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An Observational Study of Cognitive Dyfunction in Patients with Leukoaraiosis in a Tertiary Care Hospital

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ABSTRACT: Introduction: Leukoaraiosis is a very common finding in apparently 'normall individuals over the age of 60 years. Leukoaraiosis appears as low-density lesions around ventricles on CT scan, and magnetic resonance imaging (MRI) demonstrates them more clearly as hyperintensities on fluid-attenuated inversion recovery sequence.Those with Leukoaraiosis have a significantly increased risk of subsequent new stroke, dementia, and mortality. Aims: To evaluate correlation of leukoaraiosis changes in MRI Brain with clinical features especially cognitive function, executive function and gait impairment. Materials and Methods : This was a prospective observational study, done in the Department of neurology, for a period of 6 months from December 2019. Seventy five patients with Leukoaraiosis on MRI with no other additional findings were included in this study. The patients underwent a detailed neurological examination including MMSE, detailed Lobar assessment tests - executive function, Trail making test, Digit symbol test, Memory assessment test, and gait assessment. Results : The mean age of patients included was 62.01 ± 5.45 years. (Males – 62.16 ± 5.35, Females – 61.85 ± 5.65).On comparing abnormaltites in cognitive function with severity of leukoaraiosis, it was found that patients with more severe leukoaraiosis had difficulties in executive function tests and trail making test.($p<0.05$). There was no correlation between severity of leukoaraiosis and abnormalities in Digit symbol substitution test, recall, orientation and Gait.

Keywords: Leukoaraiosis, Periventricular leukomalacia, lacunar stroke, Cognitive dysfunction, executive function

I. INTRODUCTION

The story of ischemic small vessel disease of brain dates fifty years back when Fisher described lacunar infarcts in 1965. [1] This was in the days before CT or MRI when the diagnosis was done by clinical examination and careful postmortem examination after death. As neuroimaging became widely available, Hachinski et al.[2] coined the term Leukoaraiosis (LA) to denote "white matter like air" (leuko = white, araiosis = rarefaction) in 1987. Leukoaraiosis appears as low-density lesions around ventricles on CT scan, and magnetic resonance imaging (MRI) demonstrates them more clearly as hyperintensities on fluid-attenuated inversion recovery sequence. During 1987-1994, several "normal people" were observed to have Leukoaraiosis on CT scan which made physicians wonder if it was an incidental finding in old age. In the age group 65-84 years, of which 10% had periventricular and deep white matter hyperintensities increasing in incidence with age.[3] Those with Leukoaraiosis were found to have a significantly increased risk of subsequent new stroke, dementia, and mortality.

There are many studies about Leukoaraiosis from the Western parts of the world.[4,5] Patients with Leukoaraiosis were analyzed and the severity of Leukoaraiosis on MRI was graded on Fazekas scale.[6] In India, the correlates of Leukoaraiosis have not been widely reported. This study was designed to investigate the factors which correlate with Leukoaraiosis.

II. AIM

To evaluate correlation of leukoaraiosis changes in MRI Brain with clinical features especially cognitive function, executive function and gait impairment

III. MATERIALS AND METHODS

The study was a prospective observational study, done in the Department of neurology, Tirunelveli medical college, Tirunelveli for a period of 6 months from December 2019. Seventy five patients with Leukoaraiosis on MRI with no other additional findings were included in this study. Patients with Cerebral autosomal dominant arteriopathy with subcortical infarcts and leucoencephalopathy (CADASIL), cerebral amyloid angiopathy, exposure to cranial radiation, multiple sclerosis, HIV, and Hashimoto's encephalitis which may mimic Leukoaraiosis on neuroimaging were excluded. Patients with stroke,

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pregnant and lactating women, pediatric population and patients who were not cooperative for cognitive evaluation were also excluded. The patients included in the study underwent a detailed neurological examination including MMSE, detailed Lobar assessment tests - executive function, Trail making test, Digit symbol test, Memory assessment test, and gait assessment. All patients also underwent stroke workup including complete blood count, liver and renal function tests, fasting and postprandial blood sugar, serum lipid profile, electrocardiogram (ECG), echocardiography, and MRI brain imaging with FLAIR Sequence.

IV. RESULTS

A total of 75 patients were included in this study out of which (57%) were males. The mean age of patients included was 62.01 ± 5.45 years. (Males – 62.16 ± 5.35, Females – 61.85 ± 5.65). Out of the included patients, 32(42.7%) had Diabetes Mellitus, 44(58.7%) had hypertension, 24(32%) had Chronic Kidney disease, 34(45.3%) had hypothyroidism, 19(25.3%) had dyslipidemia and 14(18.7%)had hyperhomocysteinemia. Thirty-five (46.7%) patients had Grade 1 Leukoaraiosis, 19(25.3%) had Grade 2 and 21(28%) had Grade 3 Leukoaraiosis. There was no significant difference between gender and the severity of Leukoaraiosis by Fazeka's grading (Table 1). Patients with CKD and Hypothyroidism had more severe Leukoaraiosis as per Fazeka's Grading. (Table 2)

Gender	Grade 1	Grade 2	Grade 3	
Male	**21**	**11**	**11**	$\chi^2 = 0.315$
Female	**14**	**8**	**10**	
Total	**35**	**19**	**21**	$p = 0.854$

Table 1 Gender and severity of Leukoaraiosis

Pre-existing Illness	Grade 1	Grade 2	Grade 3	p value
Diabetes Mellitus	12	13	7	**0.032**
Hypertension	19	9	16	0.140
Chronic Kidney Disease	6	6	12	**0.008**
Hypothyroidism	14	3	17	**0.000**
Dyslipidemia	9	3	7	0.443
Hyperhomocysteinemia	6	5	3	0.591

Table 2Pre-existing illness and severity of Leukoaraiosis

Detailed cognitive examination was performed in all the patients. The results are summarized in Table 3.

Test	Abnormal	Normal
Trail Making test	27 (36%)	48 (64%)
Digit Symbol Test	19 (25.33%)	56 (74.67%)
Recall	24 (32%)	51 (68%)
Orientation	14 (18.67%)	61 (81.33%)
Executive function	19 (25.33%)	56 (74.67%)
Gait	16 (21.33%)	59 (78.67%)

Table 3 Neurological examination

On comparing abnormaltites in cognitive function with severity of leukoaraiosis, it was found that patients with more severe leukoaraiosis had difficulties in executive function tests and trail making test.($p<0.05$) There was no correlation between severity of leukoaraiosis and abnormalities in Digit symbol substitution test, recall, orientation and Gait.(Table 4)

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Abnormal Test	Grade 1	Grade 2	Grade 3	p value
Trail Making test	6	8	13	**0.003**
Digit-Symbol Substitution Test	8	2	9	0.057
Recall	8	6	10	0.157
Orientation	6	2	6	0.326
Executive function	6	2	11	**0.003**
Gait	6	2	8	0.074

Table 4 Correlation of neurological examination with severity of Leukoaraiosis

V. DISCUSSION

Leukoaraiosis is a diverse finding that can be associated with multiple pathological and clinical situations with a varied prevalence. There are no clinical guidelines for screening or identification of leukoaraiosis in the general population. Leukoaraiosis can be detected in 21% of patients by CT and almost 100% of the healthy population by MRI.[7] In patients with suspected cognitive impairment of vascular origin, Leukoaraiosis can be seen in between 41% and 100% by CT and 64% to 100% by MRI.[8,9]

The most accepted pathogenesis of leukoaraiosis is chronic ischemia due to damage to the penetrating blood vessels.[10] This is supported by the fact that the severity of leukoaraiosis is more in patients with hypertension, diabetes mellitus and pre-existing cardiovascular disease which are secondary to atherosclerosis.[7,11,12]

Cognitive impairment is known to occur in patients with leukoaraiosis. As the severity of leukoaraiosis increases the spectrum of manifestations of cognitive impairment widens leading to changes in memory, decreased speed of processing and executive dysfunction.[10] Leukoaraiosis is also seen in patients with AD particularly in older patients with functional impairment. Severity of Leukoaraiosis correlates with the cognitive and behavioral disability in Alzheimer's dementia from the onset of disease.[13]

The Cardiovascular Health Centre study reported that patients with progressive leukoaraiosis reported more severe impairment in performing the modified mini mental state examination test (MMSE) and the digit-symbol substitution test signifying early executive dysfunction and impaired graphomotor ability.[11]Trail making test which is another test for assessment of executive function is found to be impaired early in patients with Leukoaraiosis.[14] McMurtray A M et al found that patients with lacunar strokes with Leukoaraiosis had difficulty in MMSE, category and verbal fluency, constructional ability and verbal and non-verbal memory.[15] The Austrian stroke prevention study done on 329 volunteers from the community found a complex interplay between progression of Leukoaraiosis, brain atrophy and cognitive function. It demonstrated a significant correlation between increasing volume of Leukoaraiosis, brain atrophy and progressive declining performance in tests of memory, conceptualization and visuospatial practical skills.[16] They also found that a subgroup of patients with significant Leukoaraiosis but no brain atrophy at baseline experienced a significantly higher loss of brain matter during subsequent years than their counterparts with little or no Leukoaraiosis.[16] They concluded that this finding indicates alternate mechanisms for cognitive decline and brain atrophy other than Alzheimer's pathology which ultimately lead to Cortical and hippocampal atrophy.[17] Standard MRI sequences may not be able to identify gray matter pathology in these cases.[18]

VI. CONCLUSION

The presence of Leukoaraiosis is an important early indicator of cognitive decline in the elderly. Vascular risk factors such as diabetes mellitus, hypertension and chronic kidney disease should be adequately controlled to prevent early rapid progression of Leukoaraiosis. Memory and executive function are important cognitive functions which show early deficits in patients with Leukoaraiosis.

CONFLICTS OF INTEREST

- Authors have not received any grants from funding agencies.

DISCLOSURE

- Authors have no disclosures to make.

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