VOLUME - 13, ISSUE - 03, MARCH - 2024 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Neurology

CEREBRAL AMYLOID ANGIOPATHY RELATED INFLAMMATION(CAARI), MORE KNOWN, LESS DIAGNOSED ENTITY.

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ABSTRACT Cerebral amyloid angiopathy-related inflammation (CAARI) is a rare condition that predominantly affects elderly individuals and is characterized by amyloid deposition in cerebral blood vessels, leading to its fragility and hemorrhage. This article presents a case report of an 86-year-old gentleman with CAARI, exhibiting acute confusional state with seizure . Imaging modalities, particularly MRI with SWI and T2 weighted imaging, play a pivotal role in diagnosis, revealing characteristic features such as lobar microhemorrhages and vasogenic edema. Timely initiation of high-dose corticosteroids resulted in remarkable clinical improvement. Differential diagnosis includes various inflammatory and infectious conditions. Early recognition and treatment are crucial for prognosis, with corticosteroids demonstrating efficacy in mitigating symptoms. This abstract underscores the importance of clinical suspicion, thorough investigations, and prompt intervention in managing CAARI to prevent irreversible neurological damage.

KEYWORDS :

INTRODUCTION:

Cerebral amyloid angiopathy is a condition of elderly patients characterised by deposition of amyloid peptides in media and adventitia of small and medium-sized leptomeningeal and cortical blood vessels resulting in its fragility and cerebral haemorrhage mainly lobar bleeds. It can present in various ways includes symptomatic acute lobar intracerebral haemorrhage (ICH), chronic progressive cognitive decline, transient focal neurological episodes, and subacute cognitive disorder or behavioural changes caused by CAA-related inflammation (CAA-RI)(1).

CAARI is relatively rare and has a more aggressive course. Reid and Maloney first described CAA with vascular inflammation in a patient with AD in 1974, and subsequent cases were reported (2).

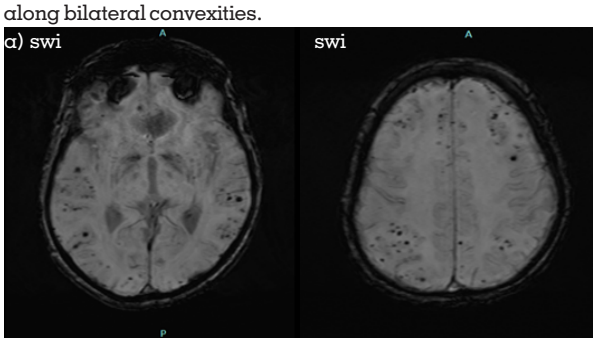
Clinical features include patient above age 40 years with acute or subacute onset of cognitive decline or behavioural changes, followed by headache or seizures or focal neurological signs, and not directly attributable to an acute intracerebral haemorrhage (3).

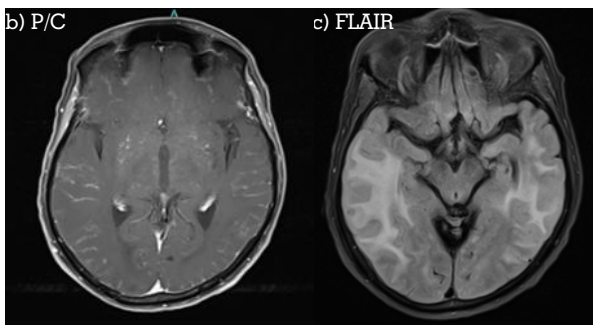
MRI brain showing multiple susceptibility artifacts in the form of one imaging marker such as cerebral microbleeds (CMBs) or cortical superficial siderosis (CSS), (ii) MRI fast fluid-attenuated inversion recovery (FLAIR) images showing corticosubcortical monolateral or bilateral hyper intensities suggestive of vasogenic oedema or sulcal effusion, (iii) clinical features associated with MRI findings, and (iiii) cerebral spinal fluid ruling out infection or malignancy.

Gold standard investigation is cortical and meningeal biopsy but is invasive. Early initiation of immunotherapy in the form of steroids results in dramatic improvement.

Case Report:

We present case report of a 86 year old gentleman with history of hypertension and Pleural Tuberculosis on Antitubercular therapy since 5 months. He presented with 4 days history of headache followed by confused behaviour spatial and temporal disorientation, psychomotor slowness and 1 episode of generalised tonic clonic seizure. On examination he was drowsy, and in post ictal state with disorientation and extensor plantar response. There was no focal motor deficit. His routine lab reports showed normal routine cell counts, infection markers ,electrolytes and liver function tests. MRI Brain with contrast was suggestive of numerous lobar micro haemorrhages with extensive vasogenic oedema in cerebral parenchyma bilaterally, with extensive T2 white matter Hyperintensities with diffuse leptomeningeal enhancement along bilateral convexities.



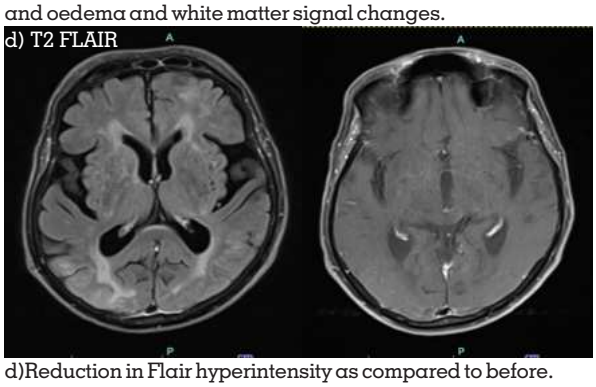


a) SWI – multiple lobar microhaemorrahages in bilateral cerebral parenchyma.
b) Post contrast leptomeningeal enhancement.
c) FLAIR – Bilateral asymmetric Flair hyperintensities in cerebral parenchyma.

CSF Study was suggestive of 2 cells, lymphocytic, normal sugar and raised proteins, negative for MTB gene expert, AFB and gram stain, negative for malignant cell cytology and ADA. Patient was given injectable dexamethasone along with antiepileptic and supportive treatment. He responded

dramatically to treatment returning to his usual state of being in a span of 2weeks. He was discharged on tapering dosages of oral steroids. 3 months later a follow up mri was done which showed complete resolution of leptomeningeal enhancement and oedema and white matter signal changes.

d) T2 FLAIR



d)Reduction in Flair hyperintensity as compared to before.

e)Reduction in post contrast leptomeningeal enhancement.

DISCUSSION:

Epidemiologically CAARI is a disease of elderly with a male preponderance (4,5) According to a systematic review which included 213 pathologically confirmed cases of CAARI (4), cognitive decline was the most common clinical manifestation(48%), followed by seizures (32%), headache (32%), encephalopathy (27%), presenting as confusion or disturbance of consciousness, weakness (16%), and aphasia (14%). Thirteen percent of patients were affected with some forms of visual impairment.

Our patient had both headache, seizures and encephalopathy. There was no motor deficit though.

Imaging:

Brain MRI, particularly FLAIR and T2□/SWI sequences, is the most important imaging modality for the identification of patients suspected of CAA-RI. Patchy or confluent T2 hyperintensity of subcortical white matter lesions, which are mostly asymmetric, in addition to the presence of multiple, strictly lobar CMBs and cSS on T2□ or SWI, which is also a typical finding in CAA. ns seen on SWI can also be identified on T2 or FLAIR images. The distribution of CMBs does not follow the regional pattern of occipital dominance in non-inflammatory CAA. The incidence of multiple lobar CMBs, as well as the total number of CMBs is significantly higher in CAA-RI patients (4–7) Gadolinium enhancement of parenchyma or leptomeninges may or may not be present.

Based on the criteria of leptomeningeal enhancement, the sensitivity and specificity of recognizing CAA-RI from CAA patients are reported to be 70.4% and 92.6%, respectively.

Magnetic resonance angiography (MRA) or cerebral angiography is unremarkable in CAA-RI, due to the small calibre of the involved blood vessels, which prevents the lesion from being captured (8) Our case had cortical microbleeds with white matter signal changes and diffuse leptomeningeal enhancement.

Blood tests may reveal signs of inflammation. An increase in inflammatory biomarkers has been observed in CAA-RI patients in different studies (4,5) The erythrocyte sedimentation rate was increased in 37.5% of patients, while C-reactive protein (CRP) was elevated in 60% (5) The APOE e4 allele is currently the only confirmed risk factor for CAA-RI.

The results of lumbar puncture revealed that more than 80% of patients had increased CSF protein, 44% had pleocytosis, (4) and generally no oligoclonal bands were detected. In our case cells were absent with elevated protein.

Diagnostic Creiteria:

Definite diagnosis requires neuropathological evidence of vascular inflammation and amyloid deposition within vessels of the affected area [2]

Probable and possible caa require clinical and radiological criteria. Clinical presentation of CAA-ri (9–12) includes acute/subacute onset of behavioural symptoms, altered level of consciousness, and rapidly progressive cognitive decline, as well as seizures, headache, and focal neurological signs.
Brain MRI findings include the presence of ≥ 1 of cortical and subcortical haemorrhagic lesions (12,13) including cerebral macrobleeds, cerebral microbleeds, and/or cortical superficial siderosis, associated with asymmetric unifocal or multifocal cortical subcortical or deep white matter hyperintensities, not depending by previous intracerebral haemorrhage, extending to the immediately subcortical white matter in probable CAA-ri, or with white matter hyperintensity simply extending to the immediately subcortical white matter in possible CAA-ri (13)

Differential Diagnosis

includes posterior reversible encephalopathy syndrome, reversible cerebral vasoconstriction syndrome, mitochondrial encephalopathy, lactic acidosis, stroke-like syndrome, Varicella Zoster virus and other infectious vasculitides, sarcoidosis, systemic amyloidosis, giant cell arteritis, primary angiitis of the CNS, and vascular malformations(14)

Treatment and prognosis:

Most studies have shown that empirical high dose corticosteroids with or without additional immunosuppressive therapy can mitigate symptoms and imaging abnormalities and can improve the prognosis of CAARI.

Immunosuppressants can be administered in cases showing no response to glucocorticoids or for preventing recurrence. Early diagnosis and timely treatment may improve prognosis.

The clinical and radiological manifestations may be initially relieved after glucocorticoid therapy, but can relapse after withdrawal of steroids or during dose decrease (8)

CONCLUSION:

CAA-ri a rare but increasingly recognized subset of cerebral amyloid angiopathy which manifests as a reversible encephalopathy with imaging features of inflammation and oedema.

Clinical suspicion, investigations including mri with SWI, T2 weighted imaging and post contrast study with investigations to rule out other causes are mandatory. Early treatment with steroids may improve recovery and prevent worsening.

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