CASE REPORT
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A Case Report of a 37-Year-Old Alzheimer's Disease Patient with Prominent Striatum Amyloid Retention

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With recent advancement in amyloid imaging, diagnostic application of this new modality has become a great interest among researchers. New ligands, such as 18F- florbetaben, florbetapir and flutemetamol, have been discovered to overcome limitations of preexisting ligand Pittsburgh compound B. We report here a case of a 37-year-old male patient whose initial complaints comprised of gradual cognitive decline, apraxia, disorientation and sleep disturbances. 18F-Florbetaben amyloid imaging of the patient showed diffuse amyloid retention with prominent striatal uptake. This finding supports the clinical utility of amyloid imaging in diagnostic process of early-onset AD. Moreover, striatal dominant uptake pattern demonstrated in this patient include some meaningful clinical implications that warrant special attention among clinicians.
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Key Words Early onset Alzheimer's disease, Striatum, Amyloid retention.

INTRODUCTION

Amyloid deposition has long been considered one of the pathognomonic markers of Alzheimer's disease (AD). Moreover, disruption in amyloid hypothesis has been frequently discussed as important targets of intervention for many years.[1] To date, most validated research results have been narrowed down to yield a model for biological trajectory of AD, where amyloid deposition far precedes clinical symptoms.[2] Thus, early detection of amyloid deposition has emerged a major target of intervention in AD patients. In this regard, amyloid imaging has emerged as an effective diagnostic tool that could enable early intervention in patients in AD trajectory, and the clinical utility of amyloid imaging has become a main topic of interest among researchers over the recent years.[3] If validated further, clinical usage of amyloid imaging is expected to extend beyond confirming AD pathology in patients with high risk factors, helping to differentiate AD from various types of dementia in those who present with atypical course or symptoms.[4]

Pittsburgh compound B has been the first ligand used to detect amyloid deposition in AD patients.[5] However, its short half-life and resultant limitations in applying it to clinical setting have resulted in the development of new ligands for detecting amyloid deposition, such as 18F-florbetaben, florbetapir and flutemetamol.[6] Amyloid deposition usually initiates from temporal and orbitofrontal cortices, which later extends to frontal, parietal, precuneus, anterior and posterior cingulate cortices.[7] However, differential uptake patterns in autosomal dominant gene carriers have been noted that warrant special clinical attention. While typical amyloid deposition occurs from cortical structures, those with autosomal dominant gene carriers demonstrated initial amyloid deposition in striatum.[8,9]

We report here a case where a case of early-onset AD patient who received a confirmatory diagnosis of AD by beta-amyloid imaging. There is relatively few evidence on the clinical application of beta-amyloid imaging in early-onset AD patients, and therefore, we expect our case can contribute to this line of inquiry. Moreover, validity of utilizing beta-amy-

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loid imaging in differential diagnosis of dementias will be discussed.

CASE

A 37-year old male patient visited outpatient clinic, with complaints of gradual cognitive decline which had started 3 years earlier. Working as an industrial researcher, he started to make serious calculation mistakes that made him quit the job and began working as a manager in a company. However, his frequent forgetfulness, along with aggravation in recent memory impairments hampered him from fulfilling his duties, making him change jobs frequently. Apraxia and apathy had started 2 years before his visit to our clinic, and disorientation to time and person was worsened to a degree which it became impossible to commute daily between his workplace and home. At time of his visit to our clinic, not only he was fired from his recent job, but also he needed frequent reminder from his family to maintain hygiene. His sleep disturbance became prominent, frequently waking up middle of the night self-talking.

Before his visit to our clinic, he had visited two hospitals for evaluation and management of his symptoms, but to no avail. For a thorough examination of his symptoms, he was immediately admitted to our psychiatric ward. His laboratory findings did not reveal any abnormalities, and his tests for human immunodeficiency virus, syphilis all turned out to be negative. Upon his psychiatric admission, a neuropsychological test battery was implemented to evaluate the patient's cognitive status. He scored 22 in Mini-mental status examination, 1 in Clinical dementia rating scale (CDR),[10] and 4.5 in Clinical Dementia Rating-Sum of Box score(CDR-SB).[11] In his cognitive tests, in contrast to his relatively preserved language function, he displayed serious impairments in free recall, 20-minute delayed recall and recognition.

Brain magnetic resonance imaging demonstrated global cerebral atrophy of grade 1 by cortical atrophy scale[12] and notable medial temporal lobe atrophy of grade 2 by medial temporal lobe atrophy visual rating scale (Figure 1A and B).[13] Atypically early onset of dementia symptoms made the patient an eligible candidate for amyloid positron emission tomography (PET) imaging.[14] 18-Florbetaben PET images revealed diffuse amyloid deposition with score 3 in brain beta-amyloid plaque load (BAPL),[15] with predominant amyloid deposition in the striatum (Figure 1C and D).

The patient's history, along with neuroimaging results and cognitive test results all satisfied the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association Alzheimer's (NINCDS-ADRDA) criteria[16] for probable Alzheimer's disease with high level of evidence. 5 mg of donepezil was prescribed, and the patient was discharged on the 10th day of his admission. To control his persistent cognitive decline even after the discharge, donepezil was increased up to 23 mg with combination of memantine, which was also increased up to 20 mg. His cognitive decline has been relatively plateaued, but we advised the patient and his caregiver to regularly visit the clinic for monitoring of his symptoms.

DISCUSSION

This is one of the few case reports that demonstrated diagnosis of early-onset AD by 18F-florbetaben PET imaging. The patient demonstrated early onset of cognitive decline with accelerated deterioration. The fact that he meandered along various departments at different hospitals for confirmatory diagnosis reflect major role amyloid imaging played in the diagnostic process of the patient.

Amyloid imaging is usually indicated in patients with progressive MCI with dubious etiology, patients with atypical presentations and clinical course, and patients with early-onset progressive dementias.[14] Considering the patient in the case exhibited dementia symptoms at atypically early age, amyloid imaging was appropriately prescribed to diagnose the etiology of his cognitive decline. Integration of information attained from his history, clinical data indicated his diagnosis to be early-onset AD.

There have been relatively few reports utilizing 18F-labelled

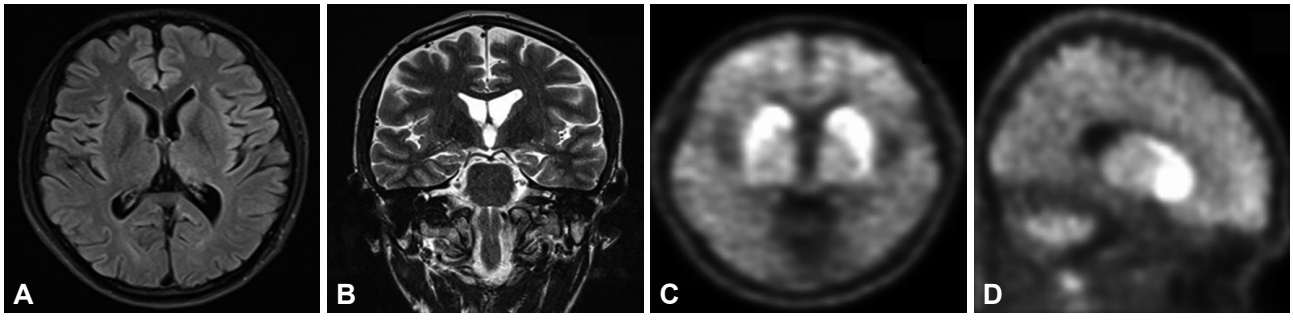

Figure 1. Brain magnetic resonance imaging of the patient. Fluid-attenuated inversion recovery (FLAIR) axial image (A), T2-weighted coronal image (B), and axial and sagittal images from amyloid imaging with 18F-florbetaben (C and D).

amyloid beta PET tracers that include clinical implications related to autosomal dominant AD. One study adopted 18F-florbetaben PET imaging in Down syndrome patients, suggesting potential role of amyloid imaging in identifying population at risk of dementia.[17] Similar study was conducted on patients with Down syndrome, but with 18F-florbetapir tracer.[18] An attempt to differentiate Down Syndrome pathology from AD has also been made with 18F-florbetapir tracer.[19] Future studies on autosomal dominant AD with 18F-labelled amyloid beta PET tracers could increase validity of adopting these new ligands in the diagnostic process.

Most notable test results in the case report arise from uptake patterns of 18F-florbetaben PET imaging. Unlike typical uptake patterns demonstrated by late-onset AD patients, where striatum is usually involved in the later course of illness, there was a dominant striatal uptake pattern in the patient. A previous study conducted on nondemented young adults with Down syndrome compared their results with that of studies conducted on autosomal dominant early-onset AD patients, where two groups of subjects concordantly showed predominant striatal uptake.[8] Indeed, previous studies on autosomal early-onset AD patients consistently showed high striatal amyloid deposition.[20,21] The aforementioned finding could explain 18F-florbetaben uptake patterns in the case.

The underlying mechanisms have been discussed in prior studies on the relatively early involvement of the striatum in autosomal dominant early-onset AD patients. Axonal mistrafficking induced by presenillin-1 gene mutation has been suggested as a potential culprit for striatal amyloid deposition in one animal study.[22] Such axonal mistrafficking is considered to stem from disruption in APP processing.[22] Indeed, APP processing patterns differed between autosomal dominant AD patients and sporadic AD patients.[23] Striatal vulnerability to early stages of tau protein accumulation in autosomal dominant AD has also been elucidated, and such phenomenon is considered more toxic to induce significant striatal neuronal injury.[24]

The most prominent limitation of our case report is lack of genotype testing in the patient. If the genetic testing had been done, one missing puzzle in the diagnosis of patient would have been complete. Nevertheless, we believe our case report affirms diagnostic usefulness and clinical application of amyloid imaging in the differential diagnosis of early-onset dementia. We expect more prevalent use of amyloid imaging with accumulation of evidences and validation studies over time.

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