

An eighty-two year-old man clinically diagnosed with argyrophilic grain disease

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Abstract

We reported an eighty-two year-old man who was clinically diagnosed as having argyrophilic grain disease. He first showed signs of amnesia at age eighty. He easily misplaced things, and forgot having moved things in the first place. He also showed mild irritability and agitation. His brain MRI revealed frontal and temporal lobe atrophy, which was relatively dominant in the anterior and medial parts of temporal lobes. Brain SPECT also showed the hypo-perfusion in the same lesions shown by MRI. We clinically diagnosed him as having argyrophilic grain disease and discussed how we should go about differentiating his disease from Alzheimer's disease.

Keywords : Argyrophilic grain disease, Alzheimer's disease, Fronto-temporal lobar degeneration, Differential diagnosis, Brain MRI, Neuropathology

Introduction

Fronto-temporal lobar degeneration (FTLD) is a term used to represent various diseases. FTLD is a common syndrome, ranking in prevalence below Alzheimer's disease [1]. Pathological lesions associated with FTLD are initially found in the frontal lobes or temporal lobes. FTLD was clinically classified by Snowden et.al [2]. Recently, FTLD has been classified based on abnormal proteins which are accumulated in neurons or glia cells [3]. FTLD-tau is a subgroup of FTLD, a characteristic of which is the abnormal accumulation of tau in neurons or glia cells. Pick's disease, progressive supranuclear palsy, cortico-basal degeneration and argyrophilic grain disease (AGD) have been included in this sub-group [3]. Argyrophilic grain disease is a common sporadic neurodegenerative

disease of old age characterized by the presence of argyrophilic grains (AGs) initially found in the ambient gyrus and from there spreading to anterior and medial temporal lobes and anterior lobes [4]. Amnesia is the most common initial symptom, with irritability and agitation also being common as initial symptoms. In contrast to the severity of amnesia, other cognitive functions are relatively spared, and the sensorimotor symptoms are not remarkable [5,6]. Differential diagnosis from Alzheimer's disease (AD) is critical because the progression of AGD is slower than that of AD. Alzheimer's disease may show amnesia, irritability and agitation as initial symptoms. We could not make a definite clinical diagnosis and it is necessary to prove the existence of argyrophilic grains in the patient's brain. In this paper, we show a patient who was clinically diagnosed

as having AGD and discuss a method to clinically differentiate a diagnosis of AGD from a diagnosis of AD.

Case report

The patient was an eighty-two year-old man who had been a forestry worker. His chief complaint was amnesia. His family history showed nothing in particular and he was not the product of consanguineous marriage. The past history showed chronic otitis media and his hearing ability was bilaterally severely disturbed. He began losing his memory from the age of eighty years old. He was unable to remember where he had placed things. He did not show hallucination or delusion but his character seemed to change. His family members noticed he had become irritable, agitated and stubborn. They took him to nearby hospital, where he was suspected to be suffering from dementia and referred to our hospital.

His general condition was not bad.

His blood pressure was 142/83 mmHg. Neurologically, his consciousness was alert but he was not sufficiently aware of his own amnesia. His hearing ability was disturbed bilaterally. His motor function was not disturbed. Muscle tonus was normal. Deep tendon reflexes were normal. Sensory function was not disturbed. Coordination was normal. No involuntary movement was seen, nor epileptic symptom.

MMSE showed 16/30; for question 1 "orientation of time" he scored 0/5, question 2 "orientation of place" 2/5, question 4 "subtraction" 2/5, and question 5 "remember names of three things" 0/3 and other questions were answered properly. He showed a normal attitude when he was seen by a doctor but he became very angry when he was given a WAIS test by a speech therapist. He complained that he could not bear receiving various tests and he insisted that he would not visit any hospital again.

His peripheral blood count showed no abnormality and his blood chemistry was also normal. His thyroid function was normal and his blood vitamin B12 level was normal. His MRI findings showed atrophy of the frontal and temporal lobes, especially the anterior and medial parts of both

temporal lobes (figure 1). VSRAD level was 3.6 [7]. His brain SPECT revealed the hypo-perfusion of the same lesions shown by MRI. He refused to check his liquor amyloidbeta42 protein, total tau and phosphorylated tau concentration. We clinically diagnosed him as having argyrophilic grain disease. We prescribed galantamine tablets for his symptoms. Two months later, his daughter visited us and said that his irritability, agitation and stubbornness were slowly becoming worse. Although he continued to insist that he never visit any hospital again, he took a pill every day. We prescribed memantine tablet in combination with galantamine tablet. His main symptoms were still amnesia, irritability, agitation and selfishness. He showed no speech disturbance, agnosia nor apraxia.

Discussion

Argyrophilic grain disease is the name of a syndrome based on the pathological findings. Many argyrophilic grains (AGs) were observed mainly in the limbic system in the brain [5,6]. AGs are common pathological findings next to senile plaques and neurofibrillary tangles in the brains of aged people. The diagnosis of AGD is applied to cases when only argyrophilic grains seem to be responsible for a demented condition [8]. AGs are stained clearly by anti-tau antibody, so it is classified in FTLD-tau [8]. AGD is not an uncommon disorder. The onset age of AGD patients is relatively older than that of Alzheimer's disease. The initial and main symptom is amnesia, while other cognitive functions seem to be spared. In addition to amnesia, irritability, agitation and selfishness are initial psychological symptoms [5,6]. The disease progression is thought to be slower than that of Alzheimer's disease [8]. MRI findings of AGD show mainly the atrophy of the anterior and medial parts of the temporal lobes. In addition, other lesions of the temporal lobes and frontal lobes also can be atrophic [5,6,8]. SPECT of AGD shows hypo-perfusion in the medial side of the temporal lobes. On the other hand, in Alzheimer's disease, hypo-perfusion is seen in the lateral side of temporal lobes and

posterior cingulate gyrus. Although AGD shows these clinical characteristics, many AGD patients can be misdiagnosed as having Alzheimer's disease [8].

This patient showed amnesia at the age of eighty but he did not show speech disturbance, agnosia nor apraxia. His character had been well-behaved and patient. Over time he became irritable, agitated and selfish. MMSE revealed normal spatial perception but revealed memory disturbance. MRI study showed the atrophy of anterior and medial lesions of both temporal lobes. Other lesions of the frontal and temporal lobes were also mildly atrophic. SPECT study showed hypo-perfusion in the same lesions shown by MRI. We clinically diagnosed him as suffering from AGD [5,6].

Pick's disease and Alzheimer's disease should be differentiated from AGD.

The symptoms of Pick's disease include difficulty in speech and thinking, behavioral changes, impaired regulation of social conduct, passivity, over-activity, pacing and wandering [9]. Onset age of Pick's disease is younger than that of AGD.

A distinguish feature seen on an MRI is local atrophy of the temporal lobe or frontal lobe. Based on these clinical features, Pick's disease can be differentiated from AGD. Typical AD symptoms include amnesia and other cognitive disturbances such as executive function, spatial perception, and speaking function. Characteristic MRI findings of Alzheimer's disease show the atrophy of para-hippocampal area and posterior region of the parietal lobe. Distinguishing SPECT findings of Alzheimer's disease are hypo-perfusion of posterior cingulate gyrus, precuneus and lateral side of temporal lobe. If we are able to check the patients' liquor, we can examine amyloidbeta protein, total tau and phosphorylated tau concentration. AD pattern of these three proteins show decreased amyloibeta, increased total tau and phosphorylated tau. On the other hand, in AGD, amyloidbeta is normal or decreased and phosphorylated tau is not increased [8]. If we could examine FDG-PET, AD will show hypo-metabolism in the lateral side of the parietal lobe, and

AGD will show hypo-metabolism in the medial side of the temporal lobe [8].

Based on these clinical and neuroimaging data, we may be able to clinically differentiate AGD from AD.

Although AGD may be differentiated from typical AD, AD may represent various types of clinical symptoms. Johnson JK et al. reported frontal variant of Alzheimer's disease [10]. Murray ME et al. reported limbic-predominant AD subtypes [11]. In his patient, liquor amyloidbeta42, tau, and phosphorylated tau showed typical AD pattern. When we diagnose patients who are strongly suspected to have AGD, we should precisely record sufficient clinical features and examine liquor amyloidbeta, tau, and phosphorylated tau concentration. The pathological examination for the patients clinically diagnosed with AGD is thought to be indispensable in establishing the accurate clinical diagnosis method and establishing the knowledge of relationship between clinical features and pathological findings of AGD. The therapy for the patients with AGD has not yet established. We may practically prescribe drugs for AD to the patients with AGD. The detailed clinical records and pathological findings may also contribute in establishing the remedy for AGD.

The patients were proved to have barely understood what was involved in a clinical trial until they participated in one. In other words, when recruiting future subjects, it is important to explain the investigational meaning and the details of the investigation clearly.

The investigational need in the social life got possible to understand only after they participated in a trial. Most subjects felt clinical trials were for "the development of better therapy". Similarly, the thing that was regarded as important on the occasion of trial participation, "the expectation to a new medicine" is big. The subjects were almost able to understand the explanation of the medical staff. If they found it hard to understand the explanation, they seem to have participated in trials based on their trust in medical staff. As for the image after clinical trial participation at our hospital, an affirmative opinion was quite partial. It is very important that consciousness for the

clinical trial of subjects is analyzed in investigational promotion. Consciousness investigation has been accomplished so far in various kinds of institutions [1,2]. These results are intended to be utilized for service and publicity work for subjects taking part in clinical trials in the future.

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