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# Late Onset Alzheimer Dementia in Patient with Genotype E3/E4: A Case Report

**Irfan Kurnia Kaban[1], Yudha Haryono[1]**

[1]Department of Neurology, Faculty of Medicine Airlangga University, Airlangga University Hospital, Surabaya, Indonesia

Corresponding Author: Irfan Kurnia Kaban

## ABSTRACT

**Background**: Alzheimer's dementia (AD) is a neurodegenerative disorder and there is progressive cognitive impairment, functional deficits and behavioral changes. This neurodegenerative disease process is classically characterized by two pathological features: amyloid- β plaque deposition and neurofibrillary tangle of tau hyperphosphorylation. The most established genetic risk factor for late-onset Alzheimer Disease is the APOE gene allele 4. We will report a case of late-onset Alzheimer's Dementia with genotype E3/E4.
**Case**: A 70-years-old woman patient, complained by her family that she often forgets. The Mini Mental State Examination showed disturbances in orientation, attention, calculation and recall. Non-contrast Brain Magnetic resonance imaging examination revealed decrease in hippocampal volume. Patient also performed a molecular examination of the Apolipoprotein E (APOE) genotype and the genotype E3/E4 was detected
**Conclusion**: The APOE E4 gene has a major role in the occurrence of Late-Onset Alzheimer's Dementia.

***Keywords*:** Alzheimer Dementia, Apolipoprotein E

## INTRODUCTION

Alzheimer's dementia is a gradual and progressive neurodegenerative disease caused by neuronal cell death. Genetic factors have a role in early and late onset Alzheimer's dementia.[1] The neurodegenerative disease process of Alzheimer's dementia is classically characterized by two pathological features: deposition of amyloid-β plaques and neurofibrillary tangles from hyperphosphorylation.[2,3]

Alzheimer's dementia is the most common form and contributes between 60-70% of all cases of dementia.[4] Increasing age and increasing prevalence of non-contagious disease are the main factors causing cognitive decline which will increase the incidence of AD and other dementias in the elderly.[5]

In 1950 the number of elderly people in the world was 205 million people and increased to 810 million people in 2012. This number is projected to continue to increase and even reach 2 billion in 2050 with an estimated number of people with dementia reaching 152 million people.[6]

The worldwide cost of dementia is estimated at US$1 Trillion in 2018 and will reach US$2 Trillion by 2030.[7]

## CASE

A 70-year-old woman, complained by her family that she often forgot about something she had just done. This forgetting complaint has been going on for about three years and is getting worse and worse. The family also complained that the patient had difficulty in counting related to his work as a trader in the market. The family said that the patient still recognized and remembered the names of his family members. Patients can still carry out their daily activities independently even though they must be supervised by their families

Patients sometimes feel offended when the husband speaks in slightly high voice, but there is no behavior that hurts her family or himself. Complaints of weakness in half of the body, facial drooping, slurred speech, and tingling did not exist.

The patient has a history of hypertension since 2015 and received captopril therapy which is taken regularly, there were no previous forgetfulness complaints. There is no family history of dementia. The patient is a high school graduate and used to work as a clothing seller in the market.

Physical examination was within normal limits, vital signs showed that stage 1 hypertension was controlled with blood pressure of 130/80 mmHg, and no neurological deficit was found.

The Mini Mental State Examination (MMSE) got a score of 16 (impaired orientation, attention, calculation and recall), the Hachinski Ischemic Score got a score of 2 (score ≤ 4 for Alzheimer's dementia), and the Geriatric Depression Scale got a score of 3 (no depression).

Hematological examination showed results within normal limits. Magnetic resonance imaging examination of the brain non-contrast showed decreased of right hippocampal volume (figure 1), decreased left hippocampal volume (figure 2). The Cella Media Index was 5.4 (normal > 4) which means there is no global atrophy and the Fazekas Scale 0 (Figure 3), which means that there are no vascular lesions. Examination of Apolipoprotein E found genotype E3/E4 which is one of the risk factors for Alzheimer's dementia. We diagnosed patient with Late Onset Alzheimer's Dementia.

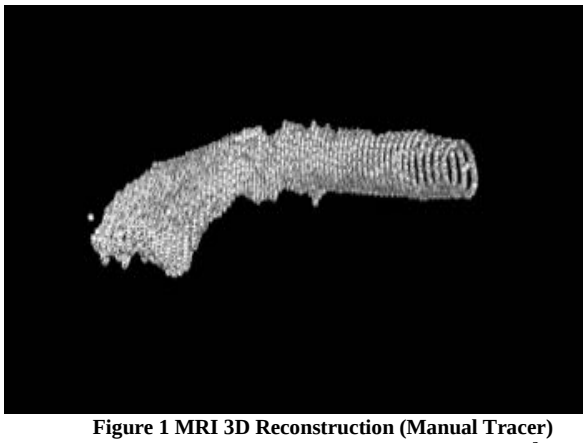

**Figure 1 MRI 3D Reconstruction (Manual Tracer) Right Hippocampal volume 0.9716 cm$^3$**

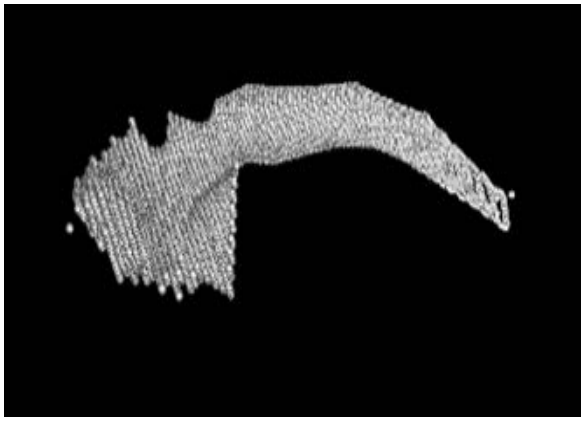

**Figure 2 MRI 3D Reconstruction (Manual Tracer) Left Hippocampal volume 1.0513 cm$^3$**

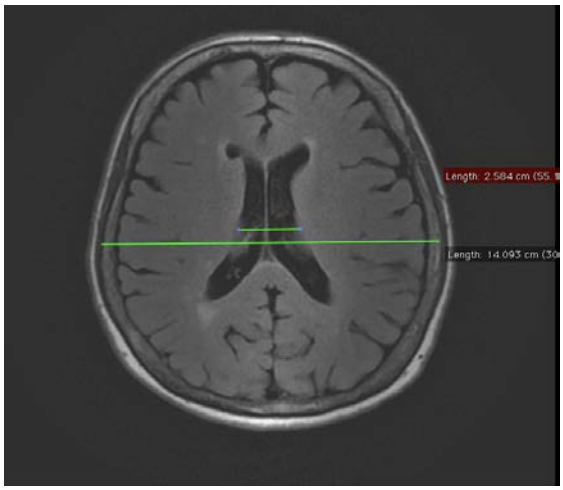

**Figure 3 FLAIR Axial Slice Brain MRI Cella Media Index 5.4 and Fazekas Scale 0**

The patient was diagnosed with Late Onset Alzheimer's Dementia. The Pharmacological therapy given is Donepezil. We also gave non-pharmacological therapy for cognitive stimulation at the Geriatric clinic Soetomo General Hospital

We evaluated the results by comparing the results of the screening at the time of arrival and the last polyclinic visit (with an interval of 6 months). Based on the results of the initial MMSE examination the score was 16 (impaired orientation, attention, calculation and recall) and at the last visit the MMSE score was 22 (impaired

orientation, attention, calculation and recall).

## DISCUSSION

Dementia is a syndrome - usually chronic or progressive in which cognitive function declines. Dementia affects memory, thinking, orientation, understanding, computation, learning abilities, language, and judgment. Consciousness is not affected. Impaired cognitive function is usually accompanied by, and sometimes preceded by, changes in mood, emotional control, behavior, or motivation.[4]

Alzheimer's dementia (AD) is a neurodegenerative disorder in which there is progressive cognitive impairment, functional deficits and behavioral changes. This neurodegenerative disease process is classically characterized by two pathological features: amyloid-β plaque deposition and a neurofibrillary tangle from tau hyperphosphorylation.[2,3,9] All of these brain changes lead to memory loss and changes in thought processes and other brain functions. AD usually develops slowly and gradually worsens as more and more brain cells death.[10]

The most common cognitive symptoms of AD are short-term memory deficits, impaired executive function, visuospatial and praxis dysfunction. Motor impairment is not found except in the late stages of the disease. Impaired behavior and dependence in activities of daily living following episodic memory impairment support the diagnosis of this disease. This disease affects the elderly, especially those aged > 65 years, although it can be found at a younger age.[2]

The risk factors for Alzheimer's dementia are divided into non-modifiable risk factors, namely age, gender, genetics and family history of disease, intellectual disability and Down's syndrome and modifiable risk factors, namely education, physical activity, diet and nutrition, sleep and circadian rhythms, psychological risk factors and cardiovascular risk factors.[11]

AD based on the onset is divided into early onset and late onset. Early-onset Alzheimer Disease was defined as AD with clinical onset younger than 65 years of age. The age of Early-Onset Alzheimer Disease is between 45 and 65 years.[12] Late-onset Alzheimer Disease occurs at >65 years of age and is found in 95% of AD cases and is also known as Sporadic Alzheimer's disease.[13]

A family history of AD is a well-established risk factor for late-onset AD. The most established genetic risk factors for late-onset AD are the APOE gene 4 allele which is associated with an approximately threefold increased risk of AD compared with the 3 allele, and the 2 allele which is associated with reduced risk. The role of the APOE gene in regulating cholesterol transport in the bloodstream; however, the mechanisms that contribute to AD are still poorly understood.[3,14] The presence of the APOE gene 4 allele can directly affect cognitive function is associated with decreased test scores in adults on tests involving memory and learning functions.[15] At autopsy, most individuals diagnosed with AD were found to have one or two copies of the APOE allele ε4.[14]

APOE is a protein that plays a major role in amyloid- metabolism, Tau protein hyperphosphorylation, and neuroinflammation. APOE allele ε4 is more involved in AD pathology in neuropathological studies than allele ε2.[15] Evidence from several imaging studies also suggests that the allele ε4 modifies the relationship between amyloid and cognitive function.[3]

Our patient is a 70-year-old woman with complaints of forgetfulness for 3 years. The MMSE screening examination obtained a score of 16, the MRI examination revealed a decrease in hippocampal volume and the APOE E3/E4 genotype was found which increased the risk of Alzheimer's dementia two to three times. Patients got pharmacological and non-pharmacological therapy where the MMSE value improved from 16 to 22 within 6 months.

## CONCLUSION

Alzheimer's dementia is a neurodegenerative disease, where the APOE E3/E4 genotype plays a role in the occurrence of LOAD. The role of APOE E3/E4 is mainly in the metabolism of amyloid-β, phosphorylation of Tau protein and the occurrence of neuroinflammation. Detection of the APOE E3/E4 genotype increases the risk of developing Alzheimer's dementia between up to three times.

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