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Slowly progressive amnesia without Alzheimer's disease features - SDAT mimics without radiological findings of Alzheimer's disease

Kasahata N[1]☼, Tamamoto F[2], Kato H[3]

1. Department of Medicine, Division of Neurology, Tokyo Metropolitan Ohtsuka Hospital, 2-8-1 Minamiohtska, Toshima-ku, Tokyo, 170-8476, Japan
2. Department of Radiology, Tokyo Metropolitan Ohtsuka Hospital, 2-8-1 Minamiohtska, Toshima-ku, Tokyo, 170-8476, Japan
3. Department of Laboratory Medicine, Tokyo Metropolitan Ohtsuka Hospital, 2-8-1 Minamiohtska, Toshima-ku, Tokyo, 170-8476, Japan

☼**Corresponding author:** Department of Medicine, Division of Neurology, Tokyo Metropolitan Ohtsuka Hospital, 2-8-1 Minamiohtsuka, Toshima-ku, Tokyo, 170-8476, Japan, e-mail: naoki_kasahata@tmhp.jp

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ABSTRACT

To describe a syndrome called "slowly progressive amnesia without Alzheimer's disease features" and to discuss this syndrome and its pathological background. We investigated 75 patients with dementia. We investigated the clinical characteristics, Mini-Mental Sate Examination score, magnetic resonance images (MRI) findings, and single photon emission computed tomography (SPECT) findings of these cases. Most cases showed clinical symptoms, sings MRI findings, or SPECT findings consistent with Alzheimer's disease. Seven patients lacked clinical and radiological Alzheimer's disease findings. Six of these seven patients studied were female. Six of these seven patients were over 65 years of age. This study encompasses patients with "slowly progressive amnesia" who lack clinical and radiological Alzheimer's disease features; and two subgroups of the patients. One subgroup exhibited lack of recognition of their son's faces, attitude of minding one's own business, and variability of symptoms; they showed medial frontal hypoperfusion of the cingulate gyrus on SPECT. The other subgroup showed predominantly anterograde amnesia, repeated the same behavior, and demonstrated untidiness; they showed frontotemporal hypoperfusion on SPECT. Autopsy findings of one case in the first subgroup case showed a neurofibrillary tangle-predominant dementia (NFTPD). We studied characteristic slowly progressive amnesia cases that lacked Alzheimer's disease features. We found at least two subgroups among these cases, one of which may be associated with NFTPD pathology.

Keywords: Amnesia, Alzheimer Disease, Neurofibrillary Tangle-Predominant dementia, Dementia with Grain, Single Photon Emission Computed Tomography (SPECT), Senile Dementia of Alzheimer Type (SDAT)

Abbreviations: NFTPD- neurofibirllary tangle-predominant dementia, SDAT- senile dementia of Alzheimer type, SPECT-single photon emission computed tomography

1. INTRODUCTION

After Mesulam's publication of cases of slowly progressive aphasia without generalized dementia (Mesulam, 1982), another syndrome has been demonstrated, called "slowly progressive amnesia" or "pure progressive amnesia" (Barbeau, 2006; Caselli 1998; Fossard, 2006; Gankam Kengne, 2009; Joubert, 2003; Kasahata, 2005; Knight, 2009; Rusconi, 1997; Terada, 1995; Tramoni, 2009). However, most cases have been published as case reports; the semiotics, radiological features, and neuropathological diagnosis of this clinical syndrome have not established (Barbeau, 2006; Caselli, 1998; Fossard, 2006; Gankam Kengne, 2009; Joubert, 2003; Kasahata, 2005; Knight, 2009; Rusconi, 1997; Terada, 1995; Tramoni, 2009). We intended to describe characteristics of slowly progressive amnesia syndrome and to discuss this syndrome and its pathological background.

Slowly progressive amnesia: Pure progressive amnesia is used for a rare form of Alzheimer's disease. However, we presented with slowly progressive memory disturbance cases caused by other than Alzheimer's disease in this article. Therefore we used slowly progressive amnesia in this article.

Alzheimer's disease (AD) can exhibit slowly progressive amnesia; however, it becomes generalized dementia. Patients with Alzheimer's disease predominantly display amnesia, wandering, apraxia, executive dysfunction, hallucination, and aphasia. Magnetic resonance images (MRI) of patients with AD exhibit medial temporal lobe atrophy and parietal lobe dominant cerebral cortex atrophy (Bankhof, 2007; Kubota, 2005). MRI findings of dementia with Lewy bodies (DLB) exhibit mild AD. MRI findings of other dementia are not established. Single photon emission computed tomography (SPECT) as well as positron emission tomography (PET), especially with three dimensional stereotactic surface projection (3D-SSP) or the easy Z-score imaging system (eZIS), of patients with AD exhibit decreased blood flow in the posterior cingulate gyrus and temporoparietal lobes (Ashford, 2000; Bartenstein, 1997; Bonte, 1997; Bonte, 2004; Imabayashi, 2004; Jagust, 2001; Kaneko, 2004; Kubota, 2005; Minoshima, 1997; Minoshima, 2001; Mito, 2005; Petrie, 2009; Shidahara, 2006). DLB exhibit generalized low uptake on SPECT/PET perfusion scan with reduced occipital activity (McKeith, 2005). SPECT findings of other dementia are not established.

Syndrome restricted to amnesia seems to correspond to pathology restricted to hippocampus or medial temporal lobe. Possible neuropathological backgrounds that can cause slowly progressive amnesia are neurofibrillary tangle-predominant dementia (NFTPD) and dementia with grains (DG), which have pathology restricted to medial temporal lobe. Moreover, frequent neuropathologies of mild cognitive impairment in Japanese are NFTPD and DG (Murayama, 2004; Saito, 2007). These neuropathological entities present with clinical features indistinguishable from AD, particularly senile dementia of Alzheimer type (SDAT), and clinical diagnoses are difficult.

NFTPD: Neurofibrillary tangle predominant dementia is a subset of late onset dementia. Neuropathology reveals abundant allocortical neurofibrillary pathology with no or few isocortical tau lesions, absence of neuritic plaques, absence or scarcity of amyloid deposits, but neurofibrillary changes comprising both 3 and 4 repeat.

NFTPD has also been called limbic neurofibrillary tangle (NFT) dementia, senile dementia of the NFT type; tangle only dementia, senile dementia with tangles, and tangle-predominant senile dementia (Bancher, 1994; Ikeda, 1997; Ikeda, 1999; Iseki, 2006; Jellinger, 1998; Jellinger, 2007; Tolnay, 2003; Yamada, 2001; Yamada, 2003). With only rare and mild involvement of the neocortex, basal ganglia, and brainstem, the absence of neuritic plaques, and the absence or scarcity of amyloid deposits, NFTPD features cerebral atrophy with neurofibrillary tangles almost solely limited to the limbic areas (Bancher, 1994; Iseki, 2006; Jellinger, 1998; Yamada, 2003). Clinical characteristics of NFTPD include a sporadic subset of very late onset of dementia with a preponderance of cases in females over 80 years of age, less severe cognitive impairment than AD (Jellinger, 1998; Jellinger, 2007). Therefore, NFTPD can predominantly present with slowly progressive amnesia.

DG has also been called dementia with grains or argyrophilic grain disease (Braak, 1998; Jellinger, 1998). DG exhibits macroscopic severe atrophy of the medial temporal lobe, most prominent in the ambient gyrus (Saito, 2002a, b). Clinical characteristics of DG are emotional and mood imbalance such as irritability and agitation, and amnesia or episodic memory loss (Braak, 1998; Ferrer, 2008; Ikeda, 2000; Togo, 2005). Therefore, DG can present with slowly progressive amnesia.

Consequently, at least two entities (NFTPD and DG) other than Alzheimer's disease can cause slowly progressive amnesia. MRI of these diseases may not show parietal atrophy, which is characteristic finding of AD. SPECT findings may be different from AD. However, differential diagnosis from AD is clinically difficult. Autopsy studies can confirm pathological diagnosis other than AD. We encountered seven cases of slowly progressive amnesia without AD features. We herein describe the characteristics of these cases and discuss the clinical features and underlying pathological changes.

2. MATERIALS AND METHODS

We investigated the cases of 75 patients who exhibited dementia, reported forgetfulness, or showed suspected cerebral degenerative disease on an imaging study from 2008 to 2011 at Tokyo Metropolitan Ohtuska Hospital. This

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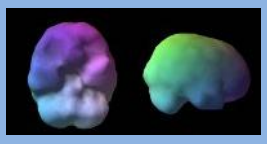
SPECT



We used 123I-iodoamphetamine (IMP) or ethyl cysteinate dimer (ECD) SPECT findings of all patients, with three dimensional stereotactic surface projection (3D-SSP) or the easy Z-score imaging system (eZIS). Patients with AD exhibit decreased blood flow in the posterior cingulate gyrus or temporoparietal lobes. DLB exhibit generalized low uptake on SPECT/PET perfusion scan with reduced occipital activity. SPECT findings of other dementia are not established.

was a retrospective review of data gathered clinical purpose. Subjects were enrolled in the study once they presented at the hospital for clinical reasons predominantly forgetfulness. Subjects were not on memory medication such as acetylcholinesterase inhibitors at the time of evaluation.

Clinical and Radiological Assessment

We investigated the clinical characteristics, Mini-Mental Sate Examination (MMSE) score, MRI findings, and 123I-iodoamphetamine (IMP) or ethyl cysteinate dimer (ECD) SPECT findings of all patients. We repeated these assessments every 1-2 years. Most cases exhibited symptoms and signs, or MRI or SPECT findings consistent with AD such as wandering, sensory aphasia, atrophy of the parietal lobe seen on an MRI scan, or posterior cingulate and/or temporoparietal hypoperfusion seen on a SPECT scan. We excluded these patients with radiological AD features. We excluded these patients consistent with PROBABLE Alzheimer's disease using NINCDS-ADRDA criteria (McKahnn, 1984). We also excluded patients suspected hippocampal sclerosis on MRI. However, 7 of 75 patients lacked both clinical features and radiological findings of AD. These subjects' characteristics are described in case reports (Table 1).

3. RESULTS

Clinical Characteristics and MMSE Score

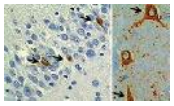
Six of the seven patients were female. Six of the seven patients were over 65 years of age. All patients reported forgetfulness and it was predominantly anterograde amnesia or encoding (memorization) disturbance (Table 1).

Cases 1 and 2 did not recognize their son's or grandson's faces. Cases 1 and 2 presented with attitudes of minding their own businesses. Cases 1 and 2 presented with a variety of symptoms daily; one day they seemed clear, and the next day they showed signs of dementia.

Cases 3 and 5 repeated the same behavior such as asking the same questions, buying the same things, and washing the same dishes because they had forgotten what they had done. Case 4 demonstrated retrograde amnesia. When case 4 was commanded to write, she continued writing until she was commanded to stop. Cases 4 and 5 demonstrated untidiness. Case 7 reported difficulty with putting events in sequence.

No cases showed hyperexcitability, wandering, apparent apraxia, apparent aphasia, or hallucinations. In most cases, the MMSE scores indicated within normal range, mild cognitive impairment or mild dementia (MMSE score 21-28). Case 4 showed moderate dementia (MMSE score 12/30) and case 3 showed severe dementia (MMSE score 4/30).

DG:



Dementia with grains, also referred to as argyrophilic grain disease, is a morphological condition in elderly individuals histologically characterized by the widespread occurrence of minute, spindle or comma-shaped arygryophilic, tau-immunoreactive structures that are predominantly located in the hippocampus and related limbic areas including the amygdala.

Magnetic Resonance Imaging Findings

All cases other than case 7 showed atrophy of the bilateral medial temporal lobes on MRI (Figure 1a, Figure 2a, Figure 3a, Figure 4a, Figure 5a, Figure 6a). Case 7 showed right side dominant medial temporal lobe atrophy (Figure 7a). Cases 1 and 3 also showed frontal lobe atrophy. All cases showed preserved or relatively preserved parietal lobes (Figure 1b, Figure 2b, Figure 3b, Figure 4b, Figure 5b, Figure 6b, Figure 7b).

Single Photon Emission Computed Tomography Findings

Cases 1 and 2 showed medial frontal hypoperfusion of the cingulate gyrus along the corpus callosum (Figure 1c, Figure 2c). The other patients showed frontotemporal or lateral frontal and temporal hypoperfusion (Figure 3c, Figure 4c, Figure 5c, Figure 6c, Figure 7c).

Neuropathological Findings of Case 1

Brain weight was 1,000g. Macroscopic findings included as follows: suspected atrophy of the bilateral frontal and left parietal lobes, and suspected atrophy of left ambient gyrus. Microscopic findings included as follows: neurofibrillary tangles detected abundantly in hippocampus and subiculum, and moderately in entorhinal cortex compatible for NFTPD. Senile changes included as follows: plaque: Braak A, tangle: Braak III (not match), NIA-AA grading: A1, B2, C1, and no Lewy bodies (Hyman, 2012, Thal 2002). Acute pontine infarction was noted. Atherosclerosis of internal carotid arteries and basilar artery was observed. Basilar artery was occluded by thrombus.

Table 1

Summary of clinical, MRI and SPECT findings

Patient	Age, sex	Clinical characteristics MMSE	MRI atrophy	SPECT findings
1	78, F 21/30	Did not recognize grandson's face, Variability, Attitude minding her own business	Bilateral MT	Bilateral cingulated gyri
2	87, F, 21/30	Did not recognize son's face, Variability, Unable to distinguish currencies, Attitude minding her own business	Bilateral MT	Bilateral cingulate gyri Bilateral operculum
3	95, M, 4/30	Severe antegrade amnesia, Forgot son's name	Bilateral MT dominant	FT
4	86, F, 12/30	Episodic amnesia, untidy	Bilateral MT	FT
5	70, F 24/30	Forgetfulness, untidy	Bilateral MT	FT
6	79, F, 26/30	Forgetfulness	Bilateral MT	Lateral FT
7	47, F, 28/30	Forgetfulness, Forget PIN code, Contextual memory disturbance	Right MT	Bilateral MT

Abbreviations

MRI: magnetic resonance imaging, SPECT: single photon emission computed tomography, MMSE: Mini-Mental State Examination, PIN: personal information number, MT: medial temporal, FT: frontotemporal

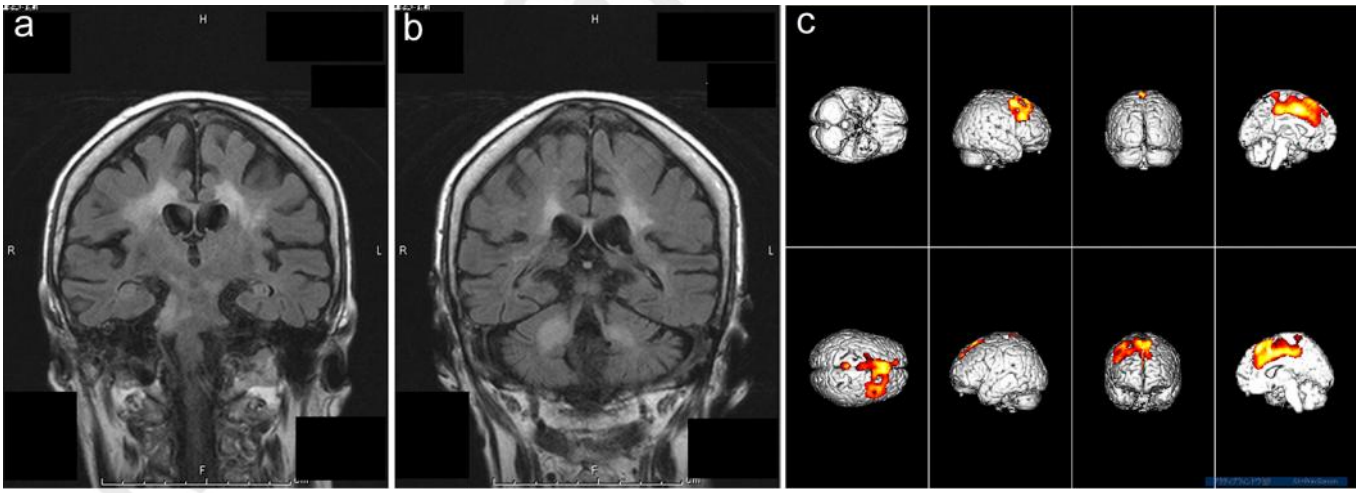


Figure 1

Magnetic resonance imaging and single photon emission computed tomography findings of case 1.

a) A fluid attenuated inversion recovery image. A coronal slice near the posterior comissure revealed mild atrophy of the hippocampus.

b) A fluid attenuated inversion recovery image. A coronal slice near the splenium of the corpus callosum revealed relatively preserved parietal lobes without remarkable atrophy.

c) The easy Z-score imaging system of ethyl cysteinate dimer-single photon emission computed tomography revealed decreased blood flow in the bilateral cingulate gyri along the corpus callosum and right precentral gyrus.

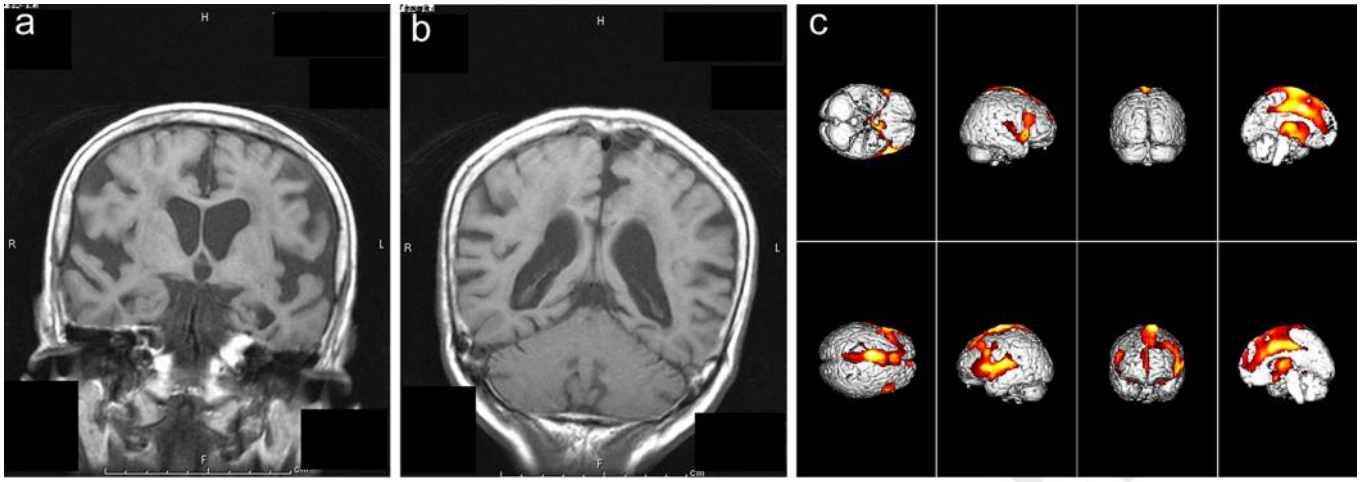


Figure 2

Magnetic resonance imaging and single photon emission computed tomography findings of case 2.

a) A T1-weighted image. A coronal slice near the mamillary body revealed atrophy of the bilateral medial temporal lobes, including the hippocampus.

b) A T1-weighted image. A coronal slice near the splenium of the corpus callosum revealed preserved parietal lobes.

c) The easy Z-score imaging system of ethyl cysteinate dimer-single photon emission computed tomography. The red (hot) color corresponded to decreased blood flow; decreased blood flow was found in the bilateral cingulate gyri along the corpus callosum and bilateral operculum.

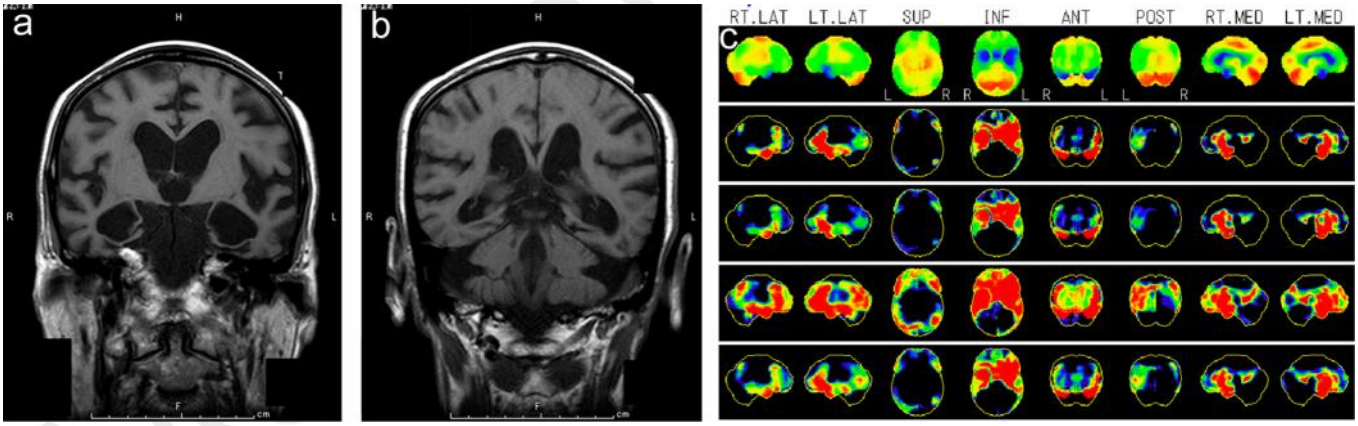


Figure 3

Magnetic resonance images and single photon emission computed tomography findings of case 3

a) A T1-weighted image. A coronal slice near the mamillary bodies revealed atrophy of the medial temporal lobes, the medial walls appeared very thin, and the inferior horns of the lateral ventricles were dilated.

b) A T1-weighted image. A coronal slice one slice posterior to the splenium revealed relatively preserved parietal lobes without remarkable atrophy.

c) Three-dimensional stereotatctic surface projection of iodoamphetamine-single photon emission computed tomography. Frontotemporal lobe blood flow was decreased while temproparietal blood flow was preserved.

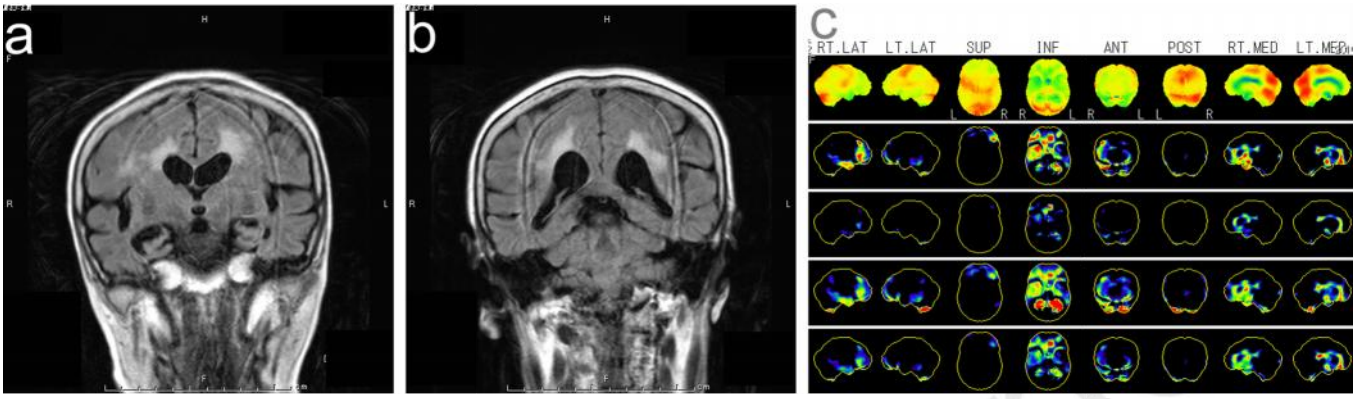


Figure 4

Magnetic resonance imaging and single photon emission computed tomography findings of case 4.

a) A fluid attenuated inversion recovery image. A coronal slice near the mamillary body revealed atrophy of the bilateral medial temporal lobes.

b) A fluid attenuated inversion recovery image. A coronal slice through the splenium of the corpus callosum revealed preserved parietal lobes.

c) Three-dimensional stereotactic surface projection of iodoamphetamine-single photon emission computed tomography revealed decreased blood flow in the bilateral frontotemporal lobes.

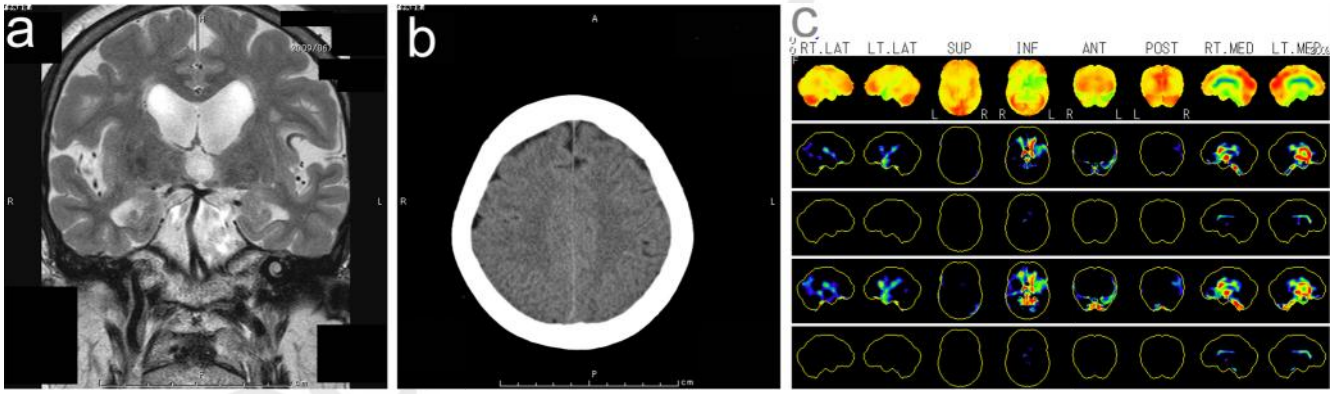


Figure 5

Magnetic resonance imaging, computed tomography, and single photon emission computed tomography findings of case 5.

a) A fluid attenuated inversion recovery image, coronal slice near the mamillary body revealed atrophy of the bilateral medial temporal lobes, including the hippocampus.

b) A computed tomography scan 7cm above the external acoustic meatus revealed preserved parietal lobes.

c) Three-dimensional stereotactic surface projection of iodoamphetamine-single photon emission computed tomography revealed decreased blood flow in the bilateral frontotemporal lobes.

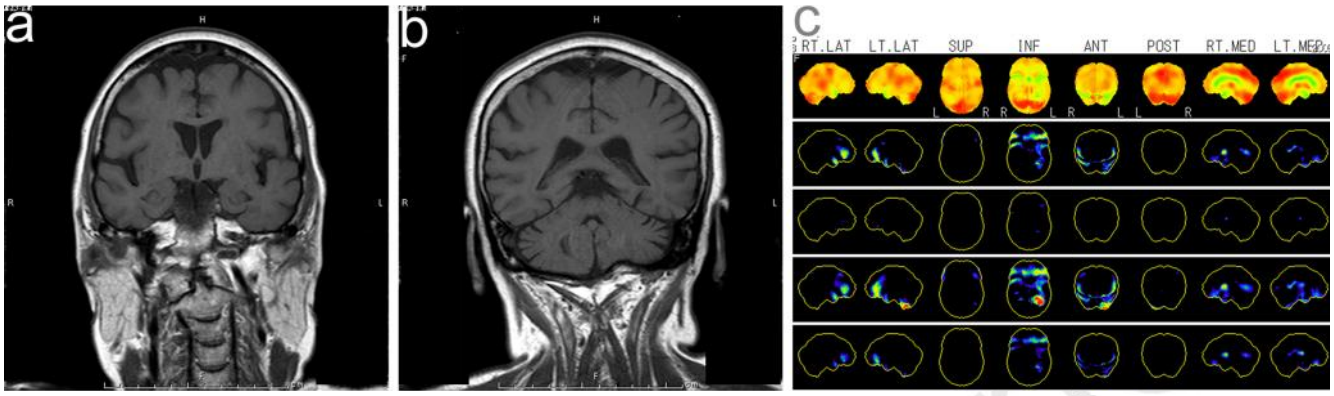


Figure 6

Magnetic resonance imaging and single photon emission computed tomography findings of case 6.

a) A T1-weighted image. A coronal slice near the mamillary body revealed mild atrophy of the bilateral medial temporal lobes.

b) A T1-weighted image. A coronal slice through the splenium of the corpus callosum revealed preserved parietal lobes.

c) Three-dimensional stereotactic surface projection of iodoamphetamine-single photon computed tomography revealed decreased blood flow in the bilateral frontal lobes.

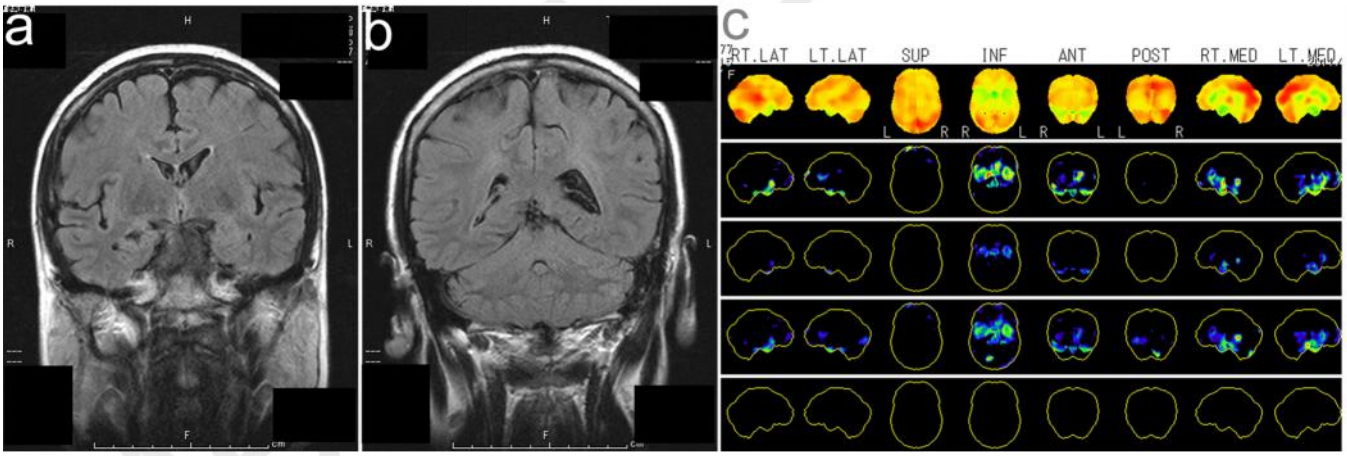


Figure 7

Magnetic resonance imaging and single photon emission computed tomography findings of case 7(a-c).

a) A fluid attenuated inversion recovery image. A coronal slice through the mamillary body revealed right hippocampal atrophy.

b) A fluid attenuated inversion recovery image. A coronal slice through splenium of the corpus callosum revealed preserved parietal lobes

c) Three-dimensional stereotactic surface projection of iodoamphetamine-single photon emission computed tomography. The red (hot) color corresponds to decreased blood flow; the blood flow in the medial temporal lobes was decreased.

Case Reports

Case 1

A 78-year-old woman came to this hospital because of forgetfulness. She was well until a few months earlier when her family noticed exacerbation of her previous forgetfulness. She forgot events that occurred 1 hour earlier. She did not recognize the face of her son. She remembered events from very long ago. She did not exhibit hyperexcitability. She was tidy. She maintained activity at a steady pace. She exhibited an attitude of minding her own business. She did not lose her way. Sometimes she was clear and at other times, she exhibited dementia.

In her 6th decade, she underwent a cholecystectomy to remove gall stones. At approximately 70 years of age, she underwent a cataract operation. Her family history was unremarkable. She did not drink or smoke. She worked as a housewife.

On examination, she was able to walk. She was disoriented regarding place. She was unable to calculate easy subtractions. Her triceps reflexes were normal bilaterally, although the remainder of her reflexes were absent. The remainder of the examinations was normal.

Her Mini-Mental State Examination (MMSE) score was 21/30. The MRI scan revealed atrophy of the bilateral medial temporal lobes and frontal lobes (Figure 1a, b). The ethyl cysteinate dimer (ECD) SPECT scan revealed decreased blood flow in the bilateral cingulate gyri along the corpus callous and right precentral gyrus (Figure 1c). After 2 years, she died of a pontine infarction. A neuropathological examination showed predominant NFTPD pathology.

Case 2

An 87-year-old woman came to this hospital because of forgetfulness.

She was well until approximately 3 months earlier when her forgetfulness worsened. She forgot events that occurred an hour earlier. She did not recognize her eldest son's face. She was unable to distinguish among currencies (1,000-yen notes, 5,000-yen notes, and 10,000-yen notes). She remembered events from the distant past. She did not show hyperexcitabilitly. She was tidy. She did things in her own way and she exhibited an attitude of minding her own business. She did not lose her way. She was clear on some days while she was not clear on other days. She did not develop hallucinations.

On examination, she was disoriented regarding place. She was unable to calculate easy subtractions. Her bilateral triceps reflexes were normal and the remainder of the deep tendon reflexes was absent. The remainder of the examinations was normal.

Her MMSE score was 21/30. The MRI scan revealed atrophy of the bilateral medial temporal lobes (Figure 2a, b). The ECD SPECT scan revealed decreased blood flows in the bilateral cingulate gyri along corpus callosum and bilateral operculum (Figure 2c).

Case 3

A 95-year-old man was admitted to this hospital because of vertigo.

He had been well until approximately 10 years earlier, when he began experiencing increasing forgetfulness. He had curiosity and asked how his son earned a living and how many grandchildren he had, but he immediately forgot the answers he was given. Thirty seconds after the answers, he repeated the same questions. He forgot his son's name. He walked every day. He took increasingly more time to come back home and his family had to look for him. Eventually, he was unable to come back home alone and his family walked with him. He did not wander around. He took a bath by himself. However, once he took a bath for a long time and his family had to check on him. He had forgotten he had washed and he washed himself repeatedly. He used to paint, but he did not want to paint and his ability to paint became worse. At 92 years old, he did not ask questions and his curiosity lessened. He was able to walk into a room until he was 94 years old. He walked with assistance. His consciousness fluctuated. He read the newspaper until 2 months previously. He did not exhibit easy excitability.

Thirty-five years earlier, he underwent a cholecystectomy. When he was young, he contracted pulmonary tuberculosis. His family history was unremarkable.

On examination, he was bed-ridden. He was disoriented regarding time and place. He was unable to calculate easy subtractions. His auditory comprehension was good. He was able to repeat sentences but he exhibited palilaria. Praxis and gnosis were difficult to determine because he did not obey the examiner's commands. He was able to state his birthdate and birthplace. He remembered the Kanto earthquake of 1923; his house was burned and he moved to Komagome (a town in Japan). He incorrectly stated his marriage age and the number of children he had. He was able to identify objects, but his visual field was difficult to examine. He exhibited ptosis. His soft palate did not elevate well. He exhibited normal bilateral biceps reflexes, decreased bilateral brachioradial reflexes, and areflexia of the remaining tendon reflexes. He exhibited no pathological reflex and his plantar responses were neutral. His coordination and sensory system could not be evaluated. The remainder of the examinations was normal.

His MMSE score was 4/30. The MRI scan revealed cerebral atrophy dominant in the medial temporal lobe with severe dilation of the inferior horns of the lateral ventricles (Figure 3a, b). The parietal lobes were relatively preserved (Figure 3b). The iodoamphetamine- (IMP) SPECT scan revealed decreased blood flow in the frontotemporal lobe (Figure 3c).

Case 4

An 86-year-old woman came to this hospital because of episodic amnesia. She was well until 6 months earlier when her memory suddenly began to have lapses. She forgot her son's name, although she knew it the previous month. She did not understand that the place was Tokyo. She confused Tokyo with Okayama, where she had been born and had lived until she was 36 years old. She was able to memorize new things. Her symptoms became worse in the evening. She repeated the same stories especially about her former workplace where she had worked as a head nurse. She did not lose her way. She cried out of loneliness when her son was absent. She had become untidy.

On examination, she was disoriented regarding time and the reflexes of her lower extremities were absent. When she was commanded to write, she continued writing long sentences until she was commanded to stop. The remainder of the examinations was normal.

Her MMSE score was 12/30. The MRI scan revealed atrophy of the bilateral medial temporal lobes (Figure 4a, b). The IMP-SPECT scan revealed decreased blood flow in the frontotemporal lobes (Figure 4c).

Case 5

A 70-year-old woman came to this hospital because of forgetfulness.

She was well until the previous autumn when her daughter noticed her forgetfulness. Thereafter, her husband, who lived with her, paid attention to her forgetfulness. She had a grandchild born in October. She was unable to recall her grandchildren's birthdays or their ages. She forgot putting something into the refrigerator after shopping. She bought things such as jam that she had already bought. She had been taking care of her stepmother. After her stepmother was admitted to the hospital in February, the woman's forgetfulness became more apparent. She recognized that she no longer needed to prepare her stepmother's food and she recognized her stepmother's hospitalization. She recognized that she had grandchildren. She was able to recount events from 10 to 20 years earlier. She neither lost her way nor wandered around. She did not exhibit hyperexcitability. She became slightly untidy. Now she cleans dishes after some time, although she previously cleaned dishes immediately.

On examination, she was able to walk. She was disoriented regarding time. The remainder of the examinations was normal.

Her MMSE score was 24/30. The MRI scan revealed atrophy of the bilateral medial temporal lobes and preserved parietal lobes (Figure 5a, b). The IMP-SPECT scan revealed decreased blood flow in the basal frontal lobes and temporal lobes (Figure 5c).

Case 6

A 79-year old woman came to this hospital because of forgetfulness.

She was well until approximately 6 months earlier when she forgot something she had heard when she was asked about it. She sometimes forgot what she had said. She did not have difficulty performing her activities of daily living.

On examination, she was able to walk. She was disoriented regarding time. She exhibited generalized areflexia, although her triceps reflexes were normal. The remainder of the examinations were normal.

Her MMSE score was 26/30. The MRI scan revealed mild atrophy of the bilateral medial temporal lobes (Figure 6a, b). The IMP-SPECT scan revealed decreased blood flow in the lateral frontal lobes and temporal lobes (Figure 6c).

Case 7

A 47-year-old woman came to this hospital because of forgetfulness.

She was well until 6 years earlier when she experienced increasing forgetfulness. Her forgetfulness became so severe that her daily life was disturbed approximately 1 month before she sought medical care. She forgot the two-digit personal identification number code for her gym locker. She was unable to make a distinction between the day's events and the previous day's events. After she put objects away, she was not able to find where they were.

On examination, she was able to walk. Her orientation was good but she was not able to calculate easy subtraction. The remainder of the examinations was normal.

Her Mini-Mental State Examination (MMSE) score was 28/30. The MRI scan revealed atrophy of the right medial temporal lobe (Figure 7a, b). The IMP-SPECT scan revealed decreased blood flow of the bilateral medial temporal lobes (Figure 7c).

4. DISCUSSION

In this study, among 75 patients with clinical dementia, seven (six females, six over age 65) showed slowly progressive amnesia without clinical and neuroimaging AD findings. All patients reported forgetfulness and demonstrated predominantly anterograde amnesia. Case 4 demonstrated retrograde amnesia. All cases exhibited bilateral or unilateral medial temporal lobe atrophy without apparent parietal atrophy. These cases could be subdividied into two groups. In the first group, cases 1 and 2 shared common features: they did not recognize their sons' faces, their symptoms varied daily and they showed medial frontal hypoperfusion on SPECT. The other cases (cases 3-7) showed frontotemporal hypoperfusion. However, case 7 was too young to suggest an age associated neurodegenerative disease. One of the first group patients (case 1) showed NFTPD pathology at autopsy.

This study demonstrated the following: 1) we found a group of patients with characteristic amnesia, called "slowly progressive amnesia", who lack clinical and radiological Alzheimer's disease features; 2) in this group are two subgroups. The patients in one subgroup (cases 1, 2) did not recognize their sons' faces, showed symptoms that varied daily, and exhibited medial frontal hypoperfusion of the cingulate gyrus along the corpus callousm on SPECT. Patients in the other subgroup (cases 3-6) showed predominantly anterograde amnesia, repeated the same behavior, demonstrated untidiness, and exhibited frontotemporal hypoperfusion on SPECT. Autopsy findings of a patient in the first subgroup demenostrated NFTPD.

Pure progressive amnesia:
Pure progressive amnesia, a form of progressive focal cortical atrophy is thought to represent stages of a rare form of Alzheimer's disease.

Previous descriptions of similar cases have been reported as case reports and have been predominantly reported as cases of "pure progressive amnesia" (Barbeau, 2006; Caselli, 1998; Fossard, 2006; Gankam Kengne, 2009; Joubert, 2003; Kasahata, 2005; Knight, 2009; Rusconi, 1997; Terada, 1995; Tramoni, 2009). Clinical characteristics of the cases in previous reports were recent memory defect, disorientation regarding time, working memory deficit, deficits tests based on recognition and recall, and deficit in the storage of context-free information, along with severe recognition memory impairment, 2) semantic amnesia, and 3) subjective impairment of episodic memory (Barbeau, 2006; Caselli, 1998; Fossard, 2006; Gankam Kengne, 2009; Joubert, 2003; Kasahata, 2005; Knight, 2009; Rusconi, 1997; Terada, 1995; Tramoni, 2009). The second subgroup patients in our study, who presented with predominantly memorizing disturbance, matched those in previous reports with recent memory defect and disorientation regarding time. However, the semiotics of the first subgroup in this study has not been reported. The MRI findings of patients in previous reports are temporal or medial temporal atrophy and our patients also showed medial temporal atrophy; only one patient showed right side (unilateral) temporal atrophy and other patients showed bilateral temporal atrophy. The SPECT findings of patients in previous reports indicated frontotemporal hypoperfusion. The second subgroup of our study also showed frontotemporal hypoperfusion, while the first subgroup showed medial frontal hypoperfusion of the cingulate gyrus along the corpus callosum. Neuropathological and genetic diagnoses in previous studies were AD and familial AD (Caselli, 1998; Gankam Kengne, 2009; Knight, 2009). Neuropathological examination revealed a case of NFTPD in one patient in the first subgroup. Therefore, the second subgroup might correspond to DG.

The limitation of the study is the small number of patients and the lack of neuropathology in the second subgroup. Because the other patients are still alive, pathological diagnosis is not possible. Neuropsychological testing may be insufficient. However, in spite of these limitations, there are cases of slowly progressive amnesia without Alzheimer's disease features and they may be divided into two subgroups. Paying attention to this syndrome might enable to make clinical diagnoses of NFTPD and DG, which have been SDAT mimics.

5. CONCLUSION

We revealed cases of characteristic slowly progressive amnesia that lack AD features. These cases may be divided into two subgroups and one of these subgroups may be associated with NFTPD pathology.

SUMMARY OF RESEARCH

1. Seven patients among 75 dementia patients lacked clinical and radiological Alzheimer's disease findings.
2. These patients were divided into two subgroups of the patients.
3. One subgroup exhibited lack of recognition of their son's faces, attitude of minding one's own business, and variability; they showed medial frontal hypoperfusion of the cingulate gyrus on SPECT.
4. The other subgroup showed anterograde amnesia, repeated the same behavior, and demonstrated untidiness; they showed frontotemporal hypoperfusion on SPECT.
5. Autopsy findings of one case in the first subgroup case showed a neurofibrillary tangle-predominant dementia.

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FUTURE ISSUES

Autopsy findings of slowly progressive amnesia patients will confirm pathological background of these patients and might enable to diagnose NFTPD or AGD.

DISCLOSURE STATEMENT

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