Journal of the Formosan Medical Association (2015) 114, 1020–1021

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.jfma-online.com

CORRESPONDENCE

Delayed diagnosis of an old Chinese woman with familial Alzheimer's disease

Yat-Fung Shea [a,*], Leung-Wing Chu [a], Angel On-Kei Chan [b], Joseph Shiu-Kwong Kwan [a]

[a] *Department of Medicine, Li Ka Shing Faculty of Medicine, University of Hong Kong, Queen Mary Hospital, Hong Kong Special Administrative Region*
[b] *Division of Clinical Biochemistry, Department of Pathology and Clinical Biochemistry, Queen Mary Hospital, Hong Kong Special Administrative Region*

Received 1 November 2014; received in revised form 10 November 2014; accepted 21 November 2014

Our patient (II2; Fig. 1) presented at 51 years of age, with a 1-year history of memory impairment. She also suffered from anomia, spatial disorientation, and apathy. During her clinical course, she also developed generalized epilepsy with tonic-clonic seizures which were controlled with phenytoin. Initial physical examination was unremarkable. Mini-Mental State Examination (MMSE) was 14/30. Vitamin B12, folate, thyroid function test, and Venereal Disease Research Laboratory test were normal. A computed tomography (CT) brain scan showed bilateral medial temporal lobes atrophy. Single photon emission CT (SPECT) showed hypoperfusion over the bilateral frontal and temporoparietal lobes. She fulfilled the National Institute of Neurological Communicative Disorders and Stroke-Alzheimer Disease and Related Disorders Association (NINCDS-ADRDA) diagnostic criteria of Alzheimer's disease (AD). Initially, there was no apparent family history of early onset AD (EOAD).

Fifteen years after II2 initial presentation, her daughter (III1), who was 49 years old, presented with amnesia and misplacement of personal items for 9 years (i.e., age of onset was 40 years). She was also found to have dysexecutive syndrome, anomia, dyscalculia, and apathy. Along the clinical course, she developed depression with low mood and suicidal ideation and was prescribed fluoxetine. Physical examination was unremarkable. MMSE was 18/30. A magnetic resonance imaging brain scan showed bilateral hippocampal atrophy. SPECT showed hypoperfusion over the left frontal, left temporoparietal lobes, and right parietal lobes. She fulfilled the NINCDS-ADRDA diagnostic criteria of AD. She was prescribed donepezil and memantine. We noted a strong family history of EOAD in this family; the patient's brother (II5) was initially diagnosed with depression at 58 years old, and subsequently developed progressive amnesia with spatial disorientation, auditory hallucination, and parkinsonism, and was finally diagnosed with AD. Another brother (II6) suffered from amnesic mild cognitive impairment and spatial disorientation. Genetic testing confirmed a heterozygous missense mutation c.2149G>A (p.Val717Ile) in the amyloid precursor protein (*APP*) gene in the index patient (II2) and her daughter (III1). The family was referred for further genetic counseling.

Our family fulfills the diagnostic criteria of familial AD (FAD).[1] It was the fourth reported FAD family with the *APP*

Conflicts of interest: The authors have no conflicts of interest relevant to this article.

* Corresponding author. Division of Geriatric Medicine, Department of Medicine, Queen Mary Hospital, the University of Hong Kong, 102 Pokfulam Road, Hong Kong Special Administrative Region.
E-mail address: syf321@ha.org.hk (Y.-F. Shea).

http://dx.doi.org/10.1016/j.jfma.2014.11.003

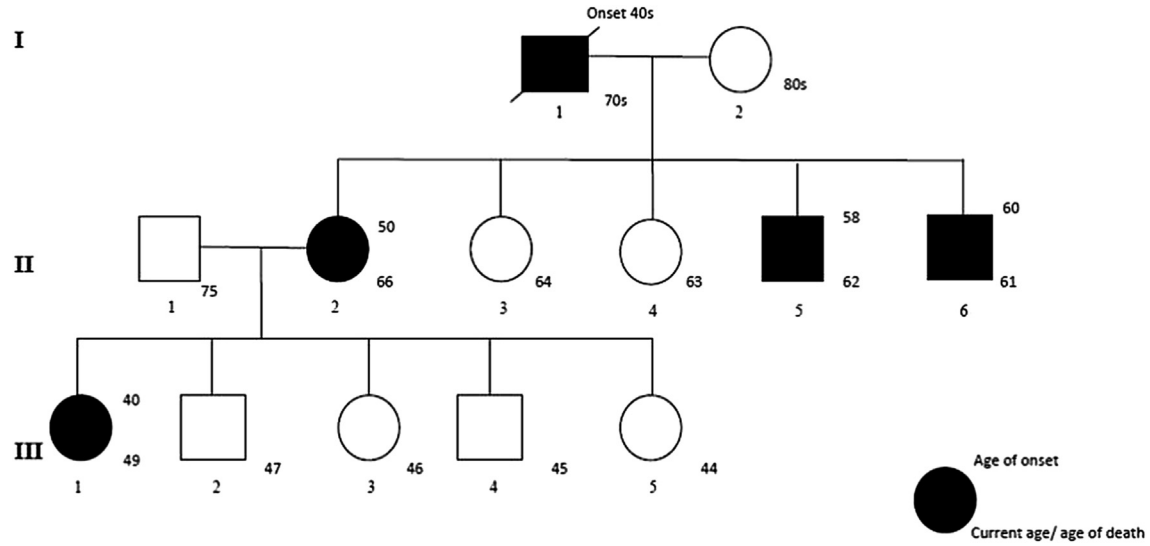

Figure 1 Pedigree of the family — squares and circles represent men and women, respectively. Affected individuals are indicated by filled symbols and unaffected individuals by open symbols. Current age, ages at onset, and age of death are shown.

mutation in Chinese people.[2,3] Within these four families, 14 patients were affected. The mean ages of onset and lifespan prior to death are 43 ± 7.0 years ($n = 13$) and 10.3 ± 5.8 years ($n = 6$), respectively. The mean MMSE on presentation was 12 ± 7.8 ($n = 3$). *APP* mutation Val717Ile is located near the γ-secretase cleavage site and hence increasing the production of Aβ42.[1] For Chinese FAD patients with the *APP* mutation, atypical phenotypes with prominent psychiatric manifestations including schizophrenic-like syndromes and behavioral and language variants had been reported.[2,3] Our family is characterized by prominent depression and one family member presented with prominent auditory hallucinations.

Our case illustrates that the clinician needs to pay attention to any new family members developing cognitive impairment, which may indicate EOAD, even when the initial family history appears unremarkable. The diagnosis of FAD is important, as the asymptomatic family members can undergo genetic counseling and consider genetic screening.[1,4] An asymptomatic carrier can consider planning their personal affairs ahead and receive appropriate treatment when they develop cognitive symptoms.

Acknowledgments

We would like to thank Dr. Kui-Kai Lau and Miss Joyce Ha for neurological and cognitive assessments of our patients and their opinion on improving the manuscript.

References

1. Wu L, Rosa-Neto P, Hsiung GY, Sadovnick AD, Masellis M, Black SE, et al. Early-onset familial Alzheimer's disease (EOFAD). *Can J Neurol Sci* 2012;**39**:436—45.
2. Peng XL, Hou L, Xu SH, Hua Y, Zhou SJ, Zhang Y, et al. Novel APP K724M mutation causes Chinese early-onset familial Alzheimer's disease and increases amyloid-β42 to amyloid-β40 ratio. *Neurobiol Aging* 2014;**35**:2657.e1—6.
3. Jiao B, Tang B, Liu X, Xu J, Wang Y, Zhou L, et al. Mutational analysis in early-onset familial Alzheimer's disease in Mainland China. *Neurobiol Aging* 2014;**35**:1957.e1—6.
4. Steinbart EJ, Smith CO, Poorkaj P, Bird TD. Impact of DNA testing for early-onset familial Alzheimer disease and frontotemporal dementia. *Arch Neurol* 2001;**58**:1828—31.