



## Early-onset Alzheimer's disease due to novel LDLR gene mutation

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### Background:

Early-onset Alzheimer's disease (EOAD), with onset in individuals younger than 65 years, comprises approximately 5% of AD. It is associated with delays in diagnosis and an aggressive course. Mutation in LDLR is a well-known cause of familial hypercholesterolemia, but genetic variants in LDLR make no significant contribution to AD risk in the general population. This is the first known case of EOAD caused by the rs140241383 variant of the LDLR gene.

### Case presentation:

A patient is a 44-year-old male who presented with spatial disorientation, short-term memory loss, and alteration in handwriting. He was also misplacing objects. MRI T2 and FLAIR sequence showed a chronic vascular lesion of the superior frontal gyrus on the left and initial atrophic changes of the cortex. Three years later, dyscalculia, constructional apraxia, clear attention deficits, and clear impairments of short-term verbal memory were noted. A score of 25 was noted on MMSE. He was diagnosed with unspecified dementia. Atorvastatin was introduced due to high LDL-cholesterol levels. Six months later significant deficits of organic type were present in terms of non-verbal functions, memory, attention, and executive functions. Decreased beta-amyloid levels and increased levels of tau and ptau were detected in CSF. PET scanning showed pathological deposition of extracellular amyloid diffusely in the cerebrum parenchyma and donepezil was introduced. Clinical exome sequencing detected a heterozygous mutation of LDLR variant rs140241383 on chromosome 19p13, also known as p.Ser265Arg. The patient was diagnosed with early-onset Alzheimer's disease. Increased levels of LDL-cholesterol were detected in the serum of the patient's two sons. They were diagnosed with familial hypercholesterolemia and were prescribed statins.

### Conclusion:

Considering that hypercholesterolemia may be an early risk factor for AD, it is necessary to keep in mind the possible development of cognitive impairment in patients with ineffective lipid metabolism. In young patients with hypercholesterolemia and dementia, LDLR mutation should be taken into consideration.

### Keywords:

Dementia; Early-onset Alzheimer's disease; Familial hypercholesterolemia; Genetics; LDLR