

The occurrence of cerebrovascular atherosclerosis in Alzheimer's disease patients

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Background: Both Alzheimer's disease (AD) and cerebrovascular atherosclerosis (CA) contributed to dementia in an aged population. Whether they share the same mechanism is unknown.

Aim: Our goal was to explore the occurrence rates of CA in AD patients.

Method: Here we examined the degree of CA in different groups of AD patients with contrast angiography. Ninety-three AD patients were recruited to the present study. Contrast computed tomography scanning and contrast angiography were performed for CA analyses.

Result: We found that the cerebrovascular plaques were common in AD patients, which was partly correlated with the severity of AD (as determined by cognitive decline).

Conclusion: We concluded that vascular dementia may partly correlate with AD pathology.

Keywords: Alzheimer's disease, cerebrovascular atherosclerosis, aging, patients

Introduction

Both Alzheimer's disease (AD) and cerebrovascular atherosclerosis (CA) contributed to dementia in an aged population.¹⁻³ Whether the two diseases share a common mechanism or pathological progression is yet unclear. It is proposed that in AD the amyloid beta peptide mutates and accumulates to form abnormal aggregates that are resistant to internal clearance,⁴⁻⁶ and these aggregates lead to amyloid plaques (senile plaques) that cause neuronal death as well as other pathological changes inside the brain, with final functional loss. Conversely, for the CA multiple small infarcts (atheromatous plaque) formed inside microvasculature and interrupted the microperfusion.⁷⁻⁹ This also leads to cognitive decline and memory loss as the final result.

Given the two distinct theories explaining the pathogenesis of AD and CA, there are increasing studies that show some common risk factors for both diseases, such as apolipoprotein E, age, smoking, inflammation, and body metabolism.^{2,10-15} In addition, the coronary atherosclerosis cases are increased in patients with AD compared to those without.¹⁶⁻¹⁸ Conceivably, the CA is higher in patients showing heart attack. Postmortem studies also reported the existence of CA in many AD patients. In the present study, we tried to employ radiological approach to investigate the occurrence of CA in AD patients.

Materials and methods

Clinical data

In the present study 93 AD patients were recruited in the Imaging Center, Nanfang Hospital of Southern Medical University, Guangzhou, People's Republic of China

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(male, 61; female, 32; aged 59–82 years; average, 71.2 years old) from January 2012 to December 2012. The patients met the criteria of the National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer's Disease and Related Disorders Association for AD, with a clinical dementia rating of 0.5 ([early AD] 17 cases); or 1 ([mild AD] 26 cases); 2 ([moderate AD] 39 cases); or 3 ([severe AD] 11 cases) (Table 1).

The study was approved by the ethics committee of medical research on human subjects at the General Hospital of Jinan Military Command, and the researchers obtained written consent from all subjects as well as their family members.

Contrast computed tomography scanning and contrast angiography were performed, atherosclerotic lesions were registered, and diameter stenosis degrees were calculated.

Statistics

The data were represented as mean \pm standard deviation and analyzed with the Statistical Package for the Social Sciences 16.0 software (SPSS; IBM Corporation, Armonk, NY, USA) for statistics. The *t*-test was used to compare intergroup differences, and $P < 0.05$ was considered statistically significant.

Results

Detection of cerebrovascular atherosclerosis

We found that atheromatous plaque is prevalent in AD patients: six of 17 (35.3%) in early AD; 14 of 26 (53.8%) in mild AD; 20 of 39 (51.3%) in moderate AD; and nine of eleven (81.8%) in severe AD. In addition, among these cases, both noncalcified and calcified atheromatous plaques were detected at different possibilities (Figure 1). The percentage of noncalcified mixed and calcified atheromatous plaques were 44%, 12%, and 44% in early AD; 47%, 21%, and 32% in mild AD; 39%, 15%, and 46% in moderate AD; and 22%, 35%, and 43% in severe AD (Figure 2).

Distribution of atheromatous plaques

We found that noncalcified atheromatous plaques were mainly distributed in the intracranial arteries (79.2%), mixed plaques in the intracranial arteries (19.1%), and intracranial internal carotid artery (ICA) (44.3%), calcified plaques in the intracranial ICA (55.2%), and extracranial arteries (24.7%) across the different AD groups. Interestingly, we found no obvious differences in plaque distribution across different staged AD patients ($P > 0.05$).

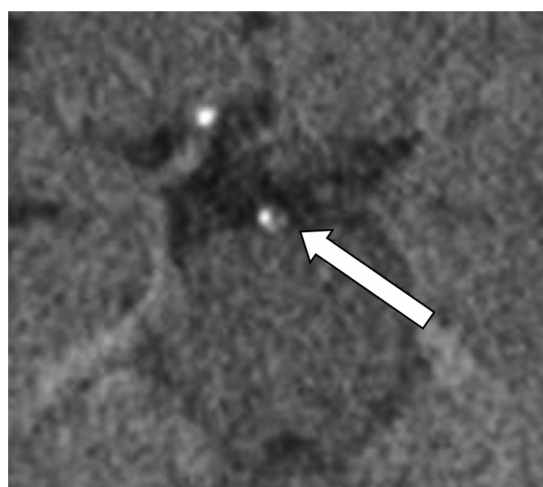


Figure 1 Nonenhanced CT detection of calcified atheromatous plaque (arrow) in a 72-year-old male patient with moderate AD.

Abbreviations: CT, computed tomography; AD, Alzheimer's disease.

Results of atheromatous plaques as vessel occlusion

The differentially composed atheromatous plaques have been shown to be associated with different levels of vessel occlusion previously. The percentage of severe stenosis ($>60\%$) and occlusion in the different AD groups were 3.1% (early), 6.7% (mild), 11.3% (moderate), and 10.7% (severe). The values were significantly different from the severe AD group to the early/mild AD groups.

Discussion

Few studies have examined the formation of CA plaques in AD patients, specifically.^{1,2,7,12} It has been shown that in an aged group with cognitive decline, atherosclerosis plaques could be used as the marker for vascular dementia.^{4,7,19}

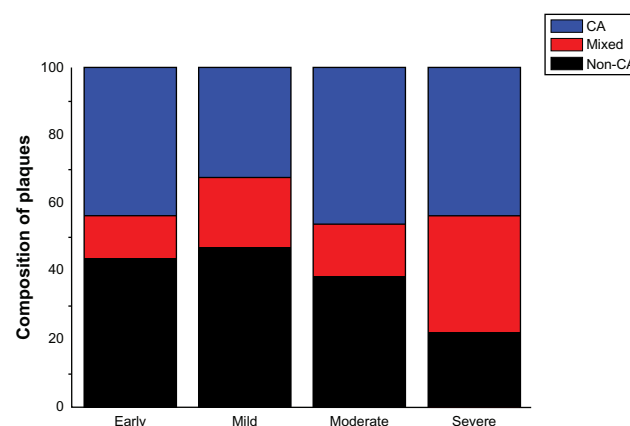


Figure 2 The composition of atheromatous plaques in different groups of AD patients.

Abbreviations: AD, Alzheimer's disease; CA, calcified; Non-CA, noncalcified.

Table I Clinical information for all patients

| CDR | Number of patients | Male | Female | Mean age (yr) | Diabetes cases | Hypertension cases | Heart disease | Smoking | Stroke |
|-----|--------------------|------|--------|---------------|----------------|--------------------|---------------|---------|--------|
| 0.5 | 17 | 11 | 6 | 68.4 | 3 | 4 | 2 | 2 | 3 |
| 1 | 26 | 16 | 10 | 71.6 | 7 | 12 | 5 | 11 | 6 |
| 2 | 39 | 21 | 18 | 73.1 | 11 | 15 | 9 | 17 | 10 |
| 3 | 11 | 4 | 7 | 69.8 | 2 | 4 | 3 | 5 | 2 |
| Sum | 93 | 52 | 41 | 71.2 | 23 | 35 | 19 | 35 | 21 |

Abbreviations: CDR, clinical dementia rating; yr, year.

In the present study, we found that cerebrovascular plaques leading to stenosis or occlusion existed in AD patients as well. Therefore, the mixed AD/CA pathology should be considered and referred in clinical diagnosis of certain aged patients with cognitive decline.

The mechanisms underlying such interactions are yet unclear. The common risk factors, such as apolipoprotein E, age, smoking, inflammation, and body metabolism, do not fully explain the increased atheromatous plaque occurrence in severe AD, rather than in early AD patients.^{2,4,5,20–23} We believe it is possible that the neuronal death and neuroinflammation in late-stage AD triggered the atheromatous plaque formation. If so, the neuroinflammation would act as the share mechanism in pathogenesis and progression in patients with severe dementia, providing the common drug target for both syndromes.

There are certain limitations of the present study. Currently, it is possible to perform magnetic resonance imaging and positron emission tomography for the tracing of plaque formation in the vessels, as well as of the amyloid plaques for AD patients.^{24–26} It will be important to perform different tests on patients to correlate the changes of CA pathology with AD pathology (senile/amyloid plaque) progression. Additionally, we did not correlate other syndromes of vascular dementia into the clinical data of AD patients, taken together with the analysis of stenosis changes of the vessels.^{12,27} We expect to perform such studies in the future. Finally, it will be important to perform these examinations on aged-matched non-AD controls to see if AD pathology causes increased atheromatous plaque formation.

In conclusion, we believe that the vascular pathology may represent one common phenomenon in AD patients. The separation of AD and CA pathology might require reconsideration.

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Disclosure

The authors report no conflicts of interest in this work.

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