Detection of Microhemorrhages in Cerebral Amyloid Angiopathy by Susceptibility Weighted MR Imaging – An Observational Study

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ABSTRACT

Introduction: Cerebral amyloid angiopathy (CAA) is a cause for approximately 10-20% of spontaneous intracerebral haemorrhage in elderly population. Susceptibility weighted imaging (SW1) is a new imaging method is clinically useful for evaluating the presence of chronic blood products in the brain, especially clinically silent microbleeds associated with cerebral amyloid angiopathy. Aim of this study was to determine the advantages of Susceptibility weighted imaging (SW1) over conventional gradient echo (GRE) technique in a probable diagnosis of Cerebral amyloid angiopathy.

Material and Methods: All patients more than 55 yrs presented with neurological signs and symptoms referred for neuroimaging, were subjected to image with MRI using T1W, T2W, FLAIR. AXIAL 2D MERGE, Diffusion weighted imaging (DWI) including apparent diffusion coefficient (ADC) and Susceptibility weighted imaging (SWI). Those cases having multiple macro and micro haemorrhages involving cortical and sub cortical region detected by either gradient or SWI included in the study.

Results: Sudden onset of neurological deficit was the most common symptom which accounted for 37% of cases. Cortical and sub cortical regions are most commonly involved sites. On comparison between gradient and SWI, 11 cases having micro hemorrgages detected only by SWI and absent in gradient.

Conclusion: GE - T2* MR imaging is currently the " standard" for identifying microhemorrhages and diagnosing cerebral amyloid angiopathy based on number and distribution of micro haemorrhages. SW1 identified many more microhemorrhages than conventional T2* weighted GE magnitude technique and may lead to earlier diagnosis of patients with CAA.

Keywords: Dementia, Cerebral Haemorrhage, Cortical and Subcortical.

INTRODUCTION

Cerebral amyloid angiopathy(CAA)is an unrecognised cause of cerebrovascular disorder characterised by deposition of B amyloid protein in small and medium sized vessels and predominantly involving cortical and leptomeningeal vessels, usually affect elderly patients. The reason of CAA is not yet established with both increased production of the peptides and abnormal clearance having been proposed as potential causes. The major risk factor for CAA is increased age. It affects both sex equally. Alzheimer's disease have a close molecular relationship with CAA. There is wide spectrum of clinical symptoms in association with cerebral amyloid angiopathy evident. Primary intracerebral hematoma and dementia are most well recognized, followed by cerebral infarct ,TIA, seizure and vasculitis etc and neuroimaging play an important role in diagnosing and assessment of disease progression. Introduction of the imaging-based Boston criteria for diagnosis of CAA in the 1990s , allowed a diagnosis of probable CAA in living patients with no available brain tissue. Susceptibility-weighted MRI is a sensitive ,non-invasive technique for identifying small microhemorrhages related to CAA and their number may predict the risk of future hemorrhage. Newer advances like functional imaging with positron emission tomography and single photon emission computerized tomography have been employed to identify and quantify amyloid protein in vivo in neurodegenerative disease e.g. Alzheimer's disease. Aim of this study was to determine the advantages of Susceptibility weighted imaging (SW1) over conventional gradient echo (GRE) technique in a probable diagnosis of Cerebral amyloid angiopathy.

MATERIAL AND METHODS

The study was hospital based and observational in nature. The study was conducted at SCB MC&H and Ashwini hospital in Cuttack, Odisha in department of Radiodiagnosis. Consecutive sampling method was used.

All patients more than 55 yrs with neurological signs and symptoms who were referred for neuroimaging from outpatient or in patient department in, during the period of January 2016 to December 2017 were included in this study. Then subjected to imaging with MRI using T1W, T2W, FLAIR. AXIAL 2D MERGE, Diffusion weighted imaging (DWI) including apparent diffusion coefficient (ADC) AND susceptibility weighted imaging (SWI). Cases who were detected by either gradient or SW1as having multiple macro and micro haemorrhages involving cortical and sub cortical region were diagnosed as probable cases of CAA and were included in the study. after excluding other possible causes of cerebral haemorrhages.

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Excluding criteria

Known hypertensive, Trauma, Post operative ,coagulopathy disorder and other possible causes of cerebral haemorrhages were excluded from the study.

The Study was conducted using 1.5 Tesla MRI scanner (signa explorer GE). The following sequences were performed, axial, coronal, sagittal, T1W, T2W, FLAIR. AXIAL 2D MERGE, Diffusion weighted imaging (DWI) including apparent diffusion coefficient (ADC) and susceptibility weighted imaging (SWI).

Imaging protocol of SWI: TR -75.7,TE 48.6 , FLIP angle 15^0, slice thickness 2mm, inter slice gap 0.2mm, band width 62.5KHZ and Field of view (FOV) 240x 200m, matrix 256x224m, acquisition time 2 minutes 53 seconds. Four sets of images generated including phase, magnitude, SWI, and minimum intensity projections which were analyzed (figures 1-8).

STATISTICAL ANALYSIS

Data were entered on an excel sheet and then analysed using licensed version of Stata 12.1 SE. Quantitative data were described using mean and standard deviation, and compared using parametric tests. Categorical data were analysed using proportions and compared using chi-square test.

RESULTS

A total of 38 cases were included in the study during the whole study period. The mean age of the patients was found to be 68.6 yrs (minimum of 56 yrs and maximum of 95 years). Maximum number of patients (21 cases, 55%) were from the age group of 66—75 yrs (Table 1).This study group comprised of 30(79%) males and 08(21%) females (table-1).

Age group (yrs)	No. of patients	Percentage
56– 65	08	21
66 – 75	21	55
76 – 85	06	16
86 – 95	03	08
Total	38	100

Table-1: Age distribution of study group (n=38)

Symptoms	Numbers	Percentage
Sudden onset of neurological deficit	14	37
Dementia	09	24
TIA like symptoms	05	13
Altered sensorium	06	16
Seizure	05	13
Others	07	18

Table-2: Presenting symptoms (n=38)

Lesion	Numbers	Percentage
Hemorrhage	18	47
Infarct	06	16
Periventricular leucoencephalopathy	07	18
Cerebral atrophy	05	13
Normal	02	05

Table-3: Lesions detected on conventional MRI

Number of micro haemorrhages	Gradient, n (%)	SW1, n (%)
Absent	11 (29)	0 (0)
2-5	13 (34)	06 (16)
5-10	08 (21)	11 (29)
Numerous	06 (16)	21 (55)

Table-4: Comparision of microhemorrhages detected by gradient mri with SW1 (n=38)

Site of involvement	No. of cases (%)
Cortical and subcortical	38 (100)
Cerebellum	13 (34.2)
Brain stem	08 (21.0)
Thalamus and basal ganglia	06 (15.7)

Table-5: Ssite of involvement of microhemorrhages detected on SW1 (n=38)

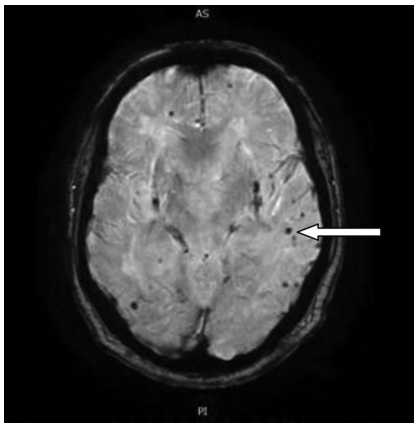


Figure-1: AXIAL SWI MR showing few cortical –sub cortical foci of signal loss consistent with chronic microhemorrhages.

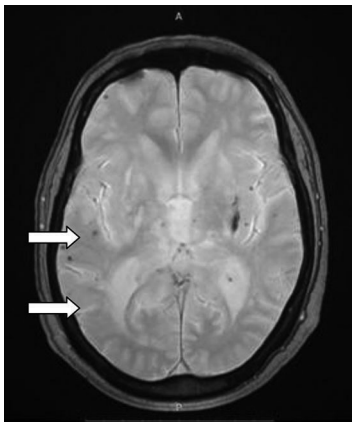


Figure-2: AXIAL GRE MR showing few indistinct foci of microhemorrhages.

Sudden onset of neurological deficit was the most common symptom which was present in 14 cases (37%). Nine patients (24%) presented with dementia, six(16%) with altered sensorium, five (13%) with transient ischemic attack (TIA) like symptom and another five (13%) with seizure. Some of the cases had more than one presenting symptom (Table 2). Haemorrhage was the most common type of lesion detected (18 cases, 47%). Two cases were found to be normal in conventional sequences (Table 3).

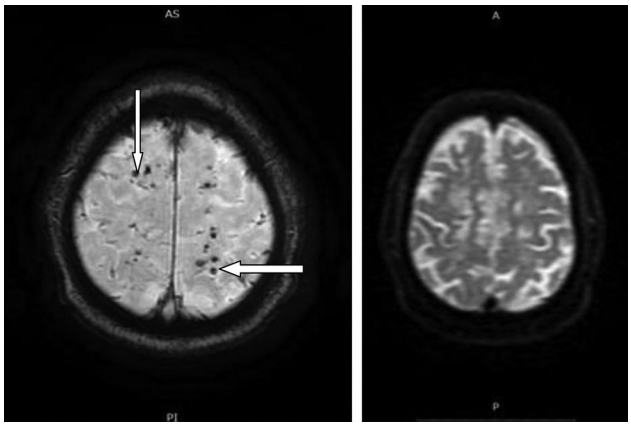
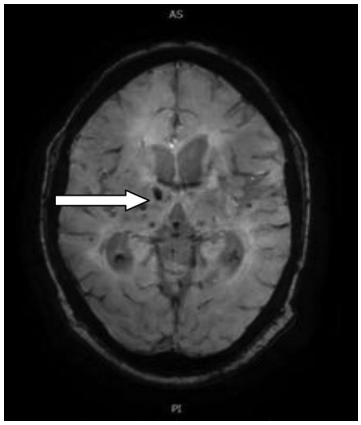
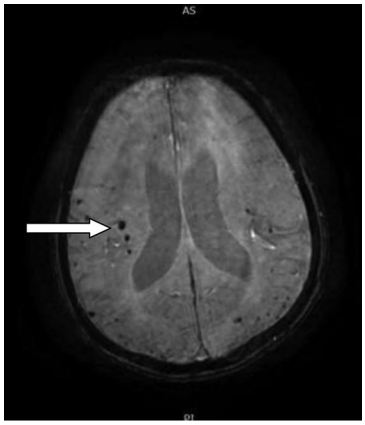


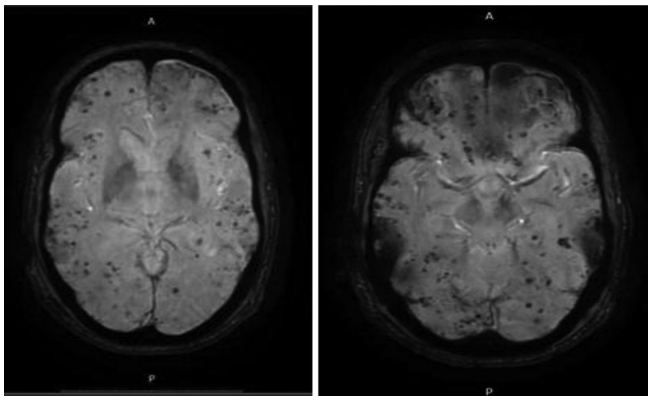
Figure-3a: AXIAL SWI MR showing microhemorrhages; **Figure-3b:** AXIAL GRE MR showing no microhemorrhages



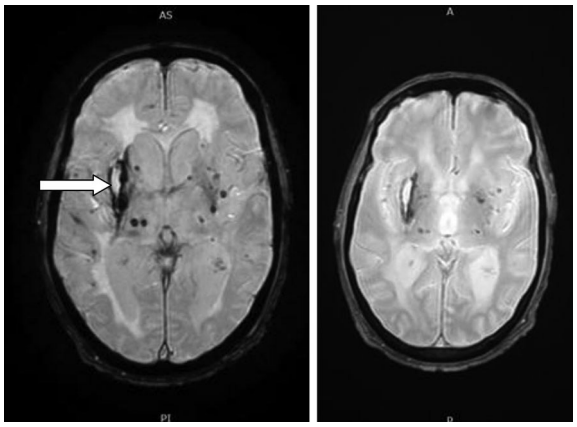
Figure–4: AXIAL SWI MR showing foci of microhemorrhages in thalamus



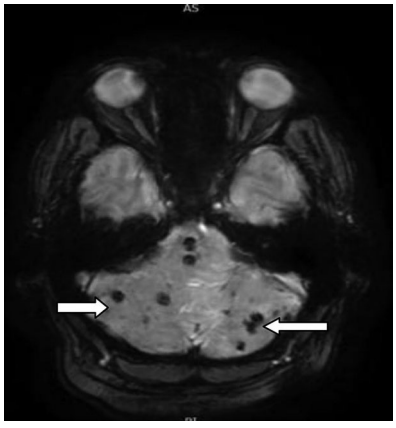
Figure–5: AXIAL SWI MR showing few foci of microhemorrhages.



Figure–6a,b: AXIAL SWI MR showing multiple foci of microhemorrhages



Figure–7a,b: AXIAL SWI MR showing both macrohemorrhage and microhemorrhages. But microhemorrhages better detected in SWI.



Figure–8: AXIAL SWI MR showing cerebellar microhemorrhages though an unusual site

There were 11 cases where micro-hemorrhages were not detectable using gradient MRI but could be detected using SW1. The sensitivity and specificity of SW1 to detect micro-hemorrhages was found to be 100% and 0% respectively. Test of association between number of micro-bleeds and type of MRI was found to be 22.38, and this was found to be statistically significant (p=0.000) (Table 4).

Cortical and sub-cortical involvement was the most common site of involvement (100% cases) (Table 5).

DISCUSSION

Cerebral amyloid angiopathy (CAA) is a small vessel disease which is characterized by deposition of amyloid B protein within the cerebral arterioles.[1,2,3,4,5] Amyloid deposition occurs in many forms, like senile amyloid plaques of Alzheimer disease, parenchymal deposition as in amyloidoma and deposition in the vasculature as in cerebral amyloid angiopathy (CAA).Incidence of cerebral amyloid angiopathy (CAA) like Alzheimer's disease is strongly age dependent.

As the B – amyloid protein deposited within the elastic lamina of vessel walls, vessels lose elasticity and become fragile leading to tiny haemorrhages (cerebral micro bleeds)

in and around the arteriole vessel wall. Repeated micro bleed can cause further loss of vessel wall elasticity, thinning of the vessel wall and vessel dilatation.[6,7]

The most concerning clinical effect of CAA is spontaneous intracranial haemorrhage which can be recurrent. Evidence of multiple lobar haemorrhages and associated subarachnoid extension is more likely in CAA.

As no in vivo imaging is available which enables either the direct visualization or quantification of the amyloid deposits, but as an indirect sign, typically microhemorrhages within and around the arteriole vessel wall, lobar micro bleeds are found related to CAA.

Studies show that CAA is associated with different conditions like aging, dementia (40%), Alzheimer's disease (90%), post radiation necrosis and spongiform- encephalopathy.CAA is not related to systemic amyloidosis.

In our study we observed maximum no. of patients (55%) were in the age group of 66 – 75 yrs and the mean age was found to be 68.6 yrs

In autopsy only 33% are of 60–70 year olds but CAA increases to 75% in patients older than 90 years.[8]

CAA-related ICH represents only 2% of all ICH but is an important cause of hemorrhage in normotensive elderly patients without trauma.[9]

In this study we observed that most common mode of presentation was sudden onset of neurological deficit (37%) followed by dementia (24%), altered sensorium (16%), TIA (13%) and seizure (13%) of cases.

The most common presentation of CAA is the development of a sudden neurologic deficit secondary to an acute ICH.[10] CAA patients may also present with symptoms resembling a TIA, progressive cognitive decline.

In this study we observed that, the most common lesion associated was intracerebral hemorrhage in 47% followed by Periventricular leucoencephalopathy (18%), infarct (16%) and Cerebral atrophy (13%) of cases.

Similar to us Carlo salvarani et al studied the varied neuro imaging spectrum including intra parenchymal lobar haemorrhage ,micro infarct ,micro haemorrhages , non enhancing T2 hyperintense infiltrative mass like lesion in white matter, and leptomeningeal disease.

Lobar haemorrhage was the the most common presentation occurring in 63% cases of CAA.[11] Usually CAA is involving the cortex and sub cortical white matter within the frontal and parietal lobes in contrast to hypertensive or atherosclerotic microangiopathy shows microhemorrhages in a deep or infratentorial location.

Christine P. Chao et al studied CAA-related ICH exhibits a distinctive cortical-subcortical distribution that generally spares the deep white matter, basal ganglia, and brainstem.[12]

We observed microhemorrhages most commonly at cortical and subcortical location in 38% of cases followed by cerebellum (13%), brain stem (8%) and thalamus and basal ganglia (16%) of cases.

CAA-related macrohemorrhages typically exhibit irregular borders (13) and may be associated with subarachnoid hemorrhage. CAA should be considered in the broad differential diagnosis of leukoencephalopathy, especially if associated with cortical-subcortical hemorrhage.[14]

Leucoencephalopathy though a non specific finding but possibility of CAA considered when associated with cortical sub cortical haemorrhages or progressive dementia.[15] CAA may also presented as multiple cortical infarct and present in 14% of cases as studied by Carlo Salvarani et al.[11]

Investigations like MR angiography, conventional angiography and digital subtraction angiography are insensitive to detect vascular disease like CAA. Neither CT nor conventional MR can detect microhemorrhages.T2*GE sequence can detect microhemorrhages (75%).

SW1 is a 3D, velocity-compensated, GE sequence that combines both magnitude information with phase information to accentuate the visibility of susceptible foci such as veins and hemorrhage. Micro haemorrhages contain hemosiderin,which is paramagnetic relative to normal tissue causing large variations in local magnetic fields and a local reduction in T2*. The loss of signal intensity is proportional to the amount of hemosiderin present.

The emphasis placed on cerebral amyloid angiopathy in medical practice and research is justified by its association with cognitive decline, dementia and, more importantly, spontaneous lobar ICH. Increased risk of thrombolysis, warfarin, aspirin and antiplatelet therapy related hemorrhagic strokes has been observed in patients with cerebral amyloid angiopathy. Also inadequate blood pressure control is associated with increased risk of intracerebral hemorrhage in cerebral amyloid angiopathy cases. Hence these risk factors of hemorrhagic stroke can be avoided if cerebral amyloid angiopathy was diagnosed in early stage.

SW1, with its unique sensitivity to blood products and haemorrhage can easily detect imaging changes consistent with CAA[16,17] and assess the rate of microhemorrhages development or regression, allowing more precise analysis of the natural history of the disease, or assessing response to therapy. Early recognition can be advantageous to patients on anticoagulant or aspirin therapy in that they are at increased risk for subsequent and possibly fatal haemorrhage reported to be as high as 38%, with a 44% mortality rate.Strict blood pressure control may also be of utility in patients with CAA related haemorrhage.

Limitation - As histopathological study is not practically possible in our institution, making SW1 and GRE an important method for probable diagnosis of CAA.

CONCLUSION

SW1 also a highly sensitive technique to iron accumulation in the brain in conditions like ageing process, diseases of iron metabolism and haemorrhages. With improved detection of microhemorrhages by SW1 than conventional T2* weighted GE, earlier detection and therapeutic response in CAA becoming possible. New therapeutic low-molecular-weight proteins that reduce amyloid fibril formation, becomes available. However large studies are still needed to determine the role of SW1 in iron measuring especially in

neurodegenerative diseases.

Abbreviations

1. CAA – Cerebral amyloid angiopathy
2. SW1 – Susceptibility weighted imaging
3. GRE – Conventional gradient echo
4. ICH – Intracerebral hemorrhage
5. TIA – Transient ischemic attack

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