Inflammation as a Catalyst in Neurodegeneration: A Case-Based Analysis of Cognitive and Structural Deterioration in CAA-ri

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INTRODUCTION

Cerebral amyloid angiopathy-related inflammation (CAAri) is an immune-mediated complication of cerebral amyloid angiopathy (CAA), often responsive to corticosteroids. While radiological remission is commonly achieved, the long-term clinical trajectory, particularly regarding cognition, remains poorly understood - especially in patients with comorbid neurodegenerative disorders.
Aim: to explore whether CAAri acts as an independent accelerator of neurodegeneration by analyzing **cognitive, functional, and radiological evolution** in three patients - with underlying neurodegenerative diseases - who developed CAAri.

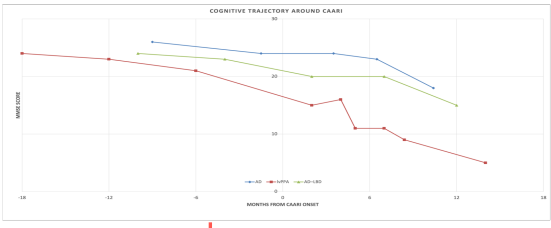
METHODS

Three female patients (aged 72–83) with prior diagnoses of Alzheimer's disease (AD), logopenic variant primary progressive aphasia (lvPPA), and mixed AD–Lewy Body Disease (LBD) were retrospectively analyzed after radiological confirmation of CAAri.

Clinical data included Mini-Mental State Examination (**MMSE**), Activities of Daily Living (**ADL**), Instrumental ADL (**IADL**), and **serial MRIs**. One patient underwent volumetric MRI analysis using SIENA (FSL) to quantify percentage brain volume change (**pBVC**).
All patients were treated with **steroids** (IV methylprednisolone 1 g/day for 5 days) followed by a gradual oral taper.

RESULTS

In all cases, the onset of CAAri marked a **turning point**, with significant and rapid clinical deterioration that contrasted with radiological improvement.



Patient with AD experienced a marked drop in MMSE from 24/30 to 18/30 within twelve months, alongside a reduction in autonomy (ADL from 6/6 to 3/6 and IADL from 8/8 to 3/8), even though follow-up MRIs showed resolution of vasogenic edema and increased microbleeds (figure 1-2).

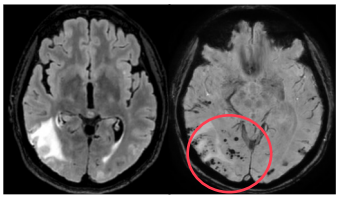


Figure 1: Axial FLAIR and SWAN during CAAri

Steroid therapy ↓ Vasogenic edema ↑ Microbleeds

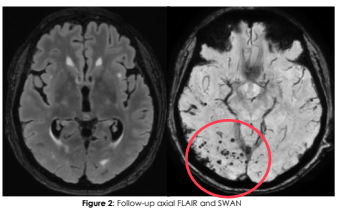


Figure 2: Follow-up axial FLAIR and SWAN

Patient with AD–LBD exhibited an MMSE decline from 21/30 to 15/30 over one year, accompanied by increased behavioral disturbances. SIENA analysis revealed an initial increase in brain volume (+2.789%) consistent with vasogenic edema during the acute phase of inflammation, followed by measurable atrophy (–0.388% over 11 months) despite resolution of imaging abnormalities (figure 3-4).

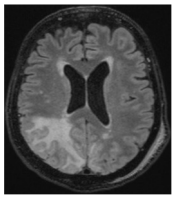


Figure 3: Axial FLAIR during CAAri

Steroid therapy

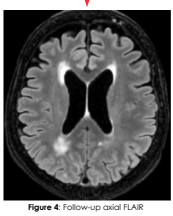


Figure 4: Follow-up axial FLAIR

Patient with lvPPA showed the most striking clinical decline: MMSE fell from 21/30 to 3/30 within 18 months of CAAri onset, accompanied by a profound loss of functional independence (ADL from 6/6 to 1/6; IADL from 2/8 to 0/8), despite radiological improvement (figure 5-6).

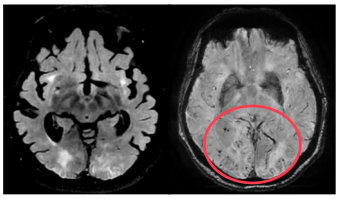


Figure 5: Axial FLAIR and SWAN during CAAri

Steroid therapy ↓ Vasogenic edema ↑ Microbleeds

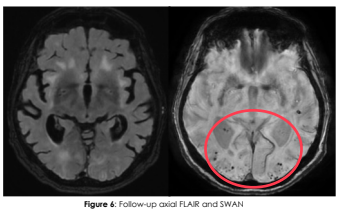


Figure 6: Follow-up axial FLAIR and SWAN

CONCLUSIONS

CAAri appears to act as a potent **catalyst in neurodegeneration**, triggering rapid and irreversible cognitive decline even when imaging shows resolution of inflammation. The discrepancy between radiological and clinical outcomes suggests lasting neurotoxic effects of the **inflammatory insult**.
These findings underscore the need to monitor cognitive trajectories closely in CAAri patients and warrant further studies using quantitative imaging and inflammatory biomarkers to better understand this complex interplay.

References
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