily be specific for Aβ accumulation, depending on the tracer used[29]; correlation with either CSF Aβ measures, brain biopsy findings and/or genetic testing for non-Aβ CAAs (details below) is advised*
- ⇒ *Presence of significant inflammation might support an alternative diagnosis of CAA-related inflammation or Aβ related angiitis (ABRA)[49]*

5. Exclusion of genetic causes of Aβ CNS disease; *this should include*:

⇒ Duplications of *APP* (including Trisomy 21, where relevant)

⇒ Mutations of *APP*, *PSEN1*, *PSEN2*

⇒ In cases where CNS Aβ deposition has not been confirmed by other means (CSF Aβ measures, brain biopsy), next-generation sequencing for mutations resulting in non-Aβ CAA (*CST3*, *TTR*, *GSN*, *PRNP*, *ITM2B*) should be considered

In order for a diagnosis of probable iatrogenic CAA to be made during life, criteria 2, 3, 4 and 5 must be met as a minimum. Features in the history which are strongly suggestive of the diagnosis are highlighted. A diagnosis of possible iatrogenic CAA can be considered if criteria 1, 2 and 3 are met.

CNS, central nervous system; CSF, cerebrospinal fluid; GRE, gradient recalled echo; PET, positron emission tomography; SWI, susceptibility weighted images.

iatrogenic CAA (iCAA)

- **HISTORY OF POTENTIAL EXPOSURE**
  - Use of human CNS cadaveric material (**Highly suggestive**)
    - Lyodura (Braun) - Used massively from 1969 to 1995
    - GHh ~2000 treatments in UK between 1959 and 1985
    - Lyophilised dura foam in endovascular embolisations
  - *Relevant* neurosurgical history
    - Brain
    - Meninges
    - Spinal cord
    - Posterior eye

B Braun suspends Lyodura production and sales

This article was originally published in Clinica

08 Jul 1996 | **NEWS**

EL PAÍS

Sociedad

EDUCACIÓN · MEDIO AMBIENTE · IGUALDAD · SANIDAD · CONSUMO · LAICISMO · COMUNICACIÓN · ÚLTIMAS NOTICIAS

En España no se usa la hormona del crecimiento que condenó a muerte a 25 niños en Francia

La administración del fármaco sintético cuesta a Sanidad 10.000 millones al año

LUCIA ARGOS

Madrid - 22 JUL 1993 - 00:00CEST

iatrogenic CAA (iCAA)

- **EVIDENCE OF Aβ ACCUMULATION IN THE CNS**
  - Positive brain PET
    - Different tracers
    - Subjective component
    - Not specific for vascular accumulation of Aβ
  - Positive brain biopsy in the absence of significant inflammation
    - Positive IHC Abeta and/or Congo Red in vessels, dura mater, parenchyma, or evacuated material
  - CSF amyloidosis pattern Aβ-42 reductions; Aβ-40 with normal tau and P-tau levels.

Neurology. 2024 Oct 22;103(8):e209828. doi: 10.1212/WNL.0000000000209828. Epub 2024 Sep 16.

CSF and Plasma Biomarkers in Patients With Iatrogenic Cerebral Amyloid Angiopathy

Aβ and tau levels comparable with elderly patients with sCAA

- **EXCLUSION OF GENETIC CAUSES**
  - Male predominance in iCAA
  - Ruling out duplications (trisomy 21), APP mutations, PSEN1, PSEN2
  - In case Aβ deposits are not confirmed: sequence non-Aβ AAC mutations (CST_3, TTR, GSN, PRNP, ITM_2B)
  - **ApoE genotyping: ε3 usually present in AACi, mostly homozygous**
    - Very rare ε2/ε4 in the iatrogenic form

CLINICAL CASE SERIES

Albacete University Hospital

CASE 1

Born 1977
Cocaine abuse

1978

H. La Fe Valencia

Neonatal surgery of craniosynostosis with CSF fistula.

+

Lyophilised dura mater from cadaver **(Lyodura)**

2014

Severe headache

+

Recurrent and self-limited paroxysmal sensory-motor episodes in the left limbs

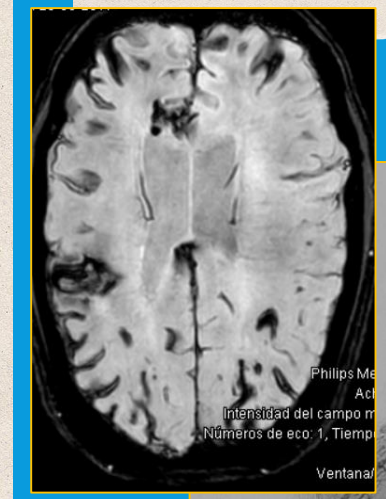
MRI:

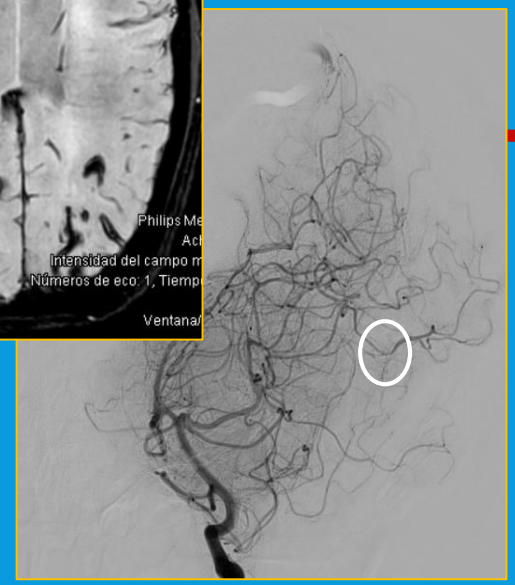
- Cortico-subcortical microbleeds
- Superficial siderosis
- Macrohaemorrhages
- cSAH

2017

Thunderclap headache

Toxic withdrawal



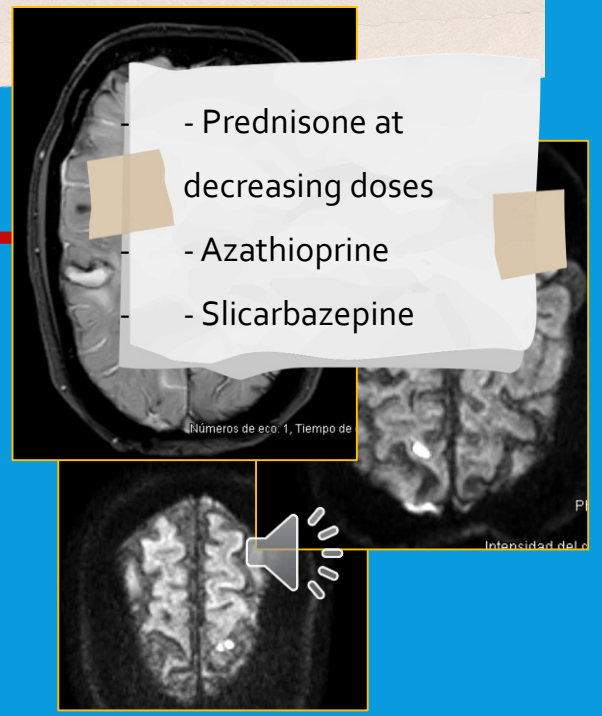


2021

Pulsatile headache

+

Paresthesias right limbs



- Prednisone at decreasing doses
- Azathioprine
- Slicarbazepine

CASE 1

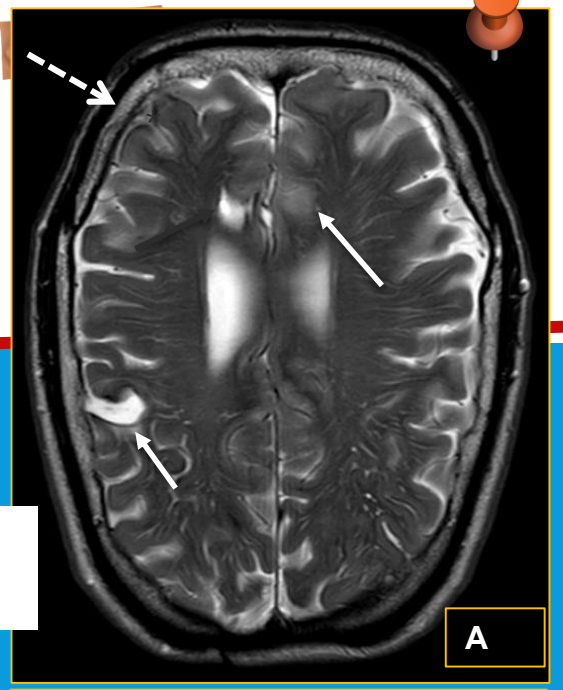
2023

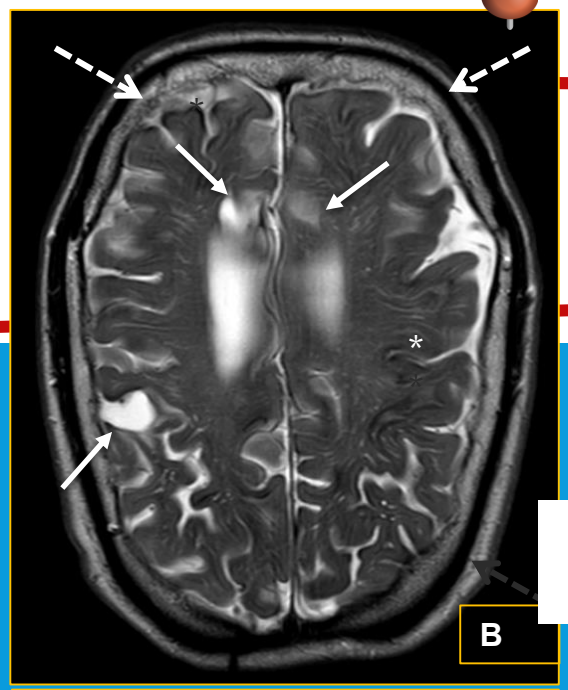
Abrupt headache, bradypsychia and instability

New left temporal macrohaemorrhage and MRI progression.

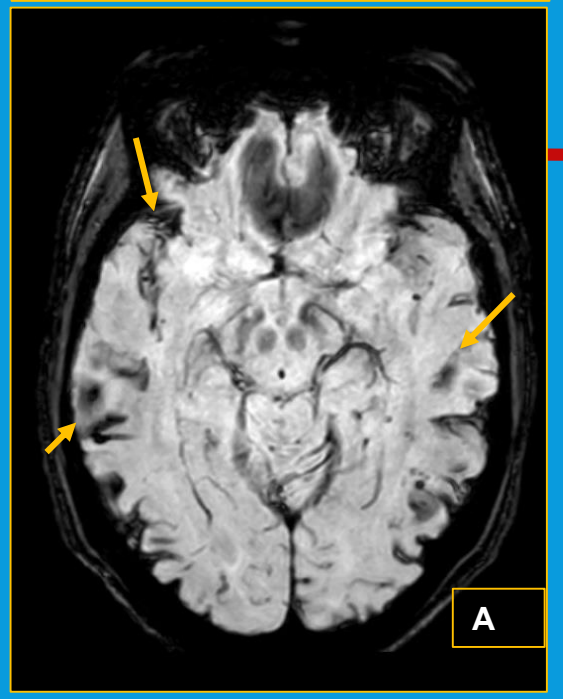
Arteriography unchanged since 2017

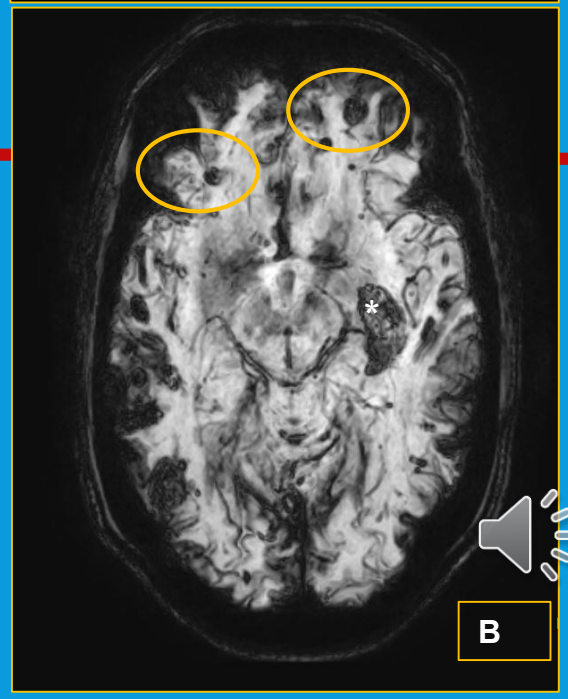
2017



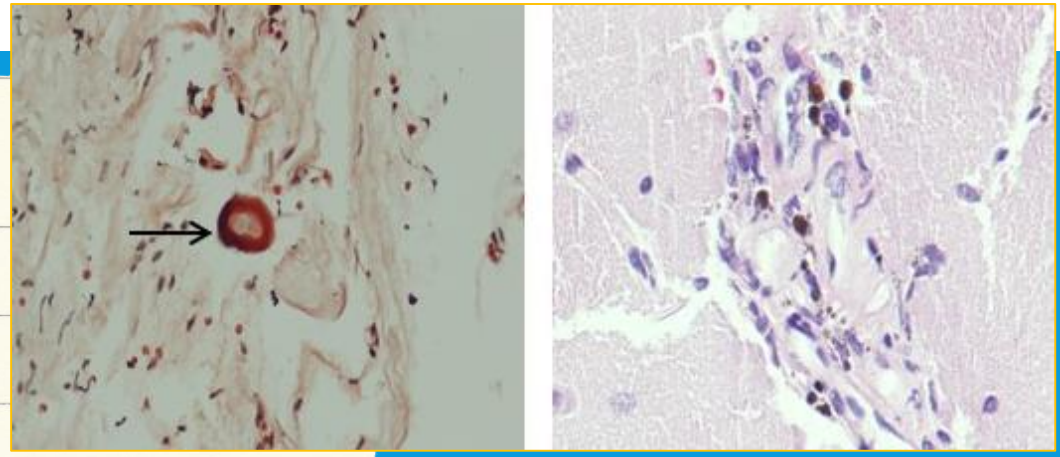


2023



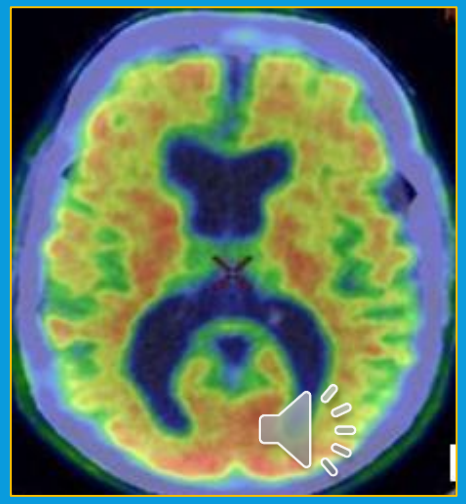


CASE 1



- **Negative genetic panels**
  - ❑ microangiopathy.
  - ❑ amiloidosis familiar, APP, PSEN1, PSEN2

- Biopsy:
  - ❑ H-E staining: reactive astrocytosis and neuropil oedema. Presence of haemosiderophages, lymphocytes and plasma cells in the vascular walls
  - ❑ **Congo red staining: Positive** in dura mater vessels (arrow) and parenchyma
- PET-CT: Positive for cortical amyloid deposition



CASE 2

Born 1967
Focal structural epilepsy

1979

Exploratory craniectomy in infancy for epileptic seizures:

TBI ischaemia (H. La Fe)

Lyodura?

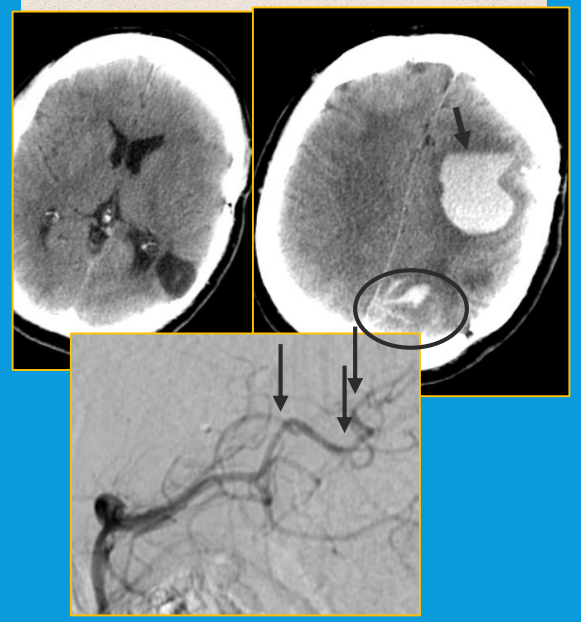
New surgery 2006:

Ganglioglioma (Fundación Jnez Díaz)

2016

49 y-o.

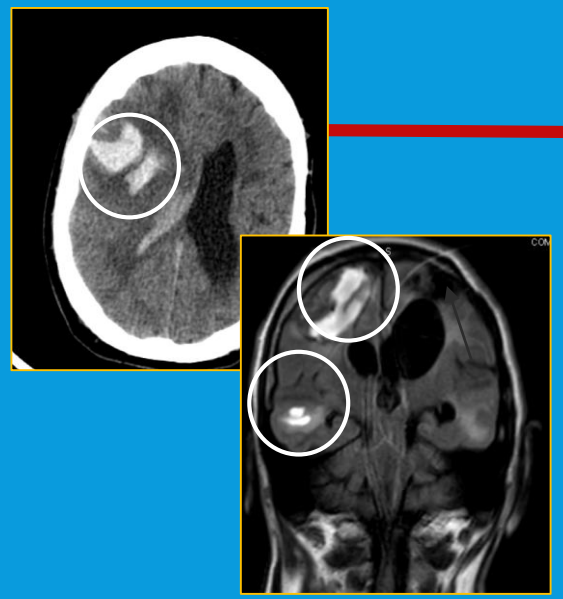
Left hemispheric Status epilepticus



2022

Right hemispheric Status epilepticus →

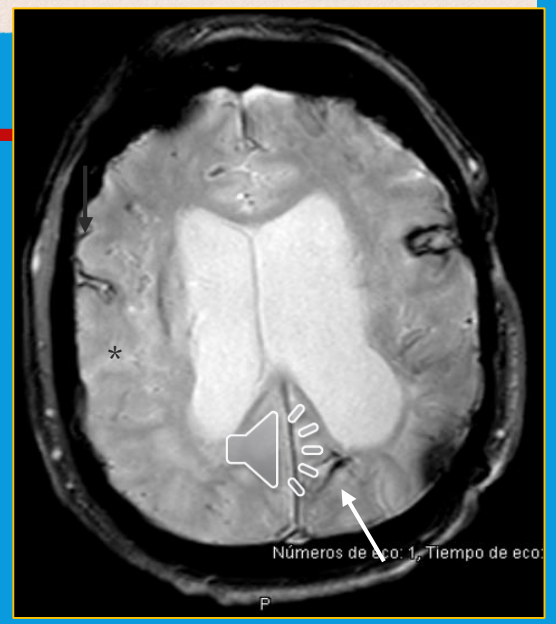
Quadriplegia + aphasia



2023

56 y-o

New frontal and left sylvian haemorrhagic foci

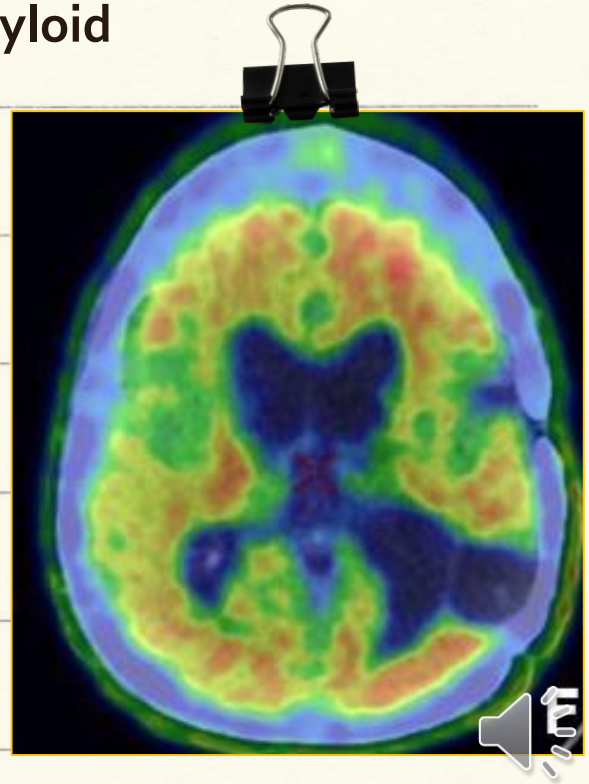


CASE 2

1967

Focal structural epilepsy, left P-T ganglioglioma?

- **PET-CT: Positive for cortical deposition of amyloid**
- Genetic panels: negative
- Lumbar Puncture:
  - ❑ Tau NORMAL (257 pg/mL)
  - ❑ P-Tau ↓ (11.1 pg/mL)
  - ❑ **βA-42 ↓ (127 pg/mL)**
  - ❑ **βA-40 ↓ (1649 pg/mL)**
  - ❑ Ratio βA-42/40 NORMAL (0.077)
  - ❑ **NFL ↑↑↑ (7094 pg/ml)**



CASE 3

Born 1972

Subependymoma IV ventricle + VP shunt valve

1978

Subependymoma IV v.

intervened x2 at 6ª

(H. La Fe)

Incomplete excision→

focal radiotherapy

+ VP valve, several

interventions due to

malfunctioning

+ Lyodura

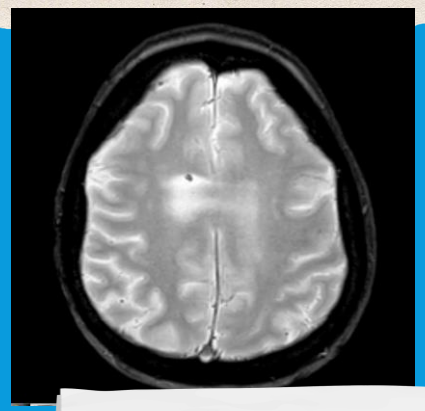
2014

Aphasia and transient

encephalopathy.

Asymmetrical inesp

EEG



- LEV 1500/12h

2016-2022

Progression:

- Amyloid-spells
- Ataxia
- Cognitive impairment:

severe hippocampal

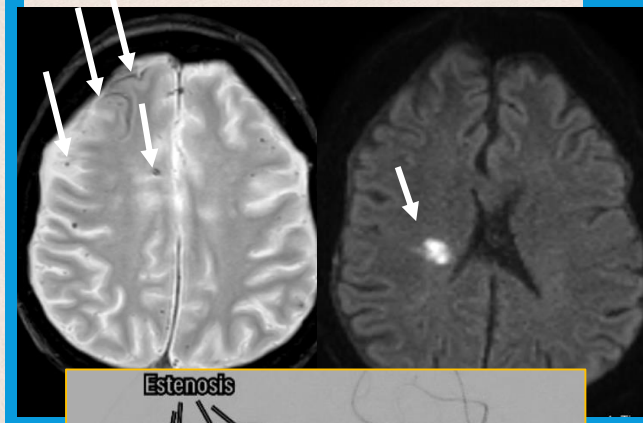
dysfunction and impaired

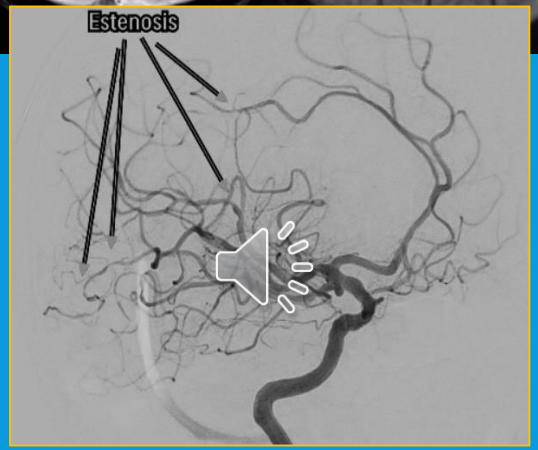
verbal episodic memory

2023

52 y-o

Left hemiplegia

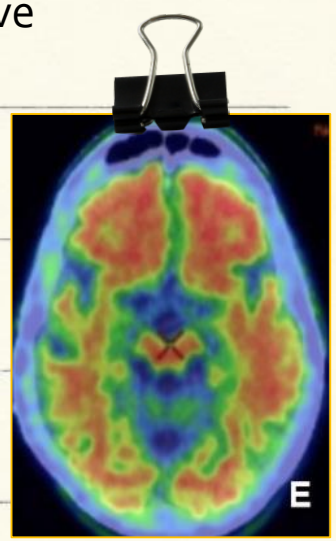


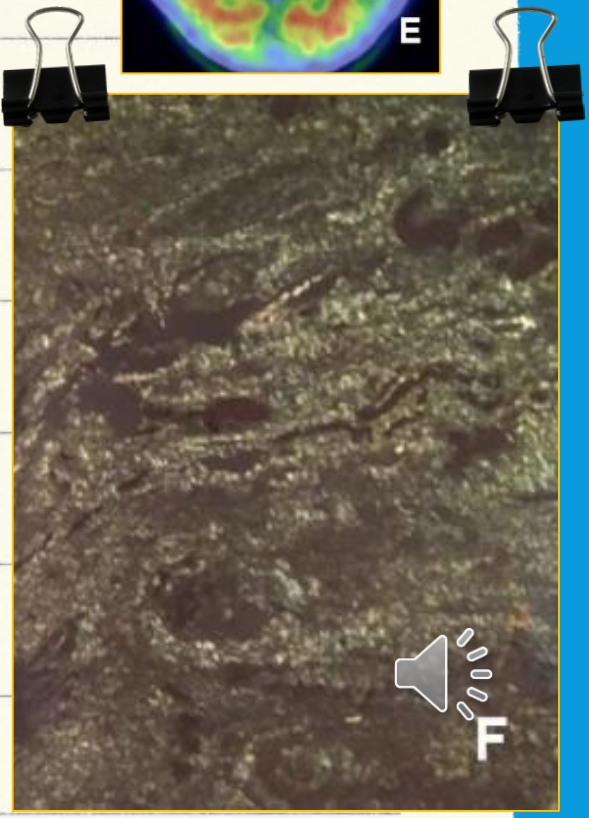


CASE 3

1972
Subependymoma IV ventricle + VP shunt valve

- **PET-CT: Positive** for cortical deposition of amyloid
- Ventricular CSF ventricular *(+ sensitivity)*:
  - ❑ **Tau ↑↑↑ (>2000 pg/mL)**
  - ❑ **P-Tau ↑↑↑ (>400 pg/mL)**
  - ❑ βA-42 NORMAL (980 pg/mL)
  - ❑ βA-40 ↑ (23334 pg/mL)
  - ❑ **Ratio βA-42/40 ↓ (0.042)**
- **Peritoneal biopsy: Congo red +, IHC AA -**
- Genetic panels: negative
- **DIAGNOSIS iCAA + COPATHOLOGY ALZHEIMER'S DISEASE**





CASE 4

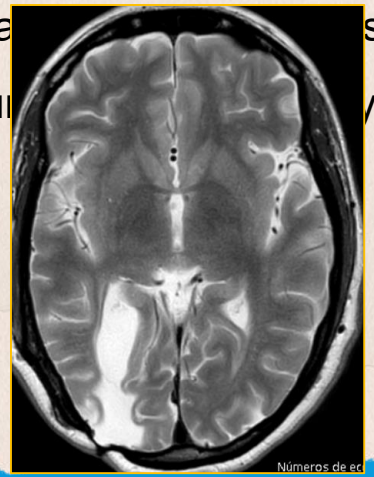
Woman, 1978
TBI

1980

Surgery for post-traumatic skull fracture (H. Ruber Madrid)

+ dural plasty of uncertain origin

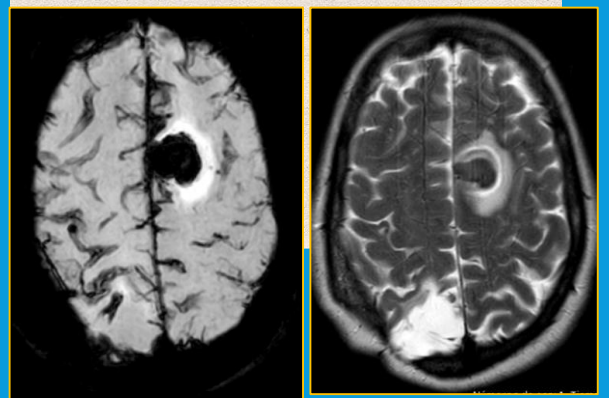
Foca sory seizu years

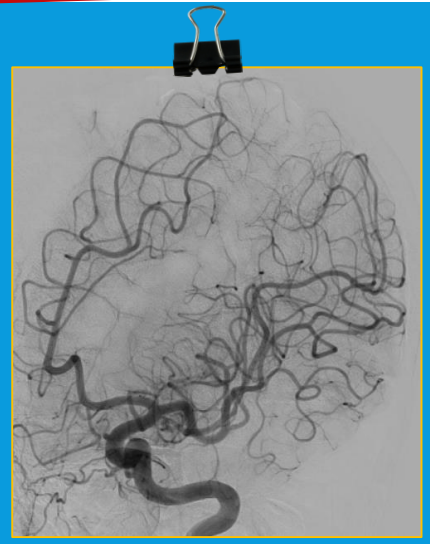


June 2024

Paroxysmal, stereotyped episodes of altered speech output lasting seconds

Oppressive holocranial headache of mild intensity



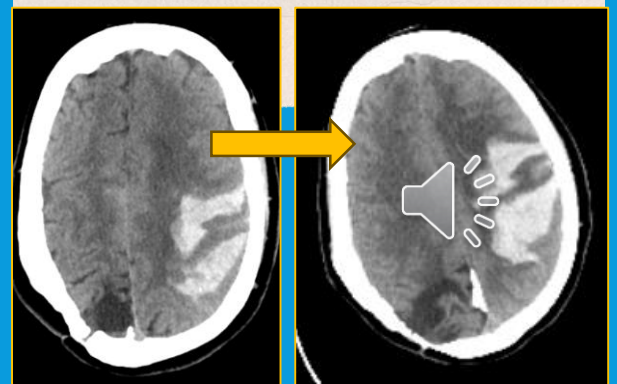


Angiogram: normal

PET-CT: overall radiotracer deposition in the main cortical reference areas

August 2024

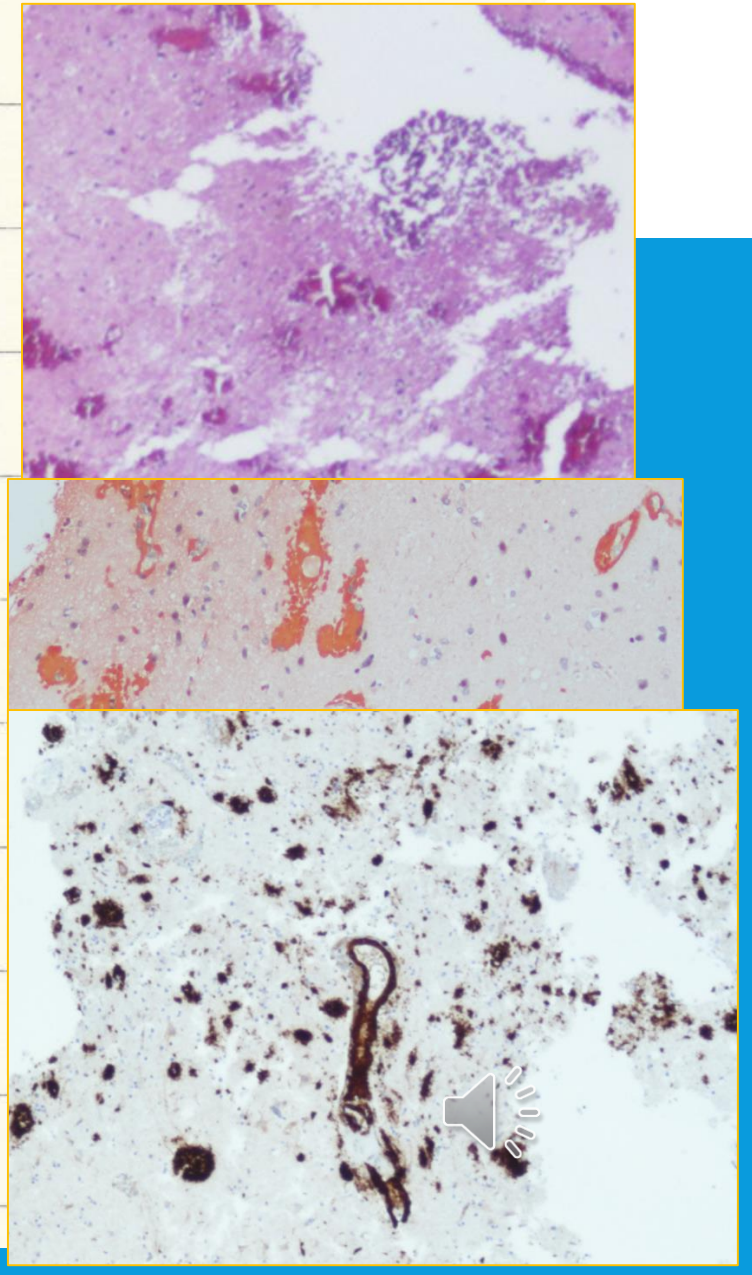
- Outpatient LP
- 3 days later: global aphasia right hemiparesis
- Rebleeding 1 day later, surgery: exitus



CASE 4

Woman, 1978
TBI

- Genetic panels: negative
- Lumbar Puncture:
  - Tau NORMAL (397 pg/mL)
  - P-Tau NORMAL (11.1 pg/mL)
  - **βA-42 ↓ (462 pg/mL)**
  - **βA-40 NORMAL (7907 pg/mL)**
  - **Ratio βA-42/40 ↓ (0.058)**
  - **NFL ↑↑ (3157 pg/ml)**
- Brain Biopsy: **β-IHC positive**



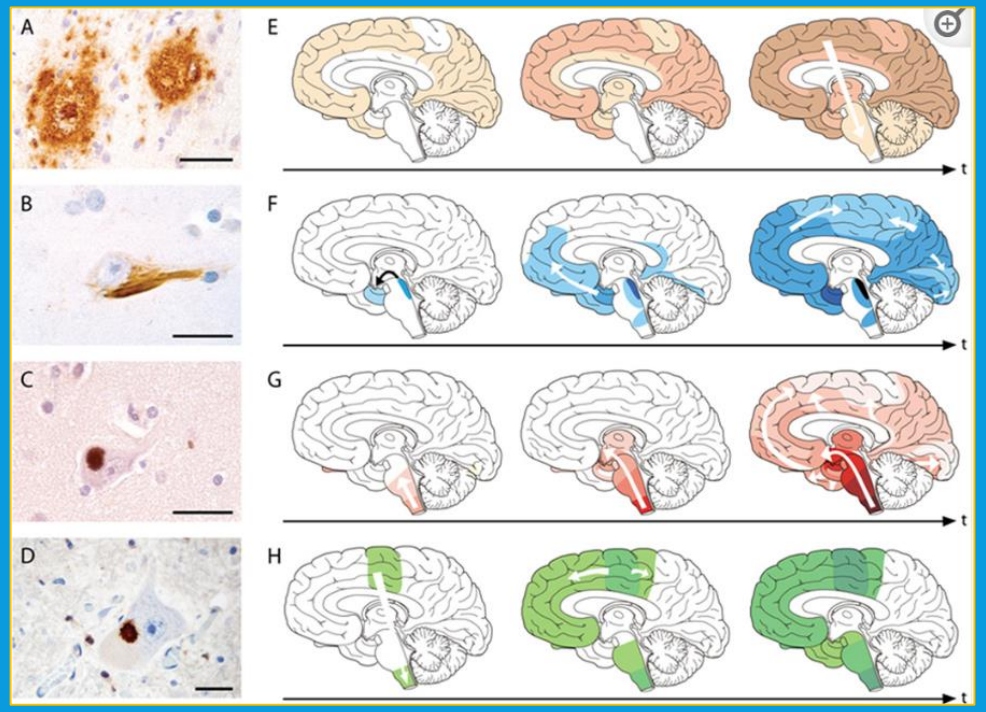
POTENTIAL RAMIFICATIONS

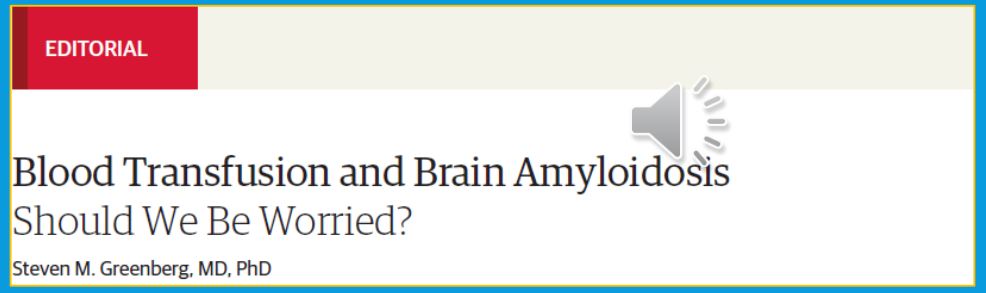
- Aβ shows prion-like characteristics: β-folding, self-replicating, assemblies, transcellular/trans-synaptic spread
- Growing evidence from cell experiments and animal models for the propagation and dissemination of misfolded protein assemblies in neurodegenerative diseases (e.g. Alzheimer's disease, Parkinson's disease, etc. J*ucker & Walker, Nature, 2013*)
- Very long latency period: projection of cases unknown

  - Apparent safety of non-disposable material

  - Doubts about transfusion of blood products and transplants

(SCANDAT registry)





POTENTIAL RAMIFICATIONS

- **Copathology with Alzheimer's disease**

Case 3: Ratio βA-42/40 ↓ (0.042), Tau ↑↑↑↑ (>2000 pg/mL) + Cognitive symptoms

nature medicine

Article

https://doi.org/10.1038/s41591-023-02729-2

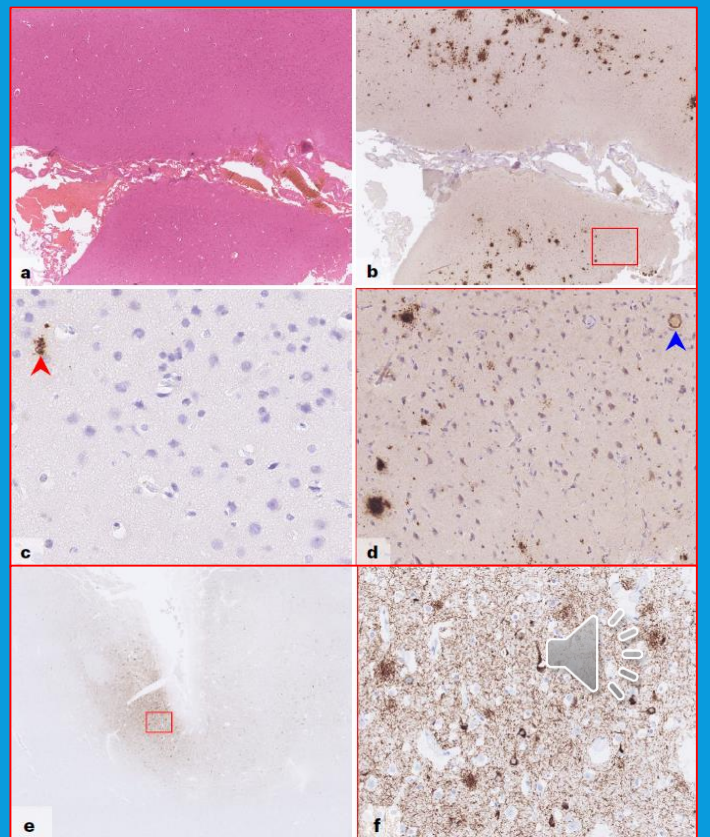
Iatrogenic Alzheimer's disease in recipients of cadaveric pituitary-derived growth hormone

Received: 3 October 2023

Accepted: 17 November 2023

Published online: 29 January 2024

Gargi Banerjee[1,2], Simon F. Farmer[3], Harpreet Hyare[4,5], Zane Jaunmuktane[6,7], Simon Mead[1,2], Natalie S. Ryan[8,9], Jonathan M. Schott[8,9], David J. Werring[10,11], Peter Rudge[1,2] & John Collinge[1,2]

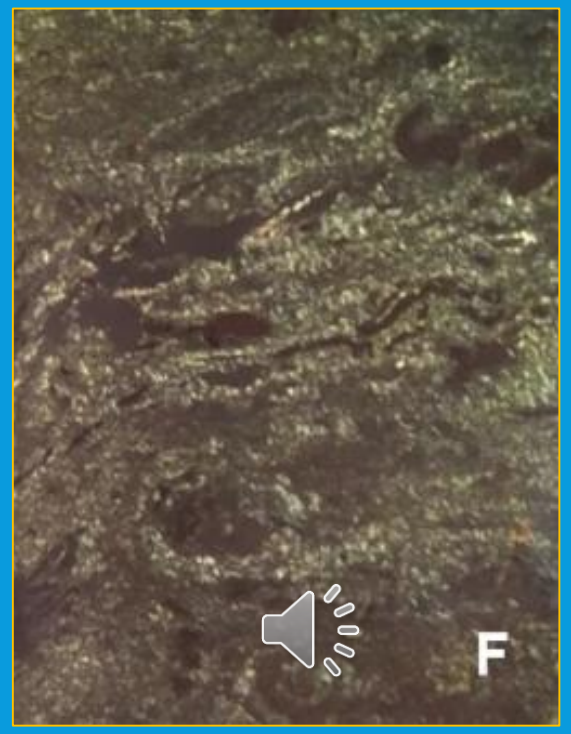


POTENTIAL RAMIFICATIONS

- **Glymphatic system and CSF clearance to other tissues as drainage.**

Case 3: peritoneal biopsy and evolution (less haemorrhagic involvement).

- ✓ Experimental brain seeding in mice and primates after peritoneal inoculation
- ✓ Studies in AD with low-flow shunting to increase circulation and CSF turnover

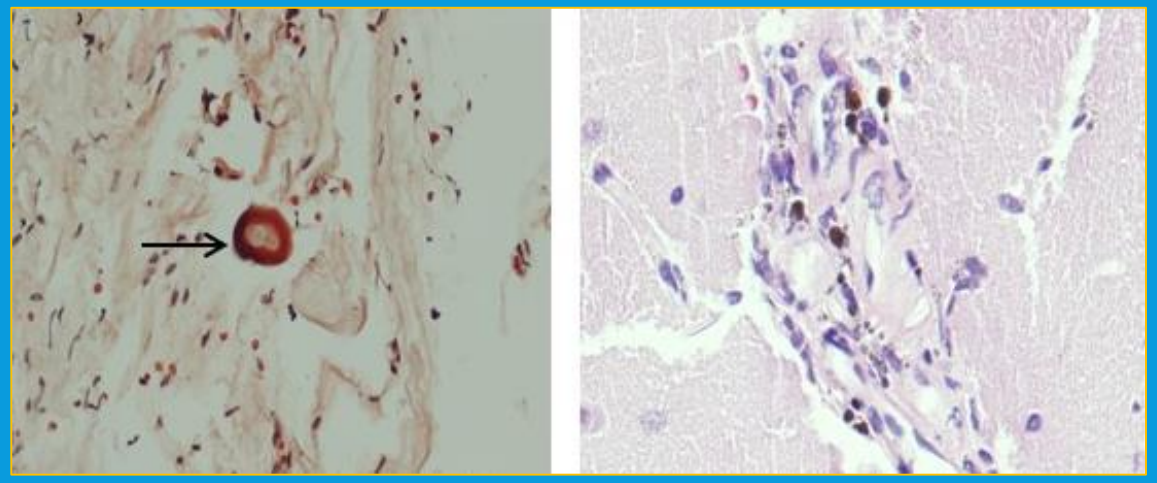


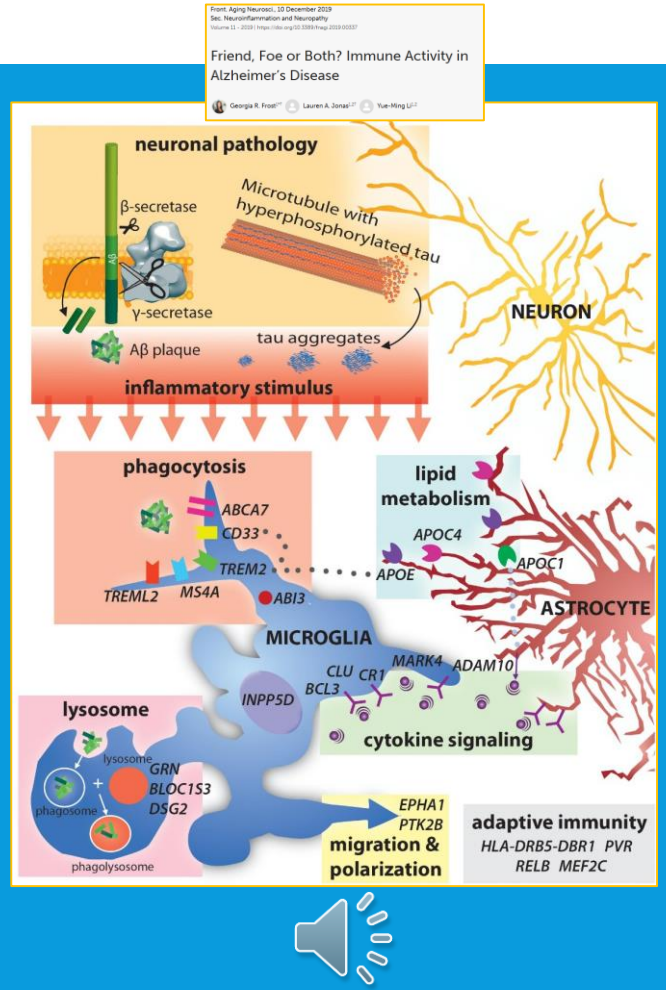
POTENTIAL RAMIFICATIONS

- **Immune response, glial activation, perivascular inflammatory exudate are involved in Aβ clearance:**

  Anti-Aβ vaccine, intranasal Copaxone, monoclonal drugs….

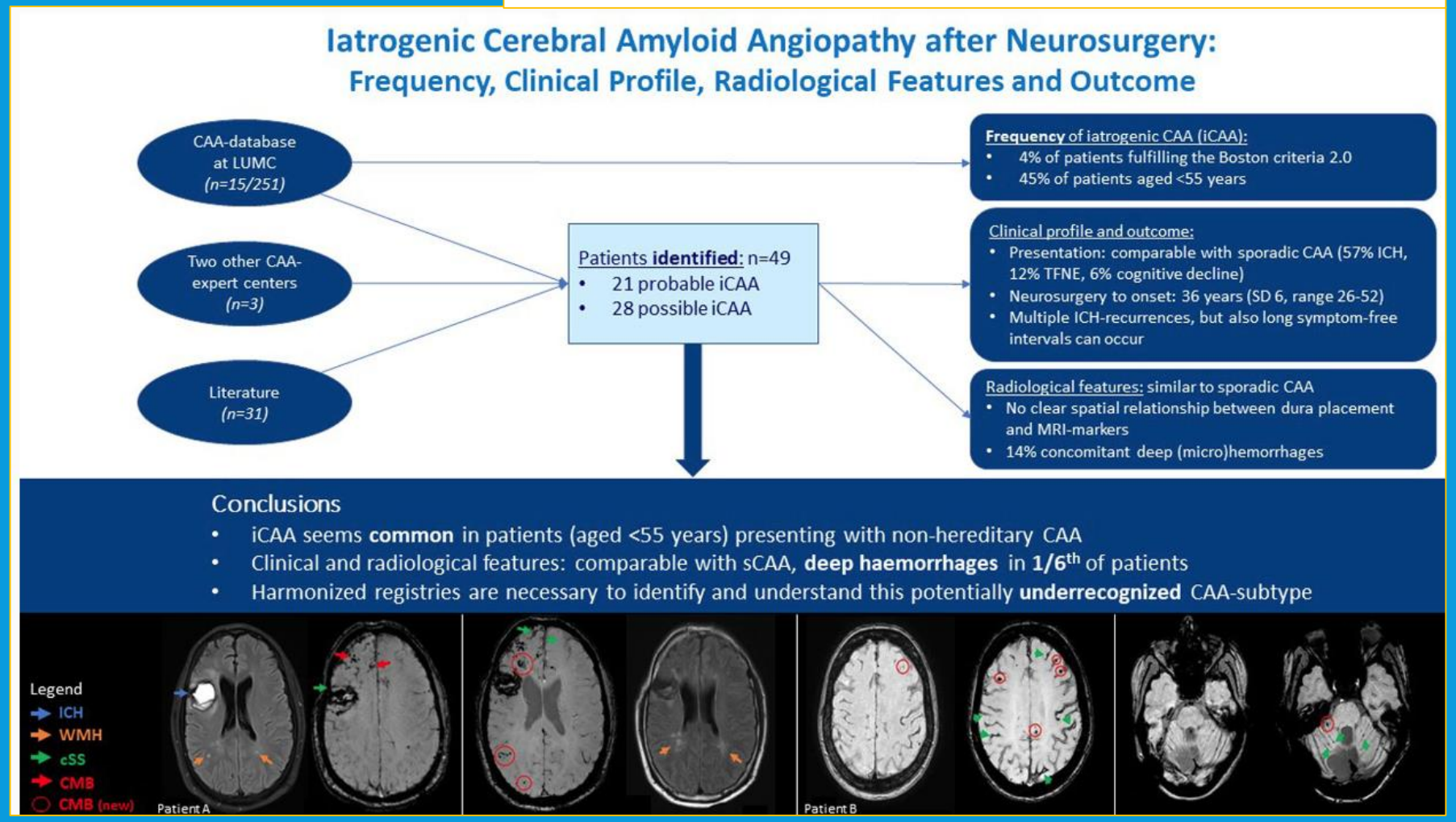
  Case 1: immune response to Aβ, biopsy with inflammation data and good evolution with immunosuppressive treatment.





POTENTIAL RAMIFICATIONS

> Stroke. 2023 May;54(5):1214-1223. doi: 10.1161/STROKEAHA.122.041690. Epub 2023 Apr 10.



RN - AACi

Registro Nacional de Angiopatía Amiloide Cerebral Iatrógena

Información General (Fecha inclusión)
Nº de Paciente
Año de nacimiento
Hospital
Departamento
Ciudad
Comunidad Autónoma
Centro de NeuroCirugía remota
Correo de contacto
Criterios Boston 2.0

Paciente
Edad Paciente al diagnóstico (años)
Edad Paciente en las primeras manifestaciones clínicas (años)
Periodo de latencia desde la primera exposición (años)
Raza
Fumador
Drogas simpatico-miméticas (cocaína, anfetaminas)
Tratamiento antitrombótico (Antiagregante o anticoagulante)
Tratamiento estatinas
Hipertensión arterial
Diabetes Mellitus 2
Antecedente de TCE
Antecedente de malformación arterio-venosa rota
Enfermedad inflamatoria crónica (especificar)
mRS al diagnóstico
Otras causas de lesión hemorrágica (detallar)
Intervención Neuroquirúrgica previa (cerebro, meninges, hipófisis, médula espinal, ojo posteri
Duramadre liofilizada de cadáver documentada
Duramadre de origen incierto
Otro material de cadáver documentado (GH, material de embolización, otros - especificar)
Drenaje LCR definitivo
Presentación primeras manifestaciones clínicas
Manifestaciones clínicas **en el momento del Diagnóstico**
- Hemorragia parenquimatosa
- Hemorragia Subaracnoidea
- Episodios Focales transitorios (amyloid spells)
- Crisis epilépticas
- Encefalopatía
- Deterioro cognitivo
- Cefalea
- Ictus isquémico
- Otros (especificar)

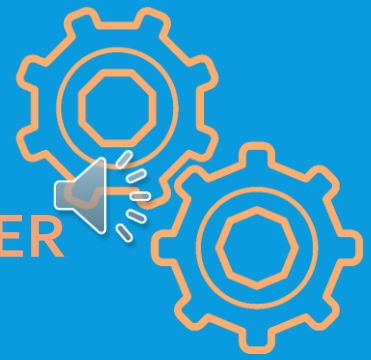
Diagnóstico - RM
RM en el momento del Diagnóstico - Año
- 3T
- T2*GRE
- SWI
- Múltiples HIC
- HIC lobular
- HIC profunda
- HIC mixta (lobular y profunda)
- HIC cerebelosa
- Microsangrados lobulares (cortico-subcorticales)
- Microsangrados profundos
- Siderosis superficial focal
- Siderosis superficial multifocal o extensa
- Hiperintensidad sustancia blanca moderada-importante
- Espacios perivasculares visiblemente dilatados
- Lesiones puntiformes alteración DWI
- Lesión isquémica definida
Diagnóstico - PET TAC
Isótopo utilizado
Afectación cortical generalizada
Afectación cortical localizada
Afectación subcortical
Positivo

Diagnóstico - Biomarcadores
Estudio genético
Genotipo ApoE
Citobioquímica LCR
A_β-42
A_β-40
Ratio A_β-42/A_β-40
p-TAU
TAU total
Neurofilamentos
Diagnóstico - Anatomía patológica
Método Diagnóstico
Hallazgos AP
- Birrefringencia/IHQ Abeta + en hematoma evacuado
- Birrefringencia/IHQ Abeta + en vasos
- Birrefringencia/IHQ Abeta + en duramadre
- Birrefringencia/IHQ Abeta + en otros tejidos
- Exudado inflamatorio de bajo/moderado grado
- Exudado inflamatorio importante
- Placas seniles (CERAD)
- Estadio ABC (NIA-AA)
- Otras enfermedades neurodegenerativas (especificar)
- Otros (especificar)
Diagnóstico - Otros
Estudio cognitivo
Perfil deterioro cognitivo
Arteriografía cerebral
EEG al diagnóstico
Otros (detallar)
Tratamiento
Quirúrgico
Médico

CONCLUSIONS

1) iCAA new emerging communicable disease
2) Mechanism of prion-like transmision
3) Other mechanisms involved: inflammation, drainage of neurodegenerative proteins
4) Copathology with Alzheimer's disease described and its implications
5) Need for comprehensive registries, research and new therapeutic targets

NATIONAL CASE REGISTER



THANKS FOR YOUR ATTENTION

fhernandezf@sescam.jccm.es