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Research article

Neuropsychiatric patterns in cerebral amyloid angiopathy and psychiatric presentations in old age: a short report

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Abstract

Background: Cerebral amyloid angiopathy (CAA) is diagnosed in various settings including stroke units, memory clinics and geriatric psychiatry. CAA is also observed in community dwelling populations. Clinical presentations including neuropsychiatric presentations were described in the last two decades. Various neuropsychological manifestations have been described which include impairment in perceptual speed, episodic memory, semantic memory, attention and executive function and global cognitive impairment. Neuropsychological manifestations included a new manifestation of high impulsivity, in addition to organic personality change, and depression. **Objective:** To explore neuropsychological impairments and psychiatric manifestations observed in CAA patients. **Methods**: Review of case notes. **Results:** Impairment in memory, organic personality change and depression are some of the key features of psychiatric manifestation of CAA. **Conclusion:** While CAA remains underreported in psychiatry, there is a possibility of a neuropsychological profile for CAA.

Key words

Amyloid Angiopathy, Neuropsychiatry, Neuropsychology

Introduction

Cerebral amyloid angiopathy (CAA) is a neurovascular disease characterised by b-amyloid fibrils deposited in the walls of cerebral blood vessels.[1] CAA is diagnosed in various settings including stroke units, memory clinics and geriatric psychiatry. CAA is observed in community dwelling populations as well.[2] Risk factors in the development of CAA include age[3] and a genetic factor, apolipoprotein E alleles.[4] Neuropsychiatric clinical presentations include symptomatic intracerebral haemorrhage, cognitive impairment and dementia, rapidly progressive cognitive and neurological decline, and transient neurological symptoms.[5] Various neuropsychological manifestations have been described which include impairment in perceptual speed, episodic memory,[6] semantic memory, attention and executive function and global cognitive impairment.[7] In one study patients exhibited significant deficits in language, processing speed and executive and memory functions compared to a control group, but were not different on attention and praxis domains.[8] Studies showed that naming was the most impaired process, followed by processing speed, executive functioning, memory and attention.[8] This pattern of frontal cognitive dysfunction was already highlighted in the CAA population.[9]

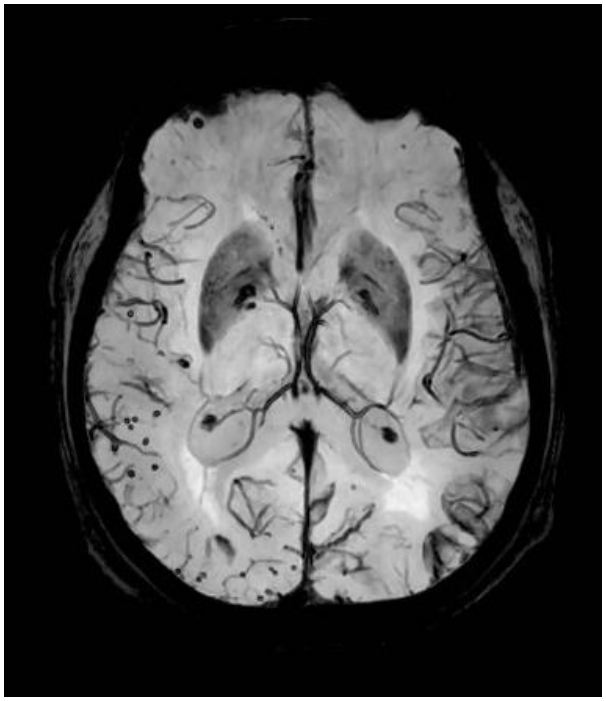
Currently there are no studies that address the psychiatric manifestations of CAA in a systematic way. We report a case series describing neuropsychiatric manifestations of four cases of CAA presented to a geriatric psychiatric unit.

Informed consent was obtained from patients who had mental capacity; or consent from next of kin in patients who did not have mental capacity or who have died.

Case 1

A 77 year old male with a background of paroxysmal atrial fibrillation presented with headache, drowsiness and left visual inattention. His computerised tomographic (CT) head scan showed a right temporal lobe acute intra parenchymal haemorrhage. A Magnetic Resonance Image (MRI) brain scan later showed a right temporal lobe residual haematoma with background evidence of amyloid angiopathy (Figure 1a) on susceptibility weighted imaging (SWI) and with T2 weighted imaging showing evidence of an evolving cortical haemorrhage in right temporal lobe (Figure 1b). On follow up he developed temporal lobe focal seizures. He was initiated on levetiracetam. There was also evidence of cognitive decline [Addenbrooke's Cognitive Examination (ACE III) score was 71/100]. He was referred to psychiatry for depression and poor sleep; with a history of inadequate response to citalopram. There were no delusions or hallucinations; and the past psychiatric history was unremarkable. The seizures were only partially controlled by levetiracetam and it had the potential to cause depression. Hence, levetiracetam was cross-titrated with carbamazepine and stopped. Citalopram was switched to mirtazapine. Following this, depression markedly improved and seizures abated.

Figure 1a: Cortical microhaemorrhages



SWI image (minimum intensity projection) showing innumerable peripheral foci of low signal consistent with extensive old cortical microhaemorrhages.

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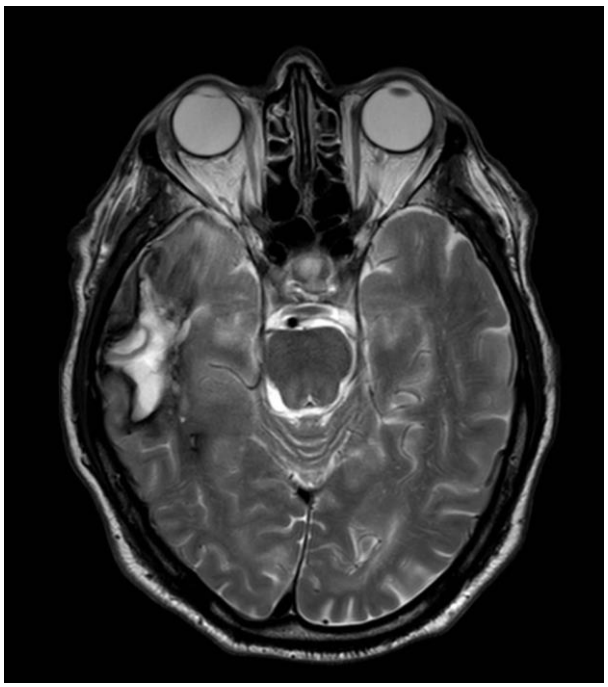
Figure 1b: Evolving cortical haemorrhage

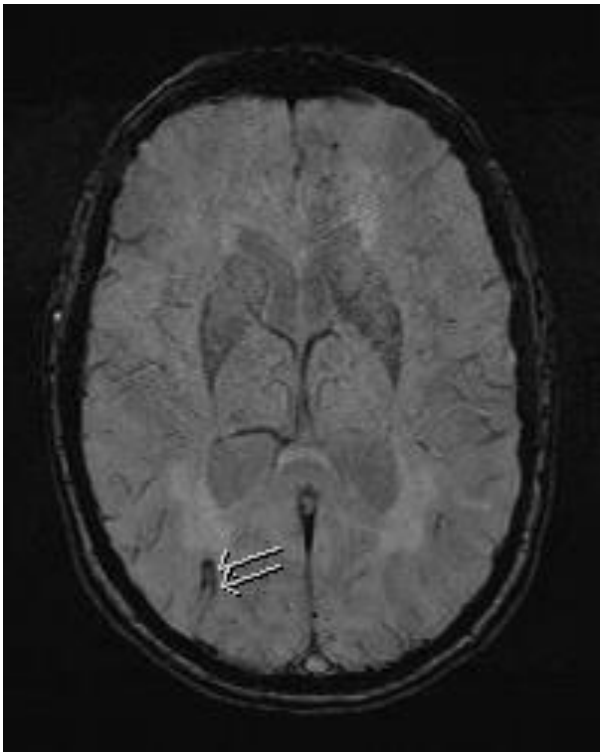


T2 weighted imaging showing evidence of an evolving cortical haemorrhage in the right temporal lobe (high T2 signal centrally with a low T2 signal rim

Case 2

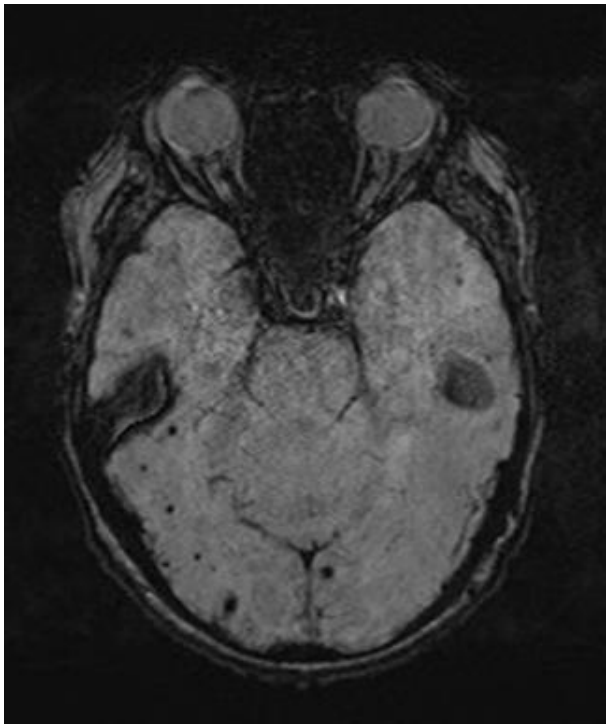
A 74 year old female with a background history of hypertension, ischemic heart disease presented with low mood, tiredness and inability to cope with recent stressful situations. Collateral information suggested changes in her personality over the last three to four years**.** Mental state examination showed low mood, no psychotic features and judgment was intact. She scored 90/100 in ACE III. On neuropsychological testing her attention, concentration and processing speed were below expectations. There was a significant decline in impulse control and cognitive flexibility. The pattern of results also indicated that she struggled to freely recall unstructured information and became overwhelmed with complex tasks. MRI imaging one year apart showed multiple bilateral foci of susceptibility in the cerebral cortex suggestive of amyloid angiopathy (Figure 2a and 2b). MRI also showed moderate small vessel ischaemic disease in the deep cerebral white matter. She was stabilized with mirtazapine 45mg, quetiapine 100mg and clonazepam 500mcg. She showed improvement in impulsivity, sleep, appetite; and became euthymic with no somatic complaints.

Figure 2a: Superficial siderosis



This is susceptibility weighted imaging showing superficial siderosis in the right occipital lobe, with a thin layer of dark signal outlining a sulcus (double arrow). This is consistent with haemosiderin staining due to prior subarachnoid haemorrhage or haemorrhages.

Figure 2b: Microhaemorrhages



SWI imaging showing several scattered microhaemorrhages within the peripheral cortex.

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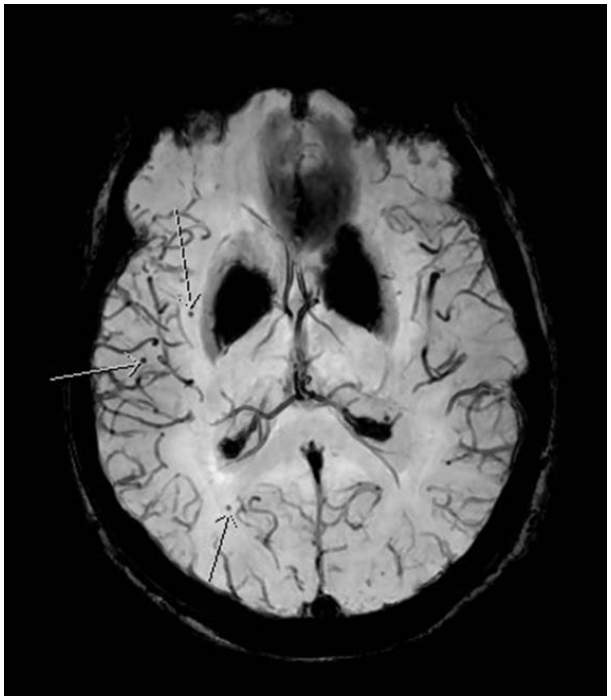
Figure 3a: Small cortical microhaemorrhages

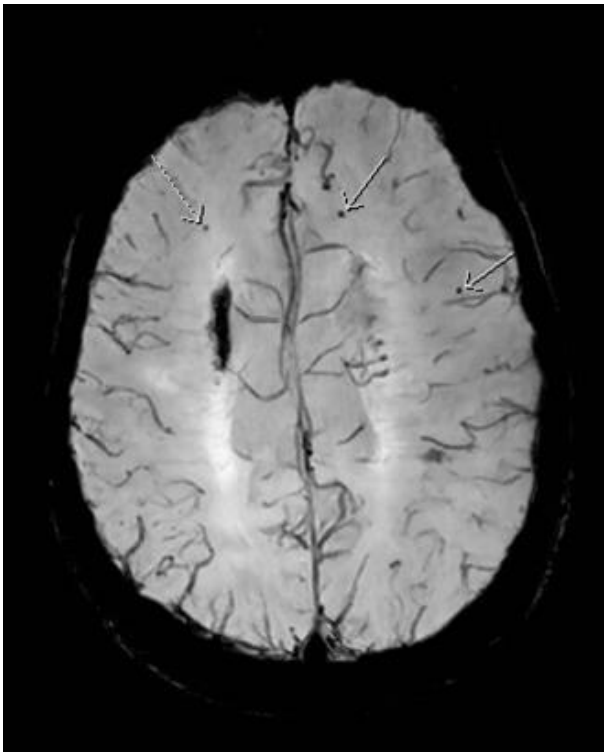


This is a susceptibility weighted image (SWI) that is used to detect evidence of prior haemorrhage. The haemorrhages show discrete foci of low signal. This imaging demonstrates at least three small cortical microhaemorrhages (3 are arrowed). There is also extensive low signal in the basal ganglia and choroid plexus consistent with calcification.

Case 3

An 80 year old female with a background of mastectomy for breast cancer and Hashimoto thyroiditis, presented with intermittent confusion, fixed false beliefs, and auditory and visual hallucinations complicated by anxiety and agitation. This culminated in an attempt to jump out of a moving car. Assessment in psychiatric unit showed delirium secondary to urinary tract infection. A brain CT showed extensive calcification within the basal ganglia and cerebellum and mild small vessel white matter ischaemic change. ACE III score was 78/100 on admission but improved to 86/100 before discharge. A lumbar puncture revealed no growth with normal protein and glucose levels. An MRI brain revealed punctate foci of susceptibility within the cerebral hemispheres peripherally in keeping with cerebral amyloid angiopathy (Figure 3a and 3b). ACE III was 83/100 and 79/100 three months later. She was treated with a small dose of risperidone and discharged home after her symptoms improved. On follow up, she developed further episodes of intermittent confusion, apathy and decline in memory. She died suddenly about six months after discharge.

Figure 3b: Cortical microhaemorrhages



SWI imaging showing at least three further cortical microhaemorrhages (3 arrowed).

Case 4

An 81 year old migrant female French language teacher presented with subjective retrieval deficits for French words five years ago. Her medical history included paroxysmal atrial fibrillation, hypertension and breast carcinoma. Her CT scan was within normal limits. On the ACE III she had 96/100 and diagnosed as amnestic

mild cognitive impairment. A year later, her ACE III score dropped to 86/100. To minimise any possibility that anastrozole may be contributing to her memory impairment, this was discontinued and her ACE III score improved to 91/100. Six months later she presented with a sudden onset ataxia and double vision. On MRI scan there were T2/FLAIR high signal foci within the periventricular and deep white matter, representing small vessel ischaemic change and numerous foci of susceptibility artefacts within the cerebral parenchyma with a cortical and subcortical distribution predominately at the cortical grey-white junction. Appearances were in keeping with amyloid angiopathy. She currently presents to psychiatry with intermittent performance anxiety mainly centred on her deficits although she continues to work as a French language teacher. She has declined psychotropic treatment but receives intermittent counselling.

Discussion

In our case series we could not demonstrate histopathological confirmation of CAA. However, these cases all met the modified Boston radiological criteria[10] for probable CAA. MRI findings in these cases (see figures) all include multiple old haemorrhages or varying size within lobar, cortical, or subcortical regions. Case one demonstrated an evolving sub-acute intra parenchymal macrohaemorrhage within the right temporal lobe but multiple factors could have contributed to his depression. The personality changes in case two may be associated with the CAA. There was executive dysfunction and exacerbation of premorbid poor impulse control was a prominent feature in her. Case three demonstrated intermittent confusion, executive dysfunction and loss of memory. Multiple etiological factors are possible in this case and CAA may be an additional factor contributed to her presentation. Case four demonstrated mild cognitive impairment and performance anxiety. CAA could be a factor contributed to her presentation. Identification of CAA was important when considering treatment methods including medications.

Psychiatric presentations are uncommon in CAA. These four cases show the importance of investigating for CAA in psychiatry settings. Psychiatrists need to be aware of CAA, particularly in the older population. In our series, two cases had depression, but it is difficult to ascribe causality, due to multiple comorbidities in these cases. The spectrum of clinical symptomatology is mainly neurological as well as cognitive decline.[11] Due to CAA being a chronic progressive illness of the central nervous system, the development of gradual psychiatric symptoms as the disease progresses is conceivable, especially in the first stages of CAA, which do not show typical, more overt clinical signs of intra cerebral bleeding or other neurological symptoms such as epileptic seizures. In case two, the patient developed organic personality change and/or exacerbation of pre-morbid personality traits in around four years. There are no attributable reasons for her personality change other than CAA. The possibility of personality change due to CAA is mentioned in literature but not substantiated with studies.[12] There was a case report of hereditary form CAA with personality change.[1] Our case is a sporadic one. Taking into account that dementia and neurodegeneration are frequently associated with behavioural problems and/or personality change[13-14] it seems plausible that CAA may also cause these clinical syndromes, although this connection has not yet been studied in a systematic way.

Our study also highlights the importance of MRI scanning in psychogeriatric population to identify cases with CAA. A caveat regarding psychiatric presentation is that in patients with suspected CAA, MRI positivity might be incidental, given that the incidence of asymptomatic CAA at autopsy in healthy aged subjects is up to 50%.[15]

Table 1.Psychiatric presentations and neuropsychological findings

Case	Neuropsychiatric presentation	Neuropsychological findings	Neuropsychological test
Case 1	Cognitive impairment Focal temporal lob seizures Depression	Poor concentration	ACE III[1]
Case 2	Depression Organic personality change	Poor cognitive flexibility Decreased processing speed Impaired free recall Impaired executive function Accentuation of poor impulse control	ACE III[1] DKEFS[2] Colour word interference test; tower, twenty questions, trail making WAIS[3] IV
Case 3	Delirium Cognitive impairment	Apathy Impaired memory Impaired executive function	ACE III Qualitative observation
Case 4	Cognitive impairment Anxiety	Performance anxiety	ACE III Qualitative observation

1 Addenbrooke's cognitive examination
2 Dells Kaplan Executive function system colour word interference test
3 Wechsler's adult intelligence scale

Neuropsychological manifestations (Table 1) in our series include cognitive impairment, organic personality change, depression, anxiety, focal temporal lobe seizure and delirium. Cognitive impairment is a well described manifestation in CAA[8-9] Three of the four cases presented here also showed cognitive impairment. Other neuropsychological issues demonstrated in these cases include accentuation of poor impulse control, impaired concentration, poor cognitive flexibility, reduced processing speed, impaired free recall, reduced executive function and apathy. All these disturbances were described in previous studies,[5,7,13] though there are no reports of organic personality change in sporadic cases or accentuation of poor impulse control. Dementia in Alzheimer's disease was considered as a differential diagnosis, but none of these cases met the criteria.

Neuropsychiatric presentations of CAA varies and various overlaps with Alzheimer's dementia and other age related pathologies exist regarding the aetiology of cognitive functional disorders, which impede unambiguous identifications of an aetiological participation of CAA, studies suggest that CAA may very well be a cause of cognitive impairments.[16,17] It seems that mainly perceptual speed and episodic memory are cognitive domains typically impaired by CAA, even taking into consideration the influences of Alzheimer's dementia and other potential covariates.[6] In Case 2 we noted decreased processing speed and impaired free recall and Case 3 showed impaired memory which goes well with available evidence. One of our cases showed organic personality change and depression. These may be brought by these neuropsychological processes impairment[5]. Otherwise, a pathognomonic clinical picture of CAA does not exist. Depression, organic personality change and behavioural problems are plausible clinical manifestations of CAA that may accompany typical neurological presentations.

Conclusion

The clinical spectrum of CAA continues to grow. Despite remarkable recent interest, CAA remains under-recognised by neurologists and stroke physicians.[5] Awareness needs to be created among psychiatrists to recognise cerebral amyloid angiopathy as a possible contributor of psychiatric presentations. More studies and insight are needed in demonstrating psychopathology, psychiatric manifestations and its relation to CAA.

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