Cerebral Amyloid Angiopathy presenting as Cognitive Decline

Krishnan Balagopal[1], **Jeyaseelan Nadarajah**[2], **Jaisurya Jaisukhalal**[3], **Mishal Raees Iqubal**[4], **Karthika Ajith**[5]

[1,3,4,5]Department of Neurology, MOSC Medical college , Kolenchery; [2]Department of Radiology, MOSC Medical college, Kolenchery

Date of submission: 23th October 2022 Date of acceptance: 2nd March 2023 Date of publication: 30th March 2023

Abstract

Cerebral amyloid angiopathy (CAA) is a disorder seen as age advances, characterized by the accumulation of amyloid within the leptomeninges and cerebral blood vessels. Lobar hemorrhages are the most common clinical manifestation seen. Cognitive decline due to repeated cerebral microhemorrhages in one of the rare presentations seen mainly in the elderly. We present here a case of a seventy year old female patient who presented with a one year history of progressive cognitive impairment. She was detected to have CAA on imaging with both cortical microbleeds and extensive superficial siderosis. She was started on cholinesterase inhibitors and antipsychotics for her symptoms. Antiplatelet agents were avoided due to increased risk of hemorrhage. This report highlights the importance of CAA as a cause of cognitive decline in elderly patients and also its therapeutic implications.

Key words: Cerebral Amyloid Angiopathy, Cognitive Decline, Superficial Siderosis

Introduction

Cerebral amyloid angiopathy (CAA) is a rare cerebrovascular disorder characterized by the accumulation of amyloid beta-peptide within the leptomeninges and small/medium-sized cerebral blood vessels[1]. The amyloid deposition results in fragile vessels that may present as lobar intracerebral hemorrhages (ICH). It may also present with cognitive impairment, incidental microbleeds, hemosiderosis of the brain parenchyma , Alzheimer disease, or transient neurological symptoms[2]. It can occur sporadically or as part of certain familial syndromes. Cerebral amyloid angiopathy is strongly age-dependent, with the prevalence of moderate to severe CAA increasing with age. When symptomatic, the most common clinical manifestation seen is spontaneous lobar hemorrhage[3]. The location and the size of the hemorrhage determines the clinical presentation. Cognitive decline is an uncommon manifestation and is seen mainly in elderly. We present here a case of a 70 year old patient with progressive cognitive decline who was detected to have CAA on imaging.

Case Report

This 70 year old female presented to the neurology outpatient department with a one year history of progressive cognitive decline. This was initially in the form of memory disturbances like forgetting where she has placed objects and names of friends and relatives. This was followed by difficulty in doing her activities of daily living, handling money matters and subsequent behavioural changes in the form of becoming withdrawn from all her pursuits and losing interest in activities like reading her newspaper, and watching television. Over the last one month, there was worsening of all symptoms along with significant disorientation to place and time and disturbed sleep. There was no history suggestive of apraxias or alien limb phenomena. There was no history of gait disturbances, difficulty in walking or tremors of the limbs. There was no headache, fever or significant weight loss. There was no history of head injury or significant drug intake.

Access this article online

Website: https://www.nepjol.info/index.php/NJN

DOI: https://doi.org/10.3126/njn.v20i1.49043

HOW TO CITE

Krishnan Balagopal, Jeyaseelan Nadarajah, Jaisukhalal J, Mishal Raees Iqubal, Karthika Ajith. Cerebral Amyloid Angiopathy presenting as Cognitive Decline. NJNS. 2023;20(1):80-83.

Address for correspondence:
Krishnan Balagopal
D.M (Neurology) ,Consultant, Department of Neurology
MOSC Medical College, Kolenchery, Kochi
E-mail: krishnan.balagopal@gmail.com
Mobile: 7592809539

ISSN: 1813-1948 (Print), 1813-1956 (Online)

Clinical examination revealed no focal neurological deficits. Mental status examination showed a Mini Mental Status Examination(MMSE) score of 20/30 and a Clinical Dementia Rating Scale score of 2. Formal Mental status examination revealed evidence of frontal executive dysfunction, impairment of immediate and recent memory, poor orientation to place and time and also impaired visuospatial functions. Writing and calculation were also significantly impaired.

Blood investigations for cognitive decline including Vitamin B12 levels ,VDRL(Venereal Disease Research Laboratories) for Syphilis , Thyroid function tests, Human Immunodeficiency Virus(HIV) and anti Thyroid Peroxidase (TPO) antibodies were negative. CSF(Cerebrospinal fluid) analysis was suggested but attenders were not willing for the same. Electroencephalogram(EEG) done showed no abnormalities.

Imaging - Magnetic Resonance Imaging (MRI)Brain – showed multiple cortical-subcortical microhemorrhages in the subcortical frontal and temporal lobes bilaterally. Gyriform dark signal intensity were noted along the frontal and parietal sulci bilaterally suggestive of superficial cortical siderosis(Figure 1). Additionally, mild to moderate small vessel disease in the bilateral cerebral deep white matter with old lacunar infarctions were found (Figure 2).

Diffusion weighted imaging(DWI/ADC) images showed no features of diffusion restriction(Figure 3)

According to the Boston criteria, the patient was diagnosed to have a probable Cerebral Amyloid Angiopathy(CAA).She was started on Donepezil for her cognitive impairment along with Quetiapine for sleep disturbances. Antiplatelet agents were not started due to increased risk of hemorrhage. She is on regular follow up.

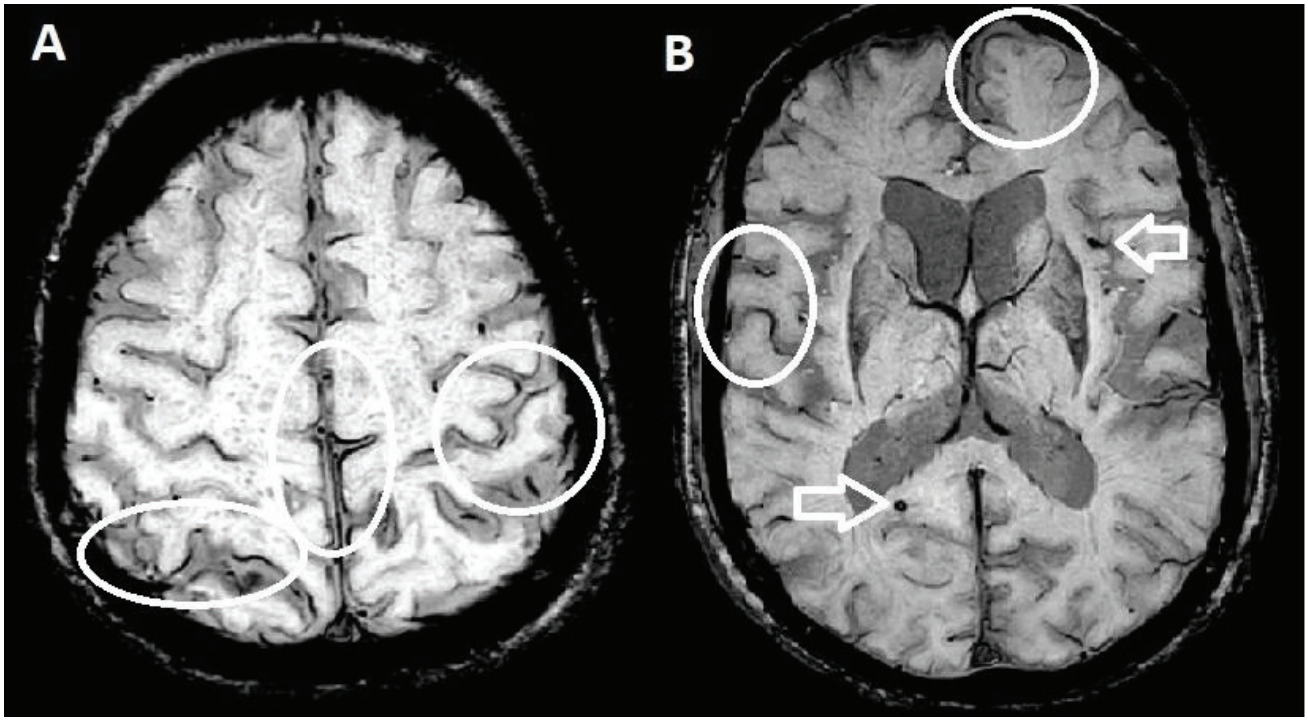

Figure 1: MRI Brain Susceptibility Weighted Imaging(SWI) showing areas of superficial cortical siderosis (A and B) appearing as black lines and small black dots representing cortical microhemorrhages(B)

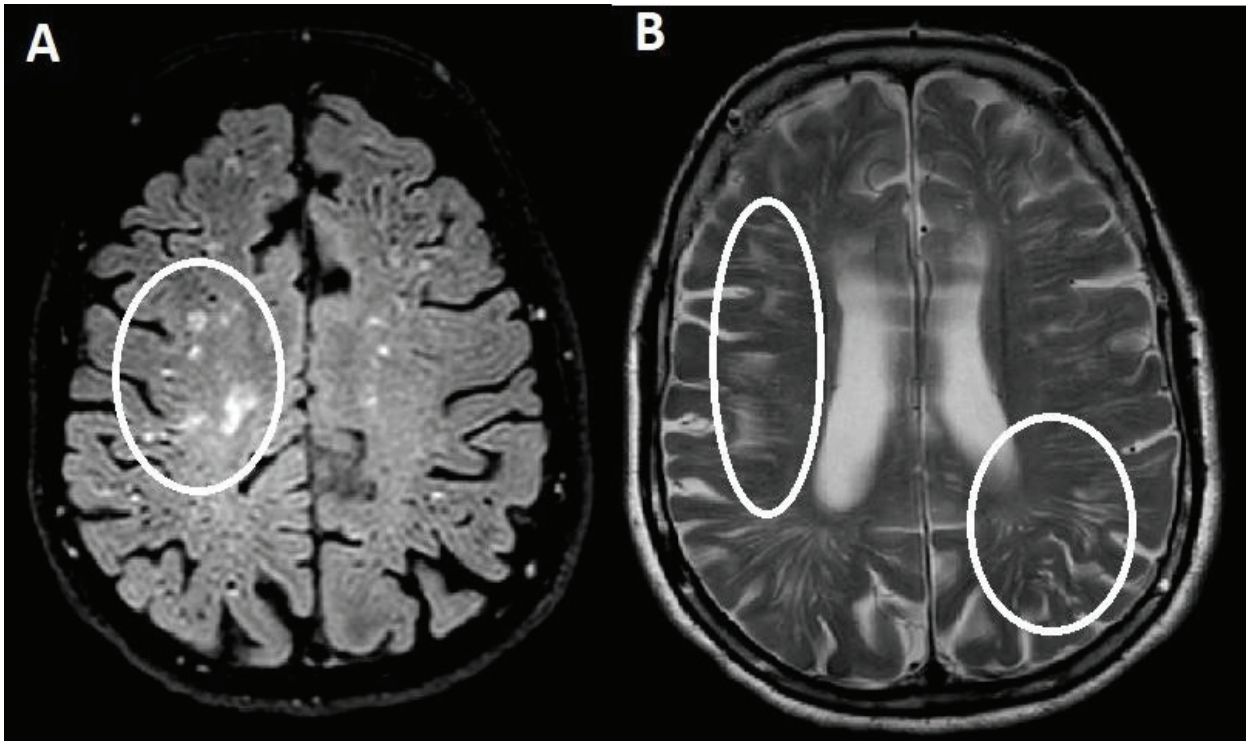

Figure 2: Showing multiple areas of hyperintensity in the subcortical areas on A-FLAIR sequences and B-T2 sequences representing ischaemic changes

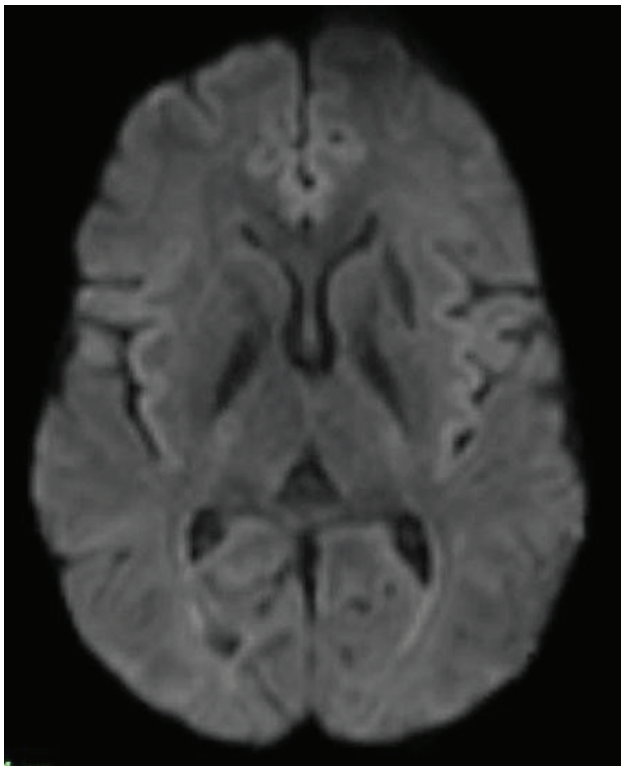

Figure 3: DWI (Diffusion Weighted Imaging) sequence showing no abnormalities

Discussion

Cerebral Amyloid Angiopathy (CAA) is a condition characterized by beta-amyloid peptide deposits within blood vessels of the brain and leptomeninges. Amyloid deposition within the media and adventitia of cerebral arteries lead to smooth muscle cell destruction, vascular wall thickening, vessel fragility and rupture[4]. Lobar microbleeds are the hallmark of CAA and occur more frequently in the temporal and occipital lobes[5]. Progressive cognitive impairment in the elderly is closely associated with CAA.. There are three main patterns of cognitive decline in CAA and they include gradual decline with microhemorrhages, lobar lacunas, microinfarcts, ischemic leukoencephalopathy; step-wise decline with recurrent lobar hemorrhages and rapidly progressive decline with cerebral amyloid angiopathy-related inflammation.

CAA may have a varied presentation with features suggestive of frontotemporal dementia, normal pressure hydrocephalus, and Diffuse Lewy body disease, which are also not usual presenting features.

Imaging findings in acute bleed can vary in size and location, but specific imaging patterns and associated findings are common in these cases. CAA-related lobar hemorrhages most commonly arise in the temporal and occipital lobes[6] . They often extend beyond the brain tissue into the subarachnoid and subdural spaces and sometimes rupture into the ventricles.

Susceptibility-weighted sequence(SWI) brain MRI obtained in patients with an acute lobar hemorrhage may also show chronic cerebral microbleeds (CMBs) along with cortical superficial siderosis . CMBs are typically asymptomatic lesions and are found in the juxtacortical and lobar regions mainly involving the temporal and occipital lobes. Superficial siderosis represents repeated subarachnoid hemorrhages in the chronic phase. It usually reflects severe CAA in the leptomeningeal vessels[7].

The presence of CAA should be suspected clinically in all patients of age 50 and above with or without a clinical manifestation of CAA who have acute or chronic hemorrhagic findings along with characteristic white matter features on brain MRI in the absence of an obvious alternative cause[8].

Because of the risk of spontaneous lobar hemorrhage in patients with CAA, there are risks and benefits of using of anticoagulant and antiplatelet agents as per the guidelines from the American Heart Association[9].

Increased risk of intracranial hemorrhage is associated with features like any past history of intracranial hemorrhage, presence of superficial siderosis on imaging and class of agent used with highest risk with warfarin, then the direct oral anticoagulants and finally antiplatelet agents. The benefit of anticoagulants or antiplatelets is determined by the clinical indication and the availability of other treatments.

Conclusion

CAA is a rare but important cause of cognitive decline in older individuals. Early diagnosis is important because of the potential risk of using medications like anti platelet agents and anticoagulation in these patients. Further studies are required to understand the wide spectrum of clinical manifestations in these patients.

References

1. Viswanathan A, Greenberg SM. Cerebral amyloid angiopathy in the elderly. Ann Neurol 2011;70:871-880. doi: 10.1002/ana.22516
2. Charidimou A, Gang Q, Werring DJ. Sporadic cerebral amyloid angiopathy revisited: recent insights into pathophysiology and clinical spectrum. J Neurol Neurosurg Psychiatry. 2012 Feb;83(2):124-37 doi: 10.1136/jnnp-2011-301308
3. Greenberg SM, Eng JA, Ning M, Smith EE, Rosand J. Hemorrhage burden predicts recurrent intracerebral hemorrhage after lobar hemorrhage. Stroke 2004;35:1415-1420 doi: 10.1161/01.STR.0000126807.69758.0e
4. Vinters HV. Cerebral amyloid angiopathy. A critical review. Stroke 1987;18:311-324. doi: 10.1161/01.str.18.2.311
5. Rosand J, Muzikansky A, Kumar A, Wisco JJ, Smith EE, Betensky RA et al. Spatial clustering of hemorrhages in probable cerebral amyloid angiopathy. Ann Neurol. 2005 Sep;58(3):459-62. doi: 10.1002/ana.20596
6. Weller RO, Nicoll JA. Cerebral amyloid angiopathy: both viper and maggot in the brain. Ann Neurol. 2005 Sep;58(3):348-50. doi: 10.1002/ana.20622
7. Charidimou A, Perosa V, Frosch MP, Scherlek AA, Greenberg SM, van Veluw SJ. Neuropathological correlates of cortical superficial siderosis in cerebral amyloid angiopathy. Brain. 2020 Dec 5;143(11):3343-3351. doi: 10.1093/brain/awaa266
8. Greenberg SM, Charidimou A. Diagnosis of Cerebral Amyloid Angiopathy: Evolution of the Boston Criteria. Stroke. 2018 Feb;49(2):491-497. doi:10.1161/STROKEAHA.117.016990
9. Rosand J, Hylek EM, O'Donnell HC, Greenberg SM. Warfarin-associated hemorrhage and cerebral amyloid angiopathy: a genetic and pathologic study. Neurology. 2000 Oct 10;55(7):947-51. doi: 10.1212/wnl.55.7.947