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## **CASE REPORT**

### **CEREBRAL AMYLOID ANGIOPATHY (CAA) AND DEMENTIA: CASE REPORT**

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**CASE REPORT****CEREBRAL AMYLOID ANGIOPATHY (CAA) AND DEMENTIA: CASE REPORT**

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**ABSTRACT**

Cerebral amyloid angiopathy (CAA) is a cerebrovascular disorder caused by the accumulation of amyloid-beta peptides in the cerebral cortical and leptomeningeal vessels. These vascular changes can lead to micro-haemorrhages and lobar intracerebral haemorrhages. CAA becomes more prevalent as age increases. According to autopsy studies, CAA tends to be associated with Alzheimer's disease in most cases. Currently, there is no disease-modifying treatment available. Despite that, early identification may assist clinicians to guide management requiring utilization of antiplatelet, anticoagulant, or thrombolytic drugs in patients with CAA. A case of a patient with cognitive impairment and suspected CAA is described.

**Keywords**

Alzheimer's Disease, Cerebral Amyloid Angiopathy, Cerebrovascular disorders, Dementia

**CASE REPORT**

A 72-year-old woman was referred to the Geriatric Outpatient Clinic for a 3-year history of progressive memory loss. This was associated with agitation and safety concerns from forgetting to switch the stove off after cooking

and wandering onto the roads. Her abilities in activities of daily living (ADLs) were intact but she required supervision, assistance, and reminders for meals and medication administration. The past medical history includes hypertension, hyperlipidemia, and

Type 2 diabetes mellitus (DM). Physical examination including neurological examination was unremarkable. Laboratory tests and an outpatient magnetic resonance imaging (MRI) of the brain was requested. A working diagnosis of Alzheimer's or mixed dementia was given, and a trial of donepezil 5 mg daily was prescribed, in addition to up-titration of amlodipine, atorvastatin and metformin, as her blood pressure, lipid profile and glycaemic control were suboptimal [1].

The blood tests did not reveal any reversible causes of cognitive impairment biochemically or serologically. However, the MRI brain demonstrated chronic small vessel ischemic changes based on extensive white matter T2/

Fluid-attenuated inversion recovery (FLAIR) hyperintensity seen throughout both cerebral hemispheres. There were signs of diffuse punctuate foci of susceptibility induced signal dropout within both cerebrum and cerebellum hemispheres, highly suggestive of microhemorrhages. The main differentials of these multiple micro-haemorrhages were chronic hypertensive angiopathy or cerebral amyloid angiopathy. At the six-month follow-up clinic, donepezil was increased to 10mg with associated improvement in her global cognitive and physical functioning as reported by family, with a reduction in repetitive conversations, less agitation and wandering, as well as less dependence on caregivers for activities of daily living.

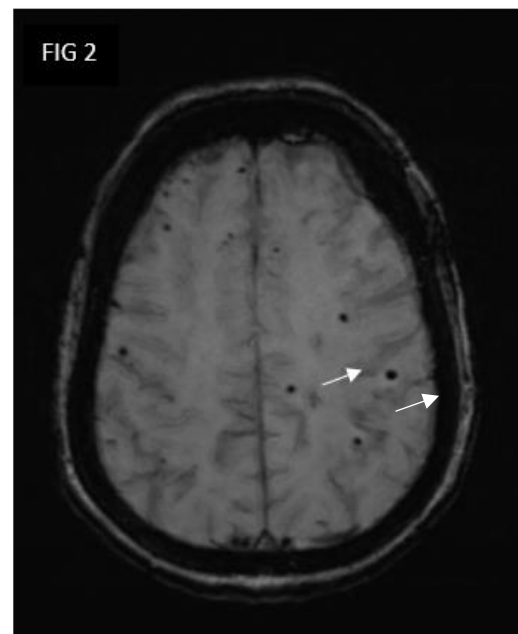
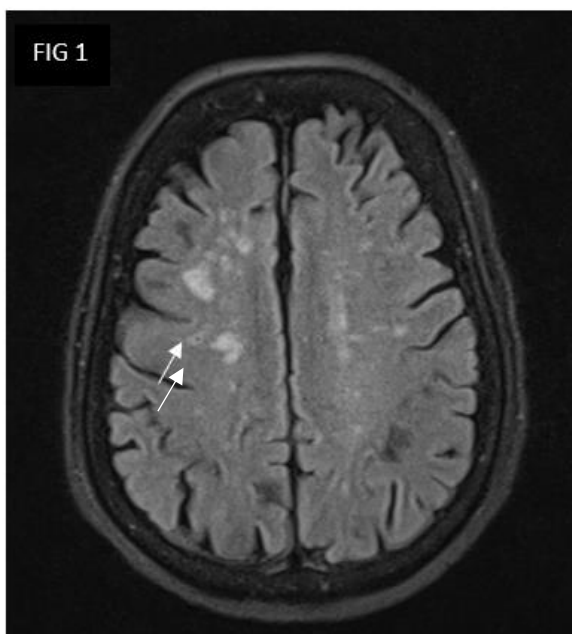


Fig 1 (Axial FLAIR) and Fig 2 (Axial SWI) demonstrated lobar-distributed multiple cortical-subcortical microhemorrhages.

## DISCUSSION

Cerebral amyloid angiopathy (CAA) is characterized by amyloid beta-peptide deposits within small- to medium-sized blood vessels of the brain and leptomeninges, which can cause lobar intracerebral hemorrhage and microbleeds in older adults. This may present with transient neurological symptoms, inflammatory encephalopathy, incidental microbleeds/hemosiderosis on MRI or like in this case, contribute to cognitive impairment [2].

The incidence of CAA has a strong relation with age. Based on autopsy cases, the incidence is 2.3% for those aged 65 to 74 years compared to 12.1% in those over the age of 85 years. Most patients diagnosed with CAA appear to have cognitive impairment in at least one domain on neuropsychological testing. An autopsy series demonstrated one-third of the study population presented with moderate to severe CAA, which was associated with a rapid decline in global cognition, perceptual speed, episodic memory, and semantic memory. These were independent of age, sex, education, Alzheimer's disease pathology and other potential covariates [3].

The prevalence of CAA among older patients with dementia is higher than those without dementia. It is estimated about 60% of patients with dementia demonstrated CAA pathology compared with less than 40% among non-dementia patients [4]. Among patients with

Alzheimer's disease, more than 80% had pathologic evidence of CAA, with 26% appearing in a moderate to severe form [5]. Another autopsy study found that patients with both CAA accompanied by Alzheimer's dementia had more severe cognitive dysfunction than patients with Alzheimer's disease alone [6]. Similarly, an MRI study of Alzheimer's disease patients found that the presence of multiple microbleeds was associated with worse cognitive performance. However, only about 25% of CAA patients appear to have a clinical history of dementia prior to their first haemorrhage [7].

With regards to vascular dementia, cerebrovascular disease may contribute to cognitive impairment in patients with CAA. Studies in population- and hospital-based subjects have correlated the number and presence of microbleeds with cognitive impairment and dementia, raising the possibility that these lesions contribute to the neurologic dysfunction and are markers of small-vessel disease [8]. Additionally, clinically silent, or subacute cerebral infarcts on diffusion weighted imaging have been detected in 15 to 23% of patients with CAA and cerebral microinfarcts on T1 and fluid-attenuated inversion recovery (FLAIR) imaging have been found in 35 to 39%. This data is consistent with autopsy and imaging studies showing an association between CAA

severity and volume of white matter hyperintensity and/or microinfarct burden [9].

The pathology of CAA involves deposition of amyloid beta-peptide within the cerebral vasculature. Vascular amyloid deposits in CAA are biochemically similar to the material comprising senile plaques in Alzheimer dementia. Despite these shared pathologic features, the pathophysiology of CAA and Alzheimer disease appear to be distinct [10].

Risk factors for CAA deposition of amyloid-beta peptide are not well-understood but genetic factors may play a big role in increasing the risk of sporadic CAA, especially autosomal dominant or carrier of amyloid precursor protein (APP) variant or Apolipoprotein E (APO-E) [11]. The deposition of amyloid-beta peptide into the media or adventitia of cerebral arteries can potentially lead to the destruction of smooth muscle, vascular wall thickening, vessel fragility and concentric splitting of vascular wall, leading to vascular rupture and bleeding. The relationship between CAA and hypertension is debatable. While most patients with CAA-related hemorrhage are normotensive, having high blood pressure will contribute to the risk of hemorrhage recurrence [12].

The commonest clinical manifestation of CAA is an acute lobar intracerebral hemorrhage (ICH). The term “lobar” refers to the location of the cortex and subcortical white matter of a

hemispheric lobe of the brain, frequently in temporal and occipital lobes. This is in contrast to the deep locations such as the putamen or pons, which are characteristic of hypertensive hemorrhage. The lobar location of hemorrhages reflects the underlying distribution of vascular amyloid deposits favoring cortical vessels and largely sparing white matter, deep gray matter, and brainstem [13]. The clinical presentation of CAA-related hemorrhage varies with lesion size and the region of the brain affected, which ranges from headache to hemiparesis and depressed consciousness [14].

Unfortunately, CAA can only be definitively diagnosed at postmortem. The next best diagnosis of probable CAA is made with clinical evaluation and weighted brain MRI. This diagnosis should be considered in clinically suspected patients aged 50 years or more, with characteristics of acute or chronic hemorrhagic findings in lobar regions, entirely sparing typical regions of hypertension hemorrhage (basal ganglia, thalamus, or pons) and/or white matter features on MRI brain in the absence of alternative causes. The Boston Criteria initially proposed in 1990 and revised in 2022 helped standardize the CAA definition through the utilization of clinical, imaging, and pathological criteria [15].

Acute CAA-related hemorrhage is treated similar to other non-traumatic intracerebral hemorrhages. Survivors of lobar hemorrhage

and patients with other clinical manifestations of CAA are at risk of hemorrhagic complications in the future. These risks need to be factored into shared decision-making when discussing the risks and benefits of medications such as antiplatelets and anticoagulants [16]. The management of patients with cognitive impairment due to CAA does not differ from other causes; the mainstay of treatment is supportive care. Older age and larger size haematomas are associated with a worse prognosis [17].

Although vascular pathology does not appear to be primarily driven by hypertension and hyperlipidemia, blood pressure and cholesterol control within normal limits is advisable. In this patient with suboptimal management of her vascular risk factors, the doses of medications for hypertension, hyperlipidaemia and diabetes mellitus were increased. A systematic review showed that donepezil in combination with nimodipine was efficacious in improving cognitive testing scores, ability to carry out activities of daily living and reduced symptom severity in patients with vascular dementia [18]. Thus, this patient was also prescribed donepezil, which was uptitrated with improvement in her symptoms.

## CONCLUSION

CAA has a strong association with progressive cognitive impairment, especially with Alzheimer's disease or vascular dementia. Early

identifications of patients with dementia together with radiological evidence of CAA is important to decide the risk versus benefit of antiplatelets and anticoagulants, emphasize the importance of blood pressure control and affects their prognosis due to its high risk of recurrent spontaneous brain hemorrhages.

## DECLARATIONS

### Author's Contributions

All authors contributed to conception, drafting and finalizing the manuscript

### Conflicts of interest

All authors declared that there are no conflicts of interests

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