

# Diagnosis of Dementia

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## Abstract

Currently, there are a few reliable biomarkers for identifying the main underlying causes of dementia and it is very difficult to use them in daily clinical work. Therefore, it is very important to identify disease-specific symptoms from a detailed history taking and medical examination of the patient after correctly understanding the pathology of each disease in order to make a comprehensive diagnosis with the help of imaging tests and other modalities. In this paper, the differential diagnoses of dementia and similar conditions, in particular senile depression and delirium, are described first, followed by the diagnostic steps on the basis of symptomatology and outlined the underlying causes of dementia. Subsequently, the symptomatology of Alzheimer's disease (AD) is discussed in detail, as correct diagnosis of AD is the basis of dementia diagnosis and AD accounts for approximately half of all dementia cases. As for causes of dementia other than AD, important points for differential diagnosis, particularly with regard to AD, are also mentioned.

**Key words** Symptomatology, Dementia, Depression, Delirium

## Introduction

Owing to an increased interest in society in dementia and advancement in treatment methods, there is an increasing need to accurately diagnose dementia at an early stage of the disease more than ever. Furthermore, different disease-specific treatment and caring strategies are recommended for different causes of dementia, increasing the importance of correctly diagnosing different types of dementia in the field of long-term care as well as medicine. However, only a few reliable biomarkers currently exist for identifying the main underlying causes of dementia, including Alzheimer's disease (AD). Therefore, it is very important to identify disease-specific symptoms from a detailed history taking and medical examination of the patient after correctly understanding the pathology of each disease in order to make a comprehensive diagnosis with the help of imaging tests and other modalities.

In this paper, the diagnostic steps for dementia developed on the basis of symptomatology are

outlined. Because AD accounts for approximately half of all dementia cases and its proper diagnosis is the basis of dementia diagnosis, important points for differential diagnosis particularly with regard to AD are also briefly described for causes of dementia other than AD.

## Diagnosis of Dementia

Prior to identification of the underlying cause of dementia, the first necessary step is to ascertain if the elderly patient suspected of dementia who visits a physician for examination for the first time does, in fact, have dementia. This step involves differentiating dementia from other conditions that are similar to dementia.

Patients with dementia have significantly reduced awareness of conditions, such as memory impairment, i.e., low insight into the disease. Therefore, the patient very rarely visits a physician for consultation or examination alone, except during the very early stages of the disease. On most visits, the patient will be accompanied by

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a family member. The characteristic of memory impairment as observed in dementia (especially in AD) is to forget an event itself. On the other hand, a person who is forgetful due to normal aging has sufficient awareness and often visits a physician alone. The characteristics of memory impairment include inability to remember people's names or dates on the spot. When a patient visits a physician for the diagnosis or treatment of dementia or "forgetfulness," the physician should first ask the patient to state the purpose of his/her visit in order to estimate the gap between the patient's words and those of his/her caregiver, so that the physician can confirm the patient's awareness about having dementia or memory impairment.

#### Differential diagnosis of senile depression

Senile depression is often accompanied by cognitive dysfunction. In many cases, complaint of sadness is not evident; however, hypochondriasis and somatic concern such as insomnia, stiff shoulders, and general malaise are obvious. Consequently, senile depression is frequently misdiagnosed as an early stage of dementia. In the revised Hasegawa's dementia scale (HDS-R) or mini-mental state examination (MMSE), patients with senile depression often have scores similar to those obtained by patients in the early stages of dementia; therefore, the total score of such assessment scales cannot be used to differentiate between depression and dementia.

A patient's awareness of his/her disease is another clue for differentiating between depression and dementia. A patient with depression often complains of his/her forgetfulness in an exaggerated manner rather than objectively stating his/her self-assessment. It is also important to confirm if the patient has a past history of depression or manic states. However, diagnosing the early stages of dementia is challenging even for a specialist because it is often accompanied by a state of depression. When in doubt, a physician should consider referring the patient to a specialist.

#### Differential diagnosis of delirium

Delirium should be first suspected if the patient shows a change in the level of consciousness or cognitive functions, or experiences visual hallucination/illusion. The possibility of an underlying condition, including electrolyte abnormalities, a

trend of circadian rhythm reversal, or prescription drug use (e.g., anti-anxiety drugs, antidepressants, and diuretics), should be considered. When drug-induced delirium is suspected, always check if more than one medical institution is prescribing similar drugs or if the patient is taking the medication as directed by the prescribing physicians. When drug-induced delirium due to benzodiazepines, tricyclic depressants,  $\beta$ -blocker,  $H_2$  blocker, furosemide, or solifenacin succinate is suspected, immediately consider switching to an alternate drug with a different mechanism of action.

Dementia can be accompanied by delirium. Hence, the diagnosis must be made carefully. The priority is to treat the delirium; once the patient's delirium improves, the presence of dementia should be verified.

#### Differential Diagnosis of Dementia and Disease-Specific Treatment

The next step involves the differential diagnosis of the underlying causes of dementia and the implementation of disease-specific treatment and care.

#### Dementia with a possibility of radical treatment (reversible causes of dementia)

First, a physician must examine the possibility of radical treatment for a given case of dementia. Radical treatment is available in approximately 10–20% of all dementia cases, but the dementia in these cases may have many different underlying causes. One difference in dementia caused by degenerative diseases such as AD (which will be discussed next) is its rapid progression. If a symptom is rapidly deteriorating over a few months, a physician should first suspect potentially reversible causes of dementia.

A head CT or MRI is essential in the diagnosis of neurosurgical diseases such as chronic subdural hematoma, normal pressure hydrocephalus, or brain tumor. Chronic subdural hematoma is strongly suspected if the patient has had a head contusion from falling, which is often undetectable during examination, and has experienced a rapidly progressive decline of cognitive function over a period of a few weeks to a few months. If a hematoma is applying pressure to the brain, the hematoma must be surgically removed immediately. In cases of idiopathic normal pressure

hydrocephalus, a patient often shows the 3 classic characteristics of gait disturbance, urinary incontinence, and memory impairment, and the coronal image from MRI shows narrowing of the subarachnoid cavity in the higher part of the fornix and the median as well as dilatation of the sylvian fissure.

Even if there is no underlying disease of the brain, it is important to address the possibility of social withdrawal due to environmental changes or disuse syndrome, which can emerge from prolonged mild physical disease such as common cold or lower back pain. In modern Japanese society, many elderly people live alone, and there are families in which the elderly are left alone at home during the daytime. A small trigger such as a mild illness can lead to reduced mental functions (e.g., lack of motivation, lowered concentration or attention) and a decline in physical functions (e.g., reduced stamina, fatigability, dizziness on standing up). If left untreated, the elderly may fall into a vicious circle of “do not want to do much” to “do not want to do anything” and “too weak to do anything,” and eventually suffer from dementia or become bedridden. Sufficient attention must be paid to such patients as dementia caused by AD or vascular dementia (VaD) (which will be discussed later in this paper) can accompany such disuse syndrome and will aggravate the symptoms further.

The best course of treatment is to break this vicious circle, that is, to take advantage of the national long-term care insurance and use the daytime care/nursing service or rehabilitation service in a short and intensive manner for improving the activity level. In such cases, the primary physician must inform the person in charge of the care or rehabilitation program of the patient’s reason for using the service.

## Alzheimer’s disease

### Cognitive dysfunction

The degenerative process of AD normally begins in the medial regions of the temporal lobe such as the hippocampus and parahippocampal gyrus, and subsequently spreads to the parietal and the temporal association area. Due to these lesions, the cognitive dysfunction caused by AD that manifests the earliest is the impairment of recent memory, which becomes the core symptom of AD. People in association with the patient in his/her everyday life commonly notice the change

through symptoms such as repeated forgetting of appointments, inability to remember where personal belongings (e.g., wallet or a pair of glasses) are kept, or repetition of the same conversation. A physician can verify such memory impairment during an examination if the patient cannot remember the name of their attending physician 5 min after being asked to recollect it, or if the patient cannot remember what he/she had for dinner the previous night.

As the degenerative process of AD advances, the manifestation of other cognitive dysfunctions, such as visual/constructional impairment, language disorder, dyscalculia, dysgraphia, which are the symptoms of the parietotemporal lobe disorder, follows memory impairment. Visual/constructional impairment is a disturbance in visuospatial ability, which can be examined by asking the patient to replicate figures or imitate finger patterns. Another common symptom observed in the relatively early stages of dementia is a disturbance in executive functions, i.e., the ability to properly respond to problems and challenges that arise in various everyday situations and to solve them. The patient also begins to have difficulty completing complicated tasks such as work and cash management, cooking, and bank transactions.

### Psychiatric symptoms and behavioral disorders

Psychiatric symptoms and behavioral disorders have been previously described as peripheral symptoms of dementia in Japan. Now, they are referred to as behavioral and psychological symptoms of dementia (BPSD), and their treatment and management is gaining attention.

In AD, apathy (reduced spontaneity and lack of interest) is believed to emerge in 70–80% of patients during the early stages of the disease, and they are considered to be the most common psychiatric symptoms. When a patient develops apathy, he/she often shows reduced spontaneity and motivation as well as a lack of interest and concern for the surroundings; his/her own low levels of spontaneity and motivation do not appear to afflict or concern the patient. Depression, a mood disorder, is another symptom that is commonly exhibited during the early stages of the disease. Delusion is also commonly exhibited in the early stages of the disease; the most common delusion is to imagine oneself as a theft victim (delusions of theft). On the other hand, the frequency of hallucinations is much lower

than that of delusion.

Wandering behavior, agitation, and irritability become evident in the middle and later stages of AD, and the patient often shows hyperactivity, restlessness, and repetitive behaviors of walking back and forth and opening and closing a drawer.

#### **Neurological symptoms**

In AD, focal neurological symptoms are rarely observed in the early stages except in some cases of familial AD. The presence of parkinsonism must be examined by signs of solidification in the wrist, which is also helpful in differentiating it from other diseases such as dementia with Lewy bodies (DLB) or corticobasal degeneration. In the progressive stage of AD, the patient exhibits neurological symptoms such as parkinsonism or myoclonus.

#### **Vascular dementia**

The clinical conditions of vascular dementia (VaD) are variable, reflecting the sites of vascular lesions and pathological heterogeneity. The most common condition accounting for more than half of all cases is subcortical VaD, primarily consisting of lacunar infarction and ischemic white matter lesions; its clinical conditions as well as pathology are relatively homogeneous. The onset of VaD can be acute, but in many cases, it is latent and the progress is slow. Therefore, differential diagnosis with degenerative dementia is required.

Gait disturbance, falling easily, urinary incontinence, pseudobulbar paralysis, and apathy are relatively common symptoms in the relatively early stage of VaD. These symptoms are helpful in differentiating VaD from AD, which shows no neurological abnormalities during the early stages of the disease.

Executive dysfunction and attentional dysfunction are the main characteristics of VaD in terms of cognitive dysfunction. The memory impairment in VaD is believed to be milder than that in AD.

The main psychiatric symptoms are emotional disorders such as emotional lability, depressed state, apathy, anxiety, irritability, hypochondriasis, and psychomotor slowing. Patients with VaD reportedly show a more pronounced degree of slowed thinking and movements, depressed states, and anxiety than patients with AD.

#### **Dementia with Lewy bodies**

Progressive cognitive impairment is the main feature of DLB, and the degree of memory impairment is believed to be mild as compared

to that in AD. On the other hand, visual perception and attentional function in DLB are more extensively impaired as compared to that in AD.

Fluctuating cognition with pronounced variations in attention and alertness, is one of the core features of DLB. Some fluctuations are observed within a day or from day to day, but some may be long-term fluctuations over a span of months. The family would report that the patient “is sometimes completely normal, but at other times is so ill, it is as if it is a different person.” A physician may observe a fluctuation in the patient’s behaviors during the examination, where the patient “is talking normally but suddenly becomes absentminded and cannot continue a conversation.”

Recurrent visual hallucinations are another core feature of DLB. The visual hallucinations often involve people, animals, or insects, and the contents are well formed and detailed, for example, “there are 3 people cleaning the restroom, but they won’t answer me when I talk to them.” Visual illusions (visual misjudgment) are also frequently observed, such as mistaking a long rope for a snake or a cloth hanging on a hanger for a person. The patient often remembers experiencing visual hallucinations/illusions, and this becomes a very important clue in differentiating between DLB and delirium.

In DLB, reportedly delusions are more variable and occur at a higher frequency than that in AD. Unlike patients with AD, a patient with DLB often misidentifies a person or place, claiming, for example, that “she (who is truly his wife) looks identical to my wife but is a different person impersonating my wife (Capgras syndrome).” The visual hallucinations-induced delusion also commonly occurs in DLB.

Depressed states are observed at a high frequency. It has been pointed out that depression appears as a precursor of DLB, and that the frequency of transition from refractory depression into DLB in the elderly is also high.

REM sleep-related behavioral disorders, including shouting out loud or moving the body to a dream, also appear often. When suspecting DLB, the physician should always ask the family members if the patient is talking or moving his/her body while sleeping.

Parkinsonism is also one of the core features of DLB, and its incidence rate is very high as compared to those of AD and VaD. While akinesia

and muscle rigidity are observed at a high rate, the frequency of tremors is believed to be low.

Additionally, the use of antipsychotic drugs in small amounts possibly aggravates parkinsonism or leads to the disturbance of consciousness or a malignant syndrome. Various autonomic symptoms are observed frequently, particularly constipation, frequent urination, urinary incontinence, and orthostatic hypotension.

### **Frontotemporal lobar degeneration**

Frontotemporal lobar degeneration (FTLD) is characterized by significant personality changes, behavioral disorder, and language disorder as the main features, and comprehensively refers to degenerative dementia with the main lesion in the anterior region of the cerebrum, namely, the frontal and frontotemporal lobes. Memory impairment, visuospatial cognitive impairment, hallucination, and delusion are not notable. AD with outstanding BPSD is sometimes misdiagnosed as FTLD or frontotemporal dementia (FTD), and it is important to check for these symptoms, as they are not observed in the early stages of FTLD. In this paper, only the major symptoms of FTD, whose main lesion is in the frontal lobe, are introduced.

Compared with patients with other types of dementia, patients with FTLD lack insight into the disease from the early stages. The patient is not aware of his/her own symptoms, and has no interest in them. Therefore, it is highly unlikely that a FTD patient willingly visits a physician for consultation.

Socially inappropriate behavior is apparent from the early stages. Ill-mannered behaviors such as bursting into laughter in the middle of a funeral or beginning to sing during a medical examination, problematic behaviors that ignore social rules such as cutting in line, or minor offenses such as urinating at the roadside, food theft, shoplifting, and ignoring traffic rules are

also common. The patient does not mean any offense and rarely reflects on his/her conduct. The patient is unconcerned when someone points out his/her misconduct and repeats the same mistake many times.

Stereotyped behavior is repeating organized or systematic behaviors. At home, it is common for the patient to eat the same food day after day (stereotyped eating) or to continue to stroll the same route for several kilometers (stereotyped walking). When stereotyped behavior develops on a certain time schedule, the day of the patient starts to resemble a time-table. The presence of such stereotyped behavior is useful in the differential diagnosis of FTLD from AD.

Some types of eating behavior abnormalities are observed frequently, which serves as an important clue for differentiating between FTLD and AD along with other stereotyped behaviors. Binge eating and changes in taste preferences are typical. The patient also starts to favor heavily seasoned dishes, sweets, and sugary juices.

### **Conclusion**

In the past, donepezil was the only drug approved for treating AD in Japan. Since 2011, however, 3 additional drugs have been approved. Disease-modified treatment for AD is becoming a reality, and the significance of correctly diagnosing dementia including AD at the early stages is increasing. The total number of cases of dementia, including mild cases, is said to be over 4 million in Japan. From a practical viewpoint and the standpoint of health economics, it is already impossible to conduct functional imaging tests such as SPECT or PET or a cerebrospinal fluid test for all cases. The importance of dementia diagnosis and care based on the symptomatology will continue to grow further in the future.

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