

LEUKOARAIOSIS: RISK FACTORS IN ETIOPATHOGENESIS

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SUMMARY

The Nature, pathophysiology and clinical significance of periventricular white-matter lucencies revealed by computed tomography and magnetic resonance scans called "leuko-araiosis" are not well understood. We studied 57 patients with leukoaraiosis detected by computed tomography scans and 45 of them had cerebrovascular disease. There were 47 (82.5%) with hypertension and 31 (54.4%) patients with hyperlipidemia. We found decline in cognitive function in 25 patients using the mental status test of Kökmen et al. Ten of them were severely demented. We suggested that control of vascular risk factors is important for controlling leukoaraiosis that may lead to intellectual impairment.

Key Words: leukoaraiosis, dementia, hypertension.

INTRODUCTION

Patchy, periventricular white-matter lucencies detected by Computed Tomography (CT) and especially by Magnetic Resonance (MR) scans are called "Leuko-araiosis" (1). Periventricular hypodense areas are usually bilateral, symmetric, not well demarcated and are mostly located in frontal and parietooccipital regions (2-4). The nature, pathophysiology and clinical significance of those hypodense areas have not been well understood, yet. Leukoaraiosis is commonly seen in elderly and hypertensive subjects (5). There is a fourfold increase in cerebral infarcts in patients with leukoaraiosis compared with normal population (6). However, while a vascular origin might be suspected from these clues, periventricular lucencies could be the result of various neurologic abnormalities such as leukodystrophies, demyelinating diseases and also normal ageing (4, 6).

One study suggests that the presence of leukoaraiosis is associated with a decline in memory and intellectual function (7). However there are other studies that disagree (8, 9). Although leukoaraiosis is not a predictor of dementia, the occurrence of leukoaraiosis is about 35% in demented patients and is especially common in vascular dementia (5,10-12).

In this study, we included patients with leukoaraiosis detected by CT scan and the clinical diagnosis,

neuropsychological test findings and risk factors of them were documented.

SUBJECTS AND METHODS

We included 57 patients admitted to hospital with various neurological disorders such as cerebrovascular diseases, tumors, dementia, headache with periventricular hypodensities revealed by CT scan, from January to July 1989. A third generation CT scanner (Phillips Tomoscan 350) set for 9mm section thickness was used. Computed tomography scans were evaluated for the presence or absence of leukoaraiosis (Table I for the criteria used). The density of lucencies was between normal white-matter and cerebrospinal fluid (CSF). Typical examples of leukoaraiosis on CT scans are illustrated in figure 1.

We determined the presence of hypertension, coronary heart disease, diabetes, hyperlipidemia with medical history, physical examination and laboratory investigations. All patients underwent the mental status test of Kökmen et al (18). Intellectual impairment was determined by a score under 20 and dementia was determined by DSM III criteria.

RESULTS

The patients' ages ranged from 37 to 85 with a mean age of 67.5 years. Twenty of the patients were women and 37 of them were men. Forty-five patients were admitted to the hospital with cerebrovascular disease. Thirty-nine of them had cerebral infarcts. Of these 39, 12 patients had large infarcts, 19 had multiple lacunar infarcts and 8 had both. Seven patients had intracerebral hematomas (Table II). There were 49 patients with hypertension and 31 patients with hyperlipidemia. Fifteen patients had diabetes and 23 patients had coronary artery disease but they were not present as a single risk factor (Table III).

We found decline in cognitive function in 25 of these patients using the mental status test. Ten of those patients had compatible with severe dementia in that they had disability to maintain their daily life by themselves. Among the demented patients, 2 of them had normal pressure hydrocephalus. Four of them had vascular dementia and one of them was consistent

with the diagnosis of Binswanger's Disease. One patient was considered to have Alzheimer's Disease. In one patient, dementia was coexistent with Down Syndrome and with vitamin B12 deficiency in another patient. Intracerebral metastatic lesions were revealed by CT scan in one patient (Table IV).

DISCUSSION

The term Leuko-araiosis has been suggested by Hachinski et al to describe the patchy periventricular white-matter lucencies (1). The presence is about 30-92 % in patients older than 60 years of age and in 22 % of subjects younger than 40 years of age (4). In this study, the mean age was 67.5 years in our 57 patients with leukoaraiosis. It appears that the frequency of leukoaraiosis increases with age but in recent studies it has been reported that age was not an independent factor after controlling for the effect of other variables (5). Prevalence of stroke and hypertension is significantly high in patients with leukoaraiosis (5). The presence of hypertension was reported in 78-93 % of patients (5, 13). In our study, 86 % of patients had hypertension. The presence of hypertension and hyperlipidemia together was in highest proportion (47.4 %).

The prevalence of stroke is 3.6-100 % in various studies (4, 5). About 69 % of our patients had cerebral infarction in their CT scans and 33.3 % of them as multiple lacunar infarcts.

The association of leukoaraiosis with hypertension and stroke suggests the vascular origin. In postmortem studies of patients with leukoaraiosis, gliosis and multiple small infarcts were shown with "état criblé" that are periventricular dilatation, arteriosclerosis and vascular ectasia described by Durant-Fordel in 1843 (13). In pathological studies of patients with motor and cognitive deficits and leukoaraiosis, diffuse demyelination of deep white-matter was also reported (4). Ball et al suggested that cortical atrophy and rarefaction of axons in the white-matter has led to widening of perivascular (Virchow-

Robin) spaces and the increased quantity of cerebrospinal fluid in these channels might result in the appearance of hypodense lucencies of the periventricular white-matter on CT and MR images (14). Consequently, the lesions may range from normal aging to demyelination and necrosis.

The results of studies investigating the correlation between the lesions and clinical findings are still controversial. As a result of a suggestion that white-matter abnormalities might play a significant role in the development of intellectual impairment, leukoaraiosis might be considered as a predictor of dementia (7, 8). Once, the presence of leukoaraiosis had been attributed to Binswanger's subcortical arteriosclerotic encephalopathy, characterized by a history of hypertension, slowly progressive dementia with occasional temporary plateaus in the course of the illness, and prominent motor signs (13, 15). However, Rezek et al suggested that periventricular changes were not limited to Binswanger's Disease but also occur in senile dementia of Alzheimer type/Alzheimer's Disease that mechanisms other than arteriosclerotic encephalopathy appear to be responsible for presence of leukoaraiosis (11). Gray et al explained the subcortical lesions with cerebral amyloid angiopathy in patients with Alzheimer's Disease (16).

In our patients, 25 had intellectual impairment and 10 of these had dementia by DSM III criteria. One patient was suspected as having Alzheimer's Disease and 4 other patients had vascular dementia; one of them was considered to have Binswanger's Disease.

In our study, we found leukoaraiosis in patients with various neurologic diseases. The patients mostly had cerebrovascular disease and atherosclerotic risk factors. We suggest that control of vascular risk factors is important as leukoaraiosis may lead to intellectual impairment. However patient population at high risk for developing leukoaraiosis and clinical correlation should be studied prospectively with cross-sectional research designs.

TABLE I: Computed tomographic criteria for infarct and leukoaraiosis.

INFARCT:	LEUKOARAIOSIS:
Well demarcated	Ill defined
Wedge shaped, if peripheral	Patchy, diffuse
Usually have a cortical extension	White matter only
Enlargement of ipsilateral ventricle or sulcus	Ventricle and sulcus unchanged locally
Follows specific vascular territory	
May involve internal capsule, basal ganglia or thalamus, rounded lucencies or lacunae.	

TABLE II: Characteristics of patients with stroke

	no of pts	%
Cerebral infarct	39	68.4
In vascular territory	12	20.8
Lacunar infarct	19	33.3
In vascular territory	8	14.3
Lacunar infarct	7	12.3
Intracerebral hemorrhage		

TABLE III: Presence of risk factors of patients.

Risk factors	no. of pts.	%
Hypertension (HT)(alone)	22	38.5
Hyperlipidemia (HL)(alone)	4	7.0
HT + HL	27	47.4

TABLE IV: Clinical causes of dementia

	no of pts
Normal pressure hydrocephalus	2
Vascular dementia	4
Binswanger's Disease	1
Alzheimer's Disease	1
Dementia with Down Syndrome	1
Dementia with vit B12 deficiency	1
Intracerebral metastatic neoplasm	1

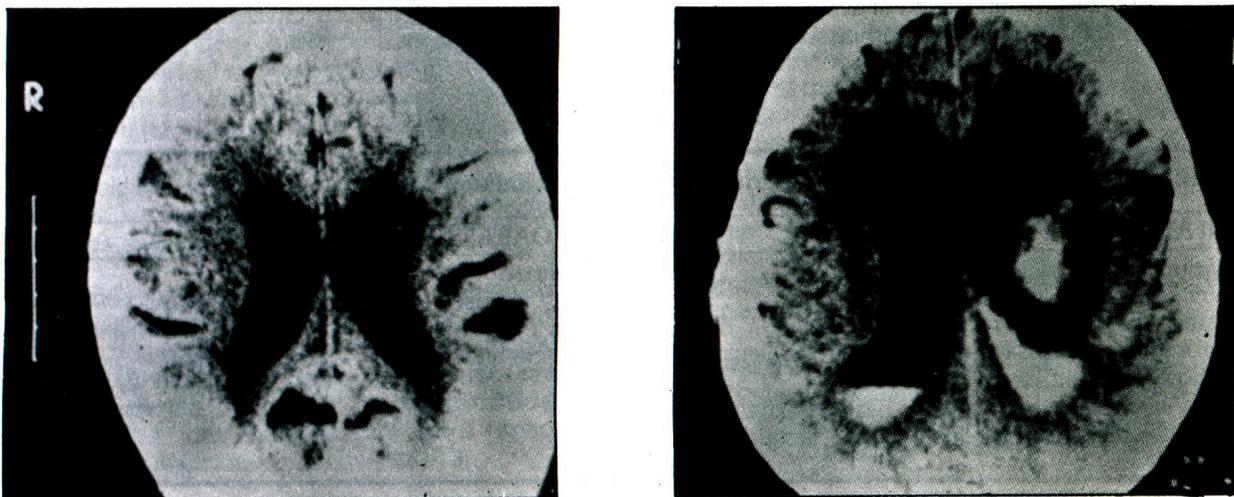


Figure 1: Representative examples of leukoaraiosis with multiple lacunar infarcts (a) and intracerebral hemorrhage (b).

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