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Case Report

Atypical presentation of cerebral amyloid angiopathy in a 42-year-old man with recurrent lobar hemorrhages and neuropsychiatric symptoms

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ABSTRACT

Background: Cerebral amyloid angiopathy (CAA) is a small- and medium-vessel cerebrovascular disease characterized by β-amyloid accumulation within cortical and leptomeningeal arterial walls. Although it most commonly manifests in older individuals as spontaneous lobar hemorrhage, uncommon cases have been reported in younger patients, especially those with risk factors such as previous head trauma, genetic predisposition, or prior exposure to cadaveric dura.

Case Description: We describe a diagnostically challenging case of suspected CAA in a 42-year-old man with a history of multiple traumatic brain injuries, prior neurosurgical interventions, neuropsychiatric symptoms, and late-onset seizures. Importantly, during treatment for head trauma in early adulthood, he received a cadaveric dura transplant. Over subsequent years, he developed recurrent lobar hemorrhages and progressive cognitive and behavioral changes, raising concern for an atypical, possibly iatrogenic, form of CAA.

Conclusion: This case highlights the need to consider CAA – even in younger patients – when recurrent lobar hemorrhages and neuropsychiatric symptoms occur in the context of relevant risk factors such as previous head trauma or cadaveric dura exposure. We believe that such exposure may underlie this patient's gradual but persistent neurological and cognitive decline.

Keywords: Atypical presentation, Iatrogenic cerebral amyloid angiopathy, Neuropsychiatric symptoms

INTRODUCTION

Cerebral amyloid angiopathy (CAA) is a cerebrovascular disorder caused by β-amyloid deposition in the walls of small-to-medium-sized cortical and leptomeningeal arteries.[2] It typically presents with spontaneous lobar hemorrhages in the elderly but can rarely occur in younger individuals, especially those with risk factors such as head trauma, genetic predisposition, or exposure to cadaveric dura.[8]

We report a case of a 42-year-old man with recurrent lobar hemorrhages and neuropsychiatric symptoms suggestive of atypical, possibly iatrogenic CAA.

CASE REPORT

A 42-year-old right-handed male, previously employed as a construction inspector, presented with a complex neurological history. He had completed secondary education and enrolled in university-level mathematics but did not complete his degree, despite reportedly achieving above-average academic performance. Before symptom onset, he was fully independent in daily activities.

His medical history is notable for multiple head traumas. At the age of three, he sustained a right sided temporal bone fracture due to a fall, requiring surgical intervention, including osteoplastic trepanation, evacuation of epidural hematoma caused by rupture of the middle meningeal artery, and the implantation of cadaveric dura mater (Lyodura®).

In 2006, he suffered a traumatic brain injury again and was found unconscious at the scene. Head computed tomography (CT) revealed left frontal intracerebral hemorrhage (ICH) and right-sided subdural hematoma, both of which were managed conservatively. Following recovery, he experienced persistent headaches and difficulties with concentration. Seizure disorder was suspected but never confirmed objectively.

In 2007, he was hospitalized due to a worsening headache, 2 weeks after another blunt head trauma event. Bilateral frontal ICH and early cerebellar atrophy were identified on head CT. Due to positive meningeal signs without other neurological deficits during hospitalization, subarachnoid hemorrhage (SAH) was suspected, but not visible on previously mentioned head CT scan. He was transferred to a tertiary center where a suspected ruptured aneurysm as the possible cause of ICH was excluded by digital subtraction angiography. Neuropsychological evaluation revealed mild, mixed-pattern cognitive impairment with associated depressive features. In 2019 and 2022, he sustained additional traumatic ICHs. Both were managed conservatively.

In July 2024, he developed a pulsating frontal headache accompanied by transient visual disturbances described as "blinking lights," lasting 1 week, followed by photophobia and mild speech difficulties. Blood pressure on admission was 138/80 mmHg. Neurological examination was unremarkable, and electroencephalography (EEG) showed no abnormalities. The headache lasted for a week and was managed effectively with naproxen and sumatriptan.

Head magnetic resonance imaging (MRI) in September 2024 showed a subacute right temporal ICH, two smaller older ICHs in the right temporobasal [Figure 1] and occipital lobe, and microhemorrhages mainly in the temporal and frontal lobes with a right-sided preponderance [Figure 2]. CT angiography did not reveal any vascular pathology.

In October 2024, he presented to the emergency neurology department with a 1-day history of headache and visual disturbances described as "dancing letters." Blood pressure at admission was 148/92 mmHg. Neurological examination revealed mild left upper limb paresis and positive plantar response on the left. An urgent head CT identified a new ICH in the right temporoparietal and temporopolar regions. He was hospitalized for further evaluation. Due to suspected CAA, a lumbar puncture was performed 14 days after the onset of headache. Cerebrospinal fluid (CSF) analysis showed elevated protein (0.84 g/L), pleocytosis (159 × 10^6/L, lymphocytic), and high tau (1534 ng/L), and neurofilament (21,360 ng/L) levels, amyloid-$ß_{42}$ level was decreased (353 ng/L). Rheumatologic and thrombophilia screening tests were negative, as were serological tests for hepatitis B surface antigen, anti-hepatitis C virus, HIV, and *Treponema pallidum*. CSF analysis was negative for oligoclonal bands. Both serum and CSF serology for *Borrelia burgdorferi* were negative. Differential diagnosis included CAA, possibly inflammatory, or aseptic meningitis due to hemorrhage. Methylprednisolone therapy (64 mg daily) was initiated and

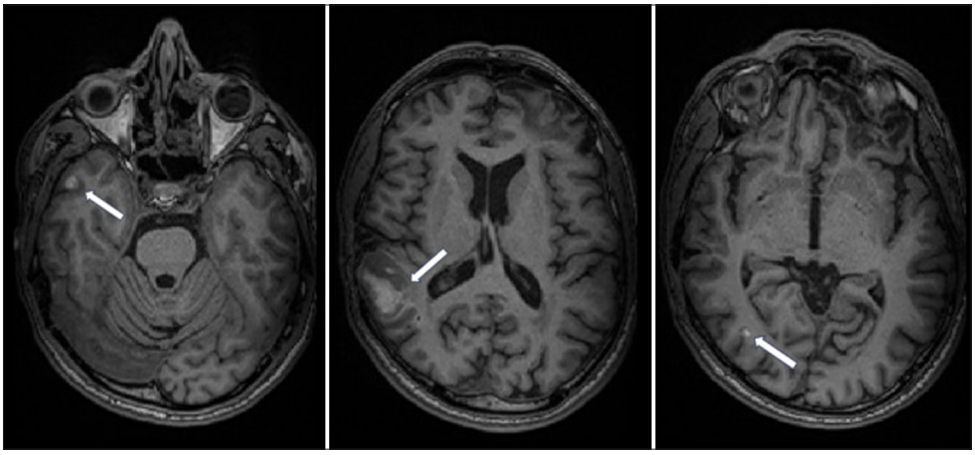

Figure 1: Axial T1MPRAGE from September 2024 demonstrating multiple subacute intracerebral hemorrhages (white arrows). T1-MPRAGE: T1-weighted magnetization-prepared rapid gradient-echo sequence

he was discharged on the 15th day of hospitalization without any residual neurological deficits.

During follow-up, he experienced cognitive symptoms such as fatigue, concentration difficulties, and irritability. Psychiatric evaluation confirmed insomnia, psychomotor slowing, hypersensitivity to sound, and anxiety. Sertraline and trazodone were recommended but he declined the therapy.

In March 2025, 8 days after discontinuing methylprednisolone, he suffered two epileptic seizures, the second being generalized tonic-clonic. Head CT showed no acute changes, but follow-up imaging 2 days later revealed a small right frontal SAH in the right frontal region [Figure 3]. Lacosamide was initiated at a dose of 100 mg twice daily. EEG revealed interhemispheric asymmetry and right temporal slowing.

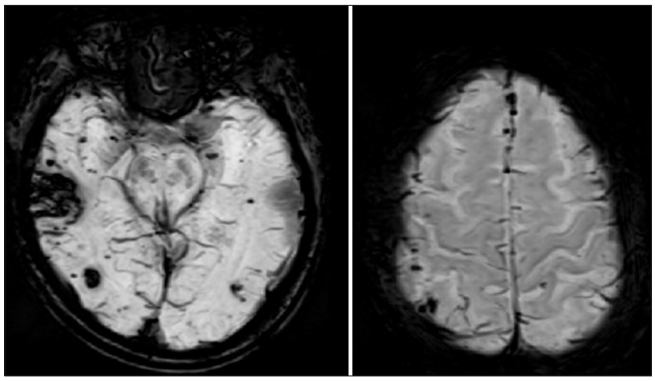

Figure 2: Susceptibility-weighted imaging magnetic resonance imaging from September 2024 demonstrating multiple microhemorrhages in the temporal and occipital lobes.

Follow-up brain MRI in March 2025 demonstrated new superficial cortical siderosis in the right hemisphere and in the left frontal lobe [Figure 4]. Multiple bilateral supratentorial lobar microhemorrhages were also visible.

In April 2025, after switching to carbamazepine due to paresthesia, he suffered generalized seizure during routine EEG. Post-ictal EEG showed frontal sharp waves and a diffuse theta-delta slowing. A repeated CSF analysis showed elevated protein with markedly increased neurofilament levels, with decreased amyloid-β_{42} and reduced amyloid-$\beta_{42/40}$ ratio.

The findings of CSF examination and head imaging were consistent with probable CAA.

In June 2025, the patient was re-evaluated by a clinical psychologist due to ongoing subjective complaints of memory and concentration difficulties, as well as fatigue during novel activities. He reported that lacosamide exacerbated his nervousness, while treatment with an antidepressant alleviated symptoms of anxiety. A comprehensive battery of neuropsychological tests revealed attention deficits and impaired executive functioning. Given his reduced ability to cope with stress, psychiatric treatment was recommended.

In July 2025, a follow-up brain MRI was performed showing radiological deterioration. New, small subacute hemorrhages in the right cerebral hemisphere were revealed, specifically in the frontal region, the precentral gyrus (9 × 6 mm), and the

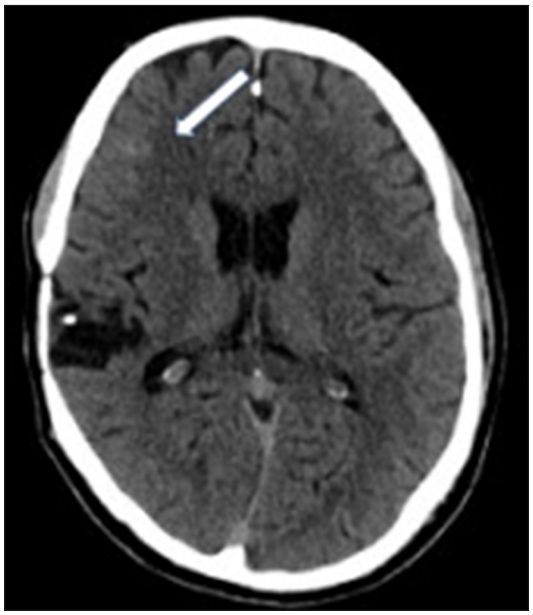

Figure 3: Non-contrast head computed tomography from March 2025 shows a right frontal subarachnoid hemorrhage (white arrow).

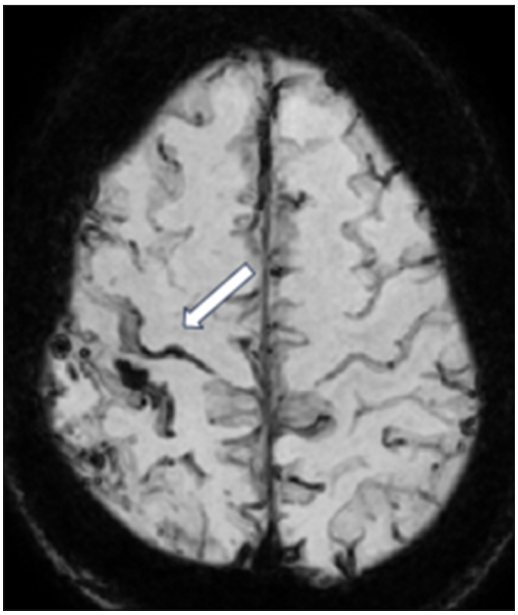

Figure 4: Susceptibility-weighted imaging magnetic resonance imaging from March 2025 reveals superficial cortical siderosis (white arrow).

occipital region (7 × 5 mm), as well as numerous hemosiderin deposits. Clinically, the patient remained stable.

The patient is still being followed up and evaluated and the amyloid positron emission tomography is planned.

DISCUSSION

This case illustrates a diagnostically complex and rare manifestation of CAA in a middle-aged patient, representing the fourth such case identified at our institution. The patient has early onset CAA and there is a history of prior exposure to cadaveric dura. While the majority of CAA cases present in older adults, early-onset CAA has been linked to prior neurosurgical exposure to cadaveric dura mater, which can transmit with prion-like amyloid-β seeding.[6,8] In this patient, an early craniotomy with Lyodura® implantation may have contributed to disease pathogenesis. At the time of his neurosurgical treatment in early childhood, cadaveric dura substitutes were frequently implanted, and no screening of the implants was conducted, as is done nowadays. Additional reported risk factors for amyloid-β seeding include contaminated neurosurgical instruments, cadaveric human growth hormone, and, more recently, blood transfusions in early childhood.[4,7,9] In our patient, a history of repeated head trauma may also be a contributing factor to his subtle cognitive decline.

Disease onset in iatrogenic CAA typically occurs two to three decades after exposure to amyloid-β seeds.[7] The latency observed in our case follows this expected pattern, with the first manifestation likely emerging three decades after Lyodura® implantation. Clinical suspicion, however, was only established a decade later, after recurrent ICHs were initially likely misattributed to trauma and possible seizures. Notably, this case demonstrates one of the longest reported disease courses in iatrogenic CAA.

Transient focal neurological episodes were the initial presentation in the most recent ICH, manifesting as visual disturbances, and can be a typical first manifestation in CAA. Although seizures are not classically associated with early CAA, they are increasingly recognized in advanced disease with extensive hemorrhagic and cortical involvement, particularly in iatrogenic forms.[1]

This case also emphasizes the diagnostic value of CSF biomarkers and advanced imaging (MRI), especially when vascular studies are unrevealing. The presence of elevated tau and neurofilament light chain, along with a reduced amyloid-$\beta_{42}/_{40}$ ratio, strengthens the diagnosis in absence of definitive histopathology.

The combination of recurrent lobar hemorrhages, cortical superficial siderosis, and cognitive and neuropsychiatric symptoms fulfills criteria for probable CAA under the modified Boston criteria version 2.0.[3] However, in iatrogenic cases, alternative diagnostic frameworks such as those proposed by Banerjee *et al*. may be more appropriate, as the disease typically occurs in younger patients.[1] The diagnostic criteria include age at onset, history of potential exposure, clinical and radiological features consistent with CAA, evidence of amyloid-β accumulation within the central nervous system, and exclusion of genetic causes of amyloid-β-related central nervous system disease.[1] Our patient fulfilled all criteria except the last, as genetic testing was not performed.

From the future perspective, the incidence of iatrogenic CAA is expected to decline given the discontinuation of cadaveric dura mater such as Lyodura® and improvements in sterilization practices. Nonetheless, uncertainty remains regarding other potential transmission routes, possibly including blood transfusion and organ transplantation such as corneal grafts.[5]

Data availability statement

All the data generated or analyzed during the study are included in this article. Further inquiries can be directed to the corresponding author.

CONCLUSION

CAA should be considered even in younger patients presenting with recurrent lobar hemorrhages, unexplained cognitive decline, and seizures – especially when there is a history of neurosurgical intervention with cadaveric materials or repeated trauma. A multidisciplinary approach with neuroimaging, CSF biomarker analysis, and close neuropsychiatric monitoring is essential for diagnosis and management.

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