Original Article

Clinical correlates of leukoaraiosis: A study of 175 patients

Rustom S. Wadia, Sandesh K. Ghiya[1], Joshita Singh[2], Santosh M. Sontakke, Vishwas Bharadwaj[3], Rahul V. Sonawane[3], Yogesh P. Bade[3], K. Shrikanth[3], Nikhil Goli[3], Rohit Singh Chauhan[3], Nilesh A. Nadkarni[4]

Consultant Neurologist, [1]Consultant Radiologist, [2]Resident at Ruby Hall Clinic, [3]Assistant Professor, Bharati Medical College, [4]Consultant Neurologist, Columbia Asia Hospital, Pune, Maharashtra, India

Abstract

Background: In India, the correlates of leukoaraiosis (LA) have not been widely reported. This study was designed to investigate the factors which correlate with LA. **Materials and Methods:** We included patients with LA who consented for the study and graded their severity on the basis of Fazekas scale. We excluded patients with LA who did not consent/cooperate for the study as also patients with other white matter changes which mimic LA. **Results:** LA is a common and under-rated cause of disability. Presentations include cognitive decline, gait disturbance, dysarthria, bladder/bowel sphincter disturbances, and increased risk of stroke. The comorbidities include hyperhomocysteinemia, hypertension, dyslipidemia, tobacco use, ischemic heart disease, previous stroke, atrial fibrillation, chronic renal failure, and bariatric surgery.

Key Words

Cognitive decline, gait and sphincter disturbances, leukoaraiosis

For correspondence:
Dr. Rustom S. Wadia, Director Neurological Services, Ruby Hall Clinic, Pune, Maharashtra, India.
E-mail: drrswadia@gmail.com

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Introduction

The story of ischemic small vessel disease of brain dates 50 years back when Fisher described lacunar infarcts in 1965.[1] This was in the days before computed tomography (CT) scan when the diagnosis was done by clinical examination during life 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. LA 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 imaging. During 1987–1994, several "normal people" were observed to have LA on CT scan which made physicians wonder if it was an incidental finding in old age. The Rotterdam Scan Study was a community-based study of apparently normal 1077 persons 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 LA were found to have a significantly increased risk of subsequent new stroke, dementia, and mortality.

There are many studies about LA from the Western parts of the world.[4,5] In India, the correlates of LA have not been widely reported. This study was designed to investigate the factors which correlate with LA.

Materials and Methods

The study was a prospective observational study carried out at a single tertiary care referral center between November 2011 and October 2014.

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Inclusion criteria

Patients with LA were analyzed. The severity of LA on MRI was graded on Fazekas scale.[6]

Clinical examination of patients included the following:

1. Mini-Mental Status Examination (MMSE)
2. Frontal lobe functions: trail making test A, trail making test B, and digit symbol test
3. Three-minute walk test.

The executive functions and walking speed were compared with age- and sex-matched controls.

Exclusion criteria

1. Patients with LA who were asymptomatic
2. Conditions such as 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 LA on neuroimaging
3. Patients with LA who in addition had infarcts more than 2 cm suggesting large vessel disease
4. Patients who did not cooperate for examination.

Investigations

All patients underwent stroke workup including fasting and postprandial blood sugar, serum lipid profile, homocysteine level, electrocardiogram (ECG), echocardiography, and MRI brain.

Results

A total 175 patients were studied. Males comprised 68% of cases. The number of patients in age groups <50, 50–60, 60–70, 70–80, and >80 years were 7, 29, 69, 55, and 15, respectively. When all outdoor and indoor patients in our tertiary care center were considered, patients with LA were found to comprise 26.98% of all cases with cerebral vascular diseases.

Comorbid conditions associated with LA are listed in Table 1.

Clinical features of patients are tabulated in Table 2. When executive function was being checked, it was found that trail making test A could be completed in 25 s only by 6% patients with LA, whereas all controls could complete in 25 s. Trail making test B was completed by all controls in 30 s, whereas only 4% patients with LA could complete in that period. Digit symbol test involving 9 digits could be completed by all controls in 80 s. However, 78%, 14%, and 8% patients with LA could, respectively, solve <5, 6–8, and all 9 digit symbols correctly in 80 s.

Table 1: Comorbid conditions in patients having leukoaraiosis

Comorbid condition	Percentage
Raised homocysteine (>15 μmol/L)	66.6
Hypertension	47.4
Dyslipidemia	23.9
Diabetes mellitus	23.4
Tobacco use (smoking plus smokeless)	17.1
Ischemic heart disease	16.5
Previous lacunar stroke	5.7
Atrial fibrillation	3.4
Chronic renal failure	2.85
Bariatric surgery	1.7

Radiologic features of the study group are shown in Table 3.

Discussion

In our study, it was noted that LA comprised 26.98% of all indoor and outdoor patients with cerebral vascular diseases presenting to our center. Even in studies done in France,[7] UK,[8] and Germany,[9] the prevalence of LA was nearly 25% of the cases of cerebral vascular diseases.

Pantoni and Garcia[10] summarized different risk factors for LA. They included older age, male gender, hypertension, history of transient ischemic attack/stroke/myocardial infarction/heart failure, left ventricular hypertrophy on ECG, elevated fibrinogen, and factor VII activity. Additional risk factors such as smoking and raised homocysteine were noted in the Rotterdam Scan Study.[3,11] Radiologically, periventricular LA is found to correlate more with aging and hypertension rather than deep white matter hyperintensities alone.[12] Comorbidities associated with LA as noted in our study are mentioned in Table 1. Identification of modifiable risk factors for LA is important as their prevention can potentially reduce morbidity and mortality.

In the present study, clinical features encountered in patients with LA include cognitive decline, dysarthria, gait impairment, sphincter disturbance, and increased risk of stroke. They compare well with the available literature.

Tarvonen-Schröder *et al*.[5] noted that dementia, dependence for basic and instrumental activities of daily living, gait impairment, urinary incontinence, mental change, and night time confusion were more common in patients with LA than those without. Lawrence *et al*.[13] observed that patients with LA had significant executive dysfunction. In a Korean study, Kim *et al*. observed lower MMSE and verbal learning test scores in patients with LA than those without.[14] In our study, 20.6% had mild cognitive impairment, whereas 39.4% had dementia.

Briley *et al*. noted increase in gait disturbances with an increase in the severity of LA.[15] Baezner *et al*. noted that walking speed and balance were inversely related to the severity of LA.[16] LA increased the risk of falls in elderly,[17] especially if it involved periventricular and frontal deep white matter.[18] Patients with LA who had gait disturbance have higher morbidity and mortality compared to those without gait disturbance.[19] In our study, patients with LA covered lesser distances than those without LA on 3-min walk test.

Poggesi *et al*. noted that urinary urgency (but not nocturia, urinary frequency, and urinary incontinence) was associated with severity of LA irrespective of their cognitive decline, gait disturbance, or depression.[20] In our study, 28% patients had bladder/bowel sphincter disturbances.

Table 2: Clinical features of patients with leukoaraiosis

	Indoor patients (*n*=80)		Outdoor patients (*n*=95)		Total (*n*=175), (%)
	Number	Percentage	Number	Percentage	
Cognitive decline					
Dementia	47	58.7	22	23	39.4
MCI	16	20	20	21	20.6
Dysarthria	37	46.25	23	24.2	34.3
Gait impairment	58	72.5	43	43.95	57.7
Bladder/bowel sphincter complaints	30	37.5	19	20	28.0
Hemiparesis	34	42.5	41	42.1	42.9

MCI = Mild cognitive impairment

Table 3: Radiologic features of patients with leukoaraiosis

Periventricular Hyperintensity Grade	Deep White Matter Hyperintensity		
	Grade I	Grade II	Grade III
Grade II	4	54	34
Grade III	2	40	41

Note: Recent lacunar infarcts recognized as diffusion restricted lesion with new neurologic deficit noted in 58 patients of whom 3 had more than 1 new lacunar infarcts. Microbleeds [3-15 mm sized perivascular hemosiderin deposits] noted in 29 patients. Small hemorrhage presenting with acute mild hemiparesis was noted in 3 patients [2 had periventricular and 1 gangliocapsular location]

Henninger *et al*. observed that presence of severe subcortical LA contributes to larger cortical infarct volumes and worse functional outcomes.[21] Patients with more severe LA are more prone for stroke recurrence within 90 days,[22] as also on 5 years follow-up.[23] Thus, LA is a marker of increased cerebral susceptibility to ischemia. In our study, 42% of patients with LA had stroke. We will like to highlight two interesting features of the strokes in LA: (1) Three of our cases had multiple new lacunar infarcts at presentation raising the possibility of embolic stroke, but no source of embolism was found. We feel that multiple infarcts in these cases occur due to hemodynamic factors resulting from low flow in the brain with widespread small vessel disease. (2) Three of our cases presenting with stroke were found to have a small hemorrhage mostly due to a small vessel rupture. Several studies have shown that these patients should be restarted on the single antiplatelet agent after the bleed subsides as the subsequent risk of ischemic stroke is actually significantly more than recurrent hemorrhage.[24,25]

Conclusion

LA is a common and under-rated cause of disability. Presentations include cognitive decline, gait disturbance, dysarthria, bladder/bowel sphincter disturbances, and increased risk of stroke. The comorbidities tend to be similar to those of ischemic strokes.

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Conflicts of interest
There are no conflicts of interest.

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Report on the 15th Annual Scientific Meeting of the Asian and Oceanian Myology Center, Hsinchu 2016

The 15th Annual Scientific Meeting of AOMC was held in conjunction with the 20th Taiwan Child Neurology Society Annual Meeting at the National Chiao Tung University in Hsinchu, Taiwan, on 27th to 29th May, 2016. Dr. Yuh-Jih Jong, AOMC 2016 Chairman and Conference President, along with International and Local Committee Members, organised the meeting for AOMC. Delegate registrations totalled 338 with 119 international participants. Highlights of the meeting included a Symposium on Spinal Muscular Atrophy with special reference to therapies being developed and updates on very promising clinical trials. A second Symposium covered Distal Myopathies in which newly-recognised phenotypes of Titanopathy and Laing Myopathy were discussed along with potential therapies for GNE Myopathy. Disappointing news regarding the results of clinical trials of three promising therapies for Duchenne Muscular Dystrophy was offset somewhat by better understanding of Ullrich Congenital Muscular Dystrophy and Facioscapulohumeral Muscular Dystrophy with hopes for therapeutic advances as a result. These reports were presented as updates on Neuromuscular Diseases in a third Symposium. Clinico-pathological case studies were again a feature of the meeting.

Allan H. Bretag

School of Pharmacy and Medical Sciences,
University of South Australia,
Adelaide, SA 5000, Australia