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Case Report

Severe Neuropsychiatric Symptoms in Multiple Cerebral Microbleeds due to Probable Cerebral Amyloid Angiopathy: A Case Study

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Abstract

Multiple cerebral microhemorrhages are a common feature of cerebral amyloid angiopathy (CAA), a cerebrovascular disorder contributing to cognitive impairment. While CAA-related cognitive and functional deterioration has been well-established within the literature, emerging work suggests that neuropsychiatric symptoms (NPS), such as depression, behavioural issues, and personality changes, are clinical manifestations of the disorder. Recent seminal work has revealed that patients with probable CAA were shown to experience various NPS, especially depression and emotional dysregulation, at a greater frequency and severity than healthy controls. Additionally, a significant association has been demonstrated between severe psychotic symptoms and advanced CAA in autopsied individuals with Alzheimer's disease. In this report, we present a case of probable CAA that highlights severe NPS within the disorder. A 72-year-old male was admitted into a local hospital to stabilize behavioural and psychological symptoms after revealing suicidal ideation to a former partner due to the state of his financial affairs. Past medical and psychiatric history revealed a three-year history of cognitive decline, long-standing personality changes, and multiple suicide attempts, with comorbidities of probable CAA, depression, and alcohol use disorder. He underwent neuropsychological testing, where he performed poorly across several cognitive domains assessed, demonstrating markedly poor executive function, processing speed, and memory. Neuroimaging revealed severe chronic microangiopathy, mild-to-moderate generalized volume loss, and multiple cerebral microhemorrhages. While the current case aligns with the reviewed literature findings, the observed suicidal behaviour, and vulnerability to financial exploitation suggest careful reconsideration of the clinical manifestations of CAA.

Keywords: CAA; Case Report; Cerebral Amyloid Angiopathy; Microhemorrhages; Neuropsychiatric Symptoms

Introduction

Cerebral microbleeds or microhaemorrhages are small, chronic brain haemorrhages that are likely caused by structural abnormalities in the small blood vessels. Multiple cerebral microbleeds are a neuroimaging marker for probable cerebral amyloid angiopathy (CAA). CAA is a cerebrovascular disorder that primarily affects older persons and is caused by the accumulation of amyloid-β (Aβ) peptide deposits within small to medium-sized arteries [1]. Aside from multiple microhemorrhages, clinical symptomatology of CAA includes lobar intracerebral haemorrhages, demyelination, neurological symptoms (e.g., headaches, focal deficits), cognitive impairment, and dementia [2, 3]. It is challenging to identify specific patterns of CAA due to its heterogeneity in presentation among individuals, and clinical similarity to other common comorbidities, such as Alzheimer's disease (AD), and other age-related pathologies (e.g., hypertension) [3]. Probable or possible cases can be evaluated based on clinical symptoms and neuroimaging results; however, a definite diagnosis of CAA can only be affirmed through post-mortem histopathological examination [3]. Hence, developing a better understanding of the clinical manifestations of CAA could facilitate early identification and treatment of the disorder. Studies have revealed a significant relationship between CAA, dementia, and cognitive impairment, showing that CAA contributes to their development and clinical presentation [2-4]. The prevalence of CAA in older persons with any form of clinically diagnosed dementia is estimated at 50-60%, signifying higher prevalence than in those without dementia (20-40%) [3]. While the relationship between CAA and cognitive impairment has been relatively well established within the current literature [2-4], minimal work has investigated the neuropsychiatric symptom (NPS) profile of CAA. Three case reports have reported depression, irritability, aggression, and personality changes in patients with CAA [5-7]. Hallucinations and delusions were also associated with advanced CAA in patients with AD or Lewy Body disease that was diagnosed with autopsy [8]. More recent work studying NPS in CAA reported that common NPS in patients with CAA are depression, irritability, agitation, apathy, and anxiety [9]. While the NPS profile in CAA has received some attention, we were unable to find any literature on the incidence of severe and/or life-threatening NPS with the condition and the vulnerability to substantial financial abuse. Here, we report a case of cerebral microbleeds with probable CAA wherein we highlight progressive development of NPS predating cognitive changes and eventually, resulting in hospital admission.

Case Description

A 72-year-old man was admitted to a local hospital after revealing an intent to end his life using sedatives and alcohol, where he was then transferred to a geriatric dementia unit to stabilize his behavioural and psychological symptoms. The patient had completed 16 years of education, earning a law degree, after which he worked as a lawyer and a university lecturer. He was twice married. He and his second former partner legally separated in 2018, after which she moved to another country. Despite their separation, she remained his power of attorney for personal care and property. According to her, the patient was a bright, charming, and committed philanthropist for many years. She described personality changes that started in 2003, worsened in 2005-2007, and were followed by cognitive changes that began in 2018. Personality changes included irritability, impulsivity, low frustration tolerance, and socially inappropriate behaviour (e.g., cursing at strangers, forced removal from event venues due to disinhibition and excess alcohol consumption, and racist remarks). Severe behaviours included two past suicide attempts; one in his early 30s where he overdosed on pills requiring stomach pumping, and another in his mid-60s (2015) through self-inflicted stabbing requiring laparotomy. Cognitive changes included a three-year history of difficulty with organization, task switching, judgment, and short-term memory. The patient's past medical history indicated that he had long-standing alcohol use from 2004 until his most recent hospitalization in 2021, which was predated by the personality changes described above. He had an extensive history of falls also likely related to alcohol intoxication. Past medical history revealed that he suffered a left cerebellar stroke in his thirties, and was involved in a car accident in 2007 that resulted in loss of consciousness and post-traumatic amnesia. Family history revealed his mother had AD.

The patient's ex-partner reported that in 2018 he stopped opening bank statements, paying membership fees, and had conflicts with his landlord concerning rental fees. In early 2019, he was no longer able to maintain employment, as he was underperforming and not able to manage his activities of daily living (ADL; e.g., mismatched clothing, feces on clothing). His ex-partner returned to the country in August 2021 due to concerns expressed by her stepchildren about the patient not returning their calls. They were also concerned about his new partner. The patient had become romantically involved with a new female partner in February 2020, who allegedly scammed him of $700k according to his children and ex-partner, and $100k according to himself; there is an ongoing investigation. Upon her visit to the patient's rental unit, the ex-partner noticed missed bill payments resulting in loss of services, progressively unkempt personal hygiene, and poor nutritional self-care (e.g., no food in the fridge). The apartment was in squalor conditions (e.g., pet urine and feces in the apartment). There were neglected pets, unfilled medications, tattered clothes, and the threat of eviction due to months of unpaid rent. The patient had not paid his hydro bills since 2020,

and his internet/cable/phone services had been disconnected due to outstanding payments. He was repetitive in conversation, disoriented, and was unable to recall the year or his age accurately. He had difficulty recalling remote and new episodic information (e.g., location/memories of his late mother's retirement home, his food preferences, past passion for cooking, recent conversations) and presented as polite but apathetic. She noticed him requiring assistance with instrumental ADLs (iADLs), specifically meal preparation, transportation, housework, laundry, medication management, and financial management. With respect to basic ADLs, he required cueing for bathing, and dressing, and was incontinent for urine and feces; however, he was able to ambulate independently and eat without assistance. On self-report, the patient denied any concerns related to his cognition, with the exception of long-standing trouble remembering names. He denied any changes or difficulties in remembering information/appointments/events, word-finding, finding his way, following multi-step instructions, managing multiple tasks simultaneously, or focusing during a conversation. He described his memory as above average when compared to his same-aged peers. Regarding iADLs, he stated he was fully independent (meal preparation, cooking, and managing finances and medications). He endorsed consuming three alcoholic beverages per day for the past 10 years and stated that his alcohol consumption never interfered with his work or relationships. He denied any difficulty managing finances and denied any romantic relationships after separating from his ex-partner. Information surrounding ADLs, alcohol use, and medical history (denied car accidents, past stroke, surgeries) were inconsistent with the informant and clinical reports reviewed. Regarding his mood, he stated that he had not felt depressed or anxious over the past two weeks.

On neuropsychological testing, the patient passed all embedded validity measures and possessed adequate vision, hearing, oral comprehension, and verbal expression. His estimated level of intelligence was in the superior range compared to same-aged peers, consistent with his educational and occupational achievements. However, he performed below expectations across all cognitive domains assessed (see Table 1). Results from the Montreal Cognitive Assessment (MoCA) [10] indicated mild impairment. Areas of relative strength included: a) average attention/working memory; b) average to low average language (phonemic fluency, semantic fluency, confrontation naming); and c) high average to low average visual object and space perception. His cognitive processing speed was variable, ranging from low average to impaired. Verbal memory and vasoconstriction/visual memory were impaired. Aspects of executive function, such as task switching, response inhibition, and self-monitoring, were also impaired. Memory encoding over repeated trials was impaired, whereas retention ranged from low average to impaired. Verbal memory was particularly susceptible to retroactive interference, and difficulties with source monitoring were evident. Based on the Mini-Mental State Exam (MMSE) [11], he was oriented to place and person, but not to time (e.g., date, year, day). Last, he did not self-report elevated symptoms of depression or anxiety. Overall, vasoconstriction, memory, cognitive processing speed, and executive function were relative weaknesses. An MRI done during the latest hospital admission revealed moderate to severe chronic microangiopathy, mild to moderate generalized volume loss, and multiple microhemorrhages (e.g., subcortical white matter, right basal ganglia, right thalamus, right cerebellum). In the context of available history and observed impairment in several cognitive domains, evidence supports that the patient has a major neurocognitive disorder. However, the etiology is uncertain and likely multifactorial. The pattern of progressive, gradual decline over three years, observed test results, and positive family history may reflect an AD ethology. His multiple vascular risk factors and MRI finding may suggest probable CAA. Note, CAA is present in approximately 80% of individuals with diagnosed AD [12]. However, a confirmatory diagnosis of CAA can only be done through histopathological studies after obtaining autopsy specimen of the brain. Other factors that may have contributed to the behavioural presentation include long-standing history of heavy alcohol use and its neurotoxic effect on the brain which may lead to personality changes over time, history of past traumatic brain injury with loss of consciousness and post-traumatic amnesia, and a possible past hypoxic/anoxic brain injury secondary to a pill overdose in his 30s.

Discussion

Previous research has reported that patients with CAA have deficits in specific domains of cognition and preservation in others [2]. Community-based autopsy research has found that both moderate and severe definite CAA (assessed via amyloid deposition in several neocortical regions) is associated with poorer perceptual speed [2,13], episodic memory [2,13] and global cognition [13], regardless of AD diagnosis. Further, clinic-based research shows that non-dementia patients with probable CAA (assessed via the Boston Criteria [14] frequently demonstrate executive dysfunction and decreased processing speed [15]. However, visuospatial skills and working memory appear intact [2], while support for impaired semantic memory is mixed [2,13]. These effects occur after correcting for comorbid neuropathologies [2,13], suggesting that CAA contributes independently to cognitive impairment. Thus far, CAA diagnosis has been based largely on cognitive and functional deterioration; however, studies have shown that behaviour is also an important component of the condition. One study proposed that NPS, such as depression, behavioural issues, and personality change, are plausible [3]. A more recent study reported that patients with probable CAA [9] (assessed via the Boston Criteria) [14] were significantly more likely to experience NPS and at a greater severity than healthy controls. They found

that depression was the most frequent NPS in CAA (49%), followed by irritability (37%), agitation/aggression (37%), apathy (35%), and anxiety (33%) [9]. They further reported that similar to patients after a stroke, the most prominent NPS in CAA were reported to be apathy and depression; agitation and aggression were less common in CAA compared to patients with mild cognitive impairment (MCI) or AD. Another study indicated a significant association between advanced CAA and severe psychotic symptoms (i.e., hallucinations and delusions) in autopsied individuals with AD, wherein CAA was more prominent in those with psychosis (85%) than those without psychosis (41%) [8]. In this report, our patient presented with executive dysfunction, reduced processing speed, memory impairments, behavioural issues, and personality changes. Further, MRI results revealed multiple microhemorrhages in subcortical regions, suggesting probable CAA, as defined by the Boston Criteria. This case illustrates that patients with probable CAA and MCI can exhibit severe NPS and personality changes early on and during the course of the illness. The severity of the NPS presented within the current case multiple suicide attempts/ideation, impulsive behaviours, and vulnerability to financial abuse suggest reconsideration of the clinical manifestations of CAA (Figure 1).

Test	Description
General Cognition MoCA [10] [a]	Mildly impaired
MMSE Orientation [11] [b]	Disoriented to time; Oriented to place
TOPF [16] (estimated pre-illness intelligence)	Superior range
Memory[b]	
California Verbal Learning Test [17]	
Total Recall Correct	Borderline impaired
Short Delay Free Recall Correct	Impaired
Long Delay Free Recall Correct	Borderline impaired to impaired
Recognition (Total Hits)	Low average to Borderline impaired
Recall Errors (Intrusions)	Impaired
Hopkins Verbal Learning Test -Revised [18]	
Trial 1 Correct	Average
Trial 2 Correct	Low average to borderline impaired
Trial 3 Correct	Borderline impaired to impaired
Learning over Trial 1 – Trial 3	Impaired
Immediate Recall	Borderline Impaired
Delayed Recall	Low average to Borderline impaired
Visual Memory (Rey Complex Figure) [19]	
30 min delayed recall	Impaired
Visuospatial Ability[c]	
Visual Object and Space Perception Battery [20]	
Screening	Within Normal Limits
Incomplete Letters	Low average
Number Location	Low average
Hooper Visual Orientation Test [21]	Average

Judgment of Line Orientation [22]	High average
Working Memory[c]	
Wechsler Adult Intelligence Scale-III Longest Digit Span Backward [23]	Average
Executive Function[b]	
Delis-Kaplan Executive Function System [24]	
Verbal Fluency - Letter Fluency: Total Correct	Average
Category Fluency	Low average
Category Switching	Impaired
Tower Test - Total Achievement Score	Average
Total Rule Violations	Impaired
Trail Making Test B [25] (Time to complete)	Impaired
Language[b]	
Boston Naming Test (Spontaneous Correct Responses)	Average
Processing Speed[b]	
Symbol Digits Modalities Test [26] – Written	Low average
Oral	Borderline impaired
Trail Making Test A (Time) [27]	Impaired
Patient Health Questionnaire -9 [28]	Normal
Generalized Anxiety Disorder -7 [29]	None

Table 1: Performance on Neuropsychological Assessments.

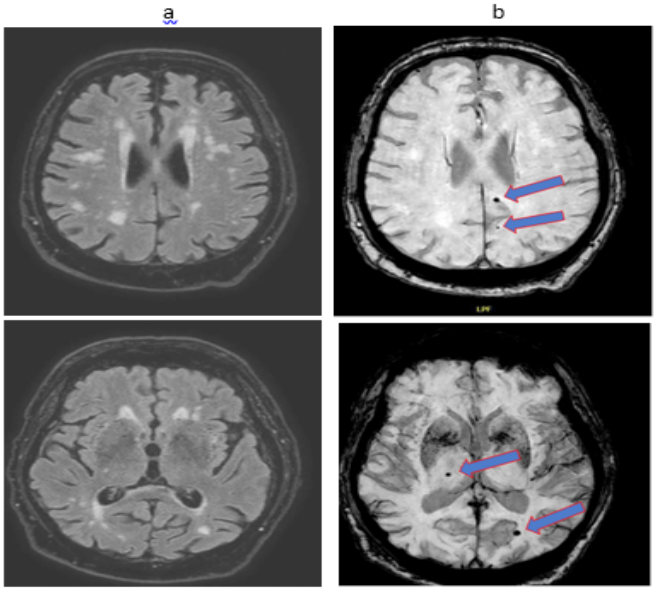

Figure 1: Magnetic resonance imaging (MRI): a) FLAIR sequences showing white matter hyper intensities b) Susceptibility Weighted Image (SWI) sequences demonstrating microbleeds (around the calcarine fissure on the right side of the image (left side of the patient). The image was read by radiology as "moderate to severe chronic microangiopathy, mild to moderate generalized volume loss, and multiple microhemorrhages".

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