Characteristic Diagnostic Imaging Findings in Alzheimer’s Disease

Shin KITAMURA
Assistant Professor,
Department of Internal Medicine, Nippon Medical School Second Hospital

Abstract: There are characteristic neuroimaging findings in Alzheimer’s disease. X-ray computed tomography (CT) and magnetic resonance imaging (MRI) reveal cerebral atrophy. The atrophy is recognized in the frontal, temporal, and parietal lobes, but not in the occipital lobe. Dilation of the inferior horn, which reflects the atrophy of the medial temporal cortex, is a characteristic finding in Alzheimer’s disease, but, cerebral atrophy is a nonspecific finding. MRI is superior as method of detecting atrophy of the hippocampus. Estimation of hippocampal volume is useful for differentiation between Alzheimer’s disease and a normal brain but it is not practical because the method is complicated. Single-photon emission computed tomography (SPECT) and positron emission tomography (PET) reveal reduced blood flow and metabolism in the temporal and the parietal cortex. Reduced blood flow and metabolism in the posterior cingulate cortex are detected by analysis using three-dimensional stereotactic surface projections. These findings are also recognized in the early stage of Alzheimer’s disease. Since functional changes in the brain, namely reduction of cerebral blood flow and metabolism, precede the morphological changes, SPECT and PET are more useful for the early diagnosis of Alzheimer’s disease than CT and MRI.

Key words: Alzheimer’s disease; Cerebral blood flow; SPECT; MRI

Introduction

Almost three years have passed since therapeutic drugs for the treatment of Alzheimer’s disease were approved in Japan. In view of such approval, it has become increasingly more important to make a definitive diagnosis of Alzheimer’s disease. In clinical practice, the diagnosis as Alzheimer’s disease may be made based on the clinical course of dementia, the neurological and neuropsychological findings, and the diagnostic imaging findings on brain.
x-ray computed tomography (X-CT), magnetic resonance imaging (MRI), positron emission tomography (PET), and single-photon emission computed tomography (SPECT). Since the various diagnostic imaging procedures provide good evidence for the diagnosis of Alzheimer’s disease, I describe in this paper, the characteristic imaging findings in Alzheimer’s disease.

**X-CT**

X-CT, which is widely employed and easily performed, allows detection of morphological changes. Cerebral atrophy, which is a macroscopic pathological finding in Alzheimer’s disease, can be detected by X-CT, although it is not specific for the diagnosis of Alzheimer’s disease (Fig. 1).

Findings suggestive of cerebral atrophy include ventricular dilatation and widening of sulci; dilatation of the inferior horn, which reflects atrophy of the medial temporal lobe including the hippocampus related to memory impairment, is one of the characteristic findings. In the early stage, cerebral atrophy in Alzheimer’s disease cannot be differentiated from that associated with normal ageing, but more significant atrophy than that seen as a normal ageing variation is increasingly revealed with the passage of time. Even in Alzheimer’s disease patients with severe dementia, only mild or no atrophy of the occipital lobe or cerebellum may be seen. A low-density area surrounding the ventricle, i.e., periventricular low density (PVL), a characteristic finding in cases of vascular dementia, may also be observed in Alzheimer’s disease. The PVL in Alzheimer’s disease, however, is rarely marked. Determination of the presence or absence of lesions associated with cerebrovascular accident (CVA), such as hemorrhage and infarction, is also im-

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**Fig. 1** Time-course changes in X-CT findings in Alzheimer’s disease

The image taken in 1991 reveals mild cerebral atrophy with dilatation of the inferior horn. With the passage of time, the extent of atrophy increased, and a PVL also became increasingly apparent.
portant for the differentiation of Alzheimer’s disease from vascular dementia.

While lesions associated with CVA may also be observed occasionally in some patients who are clinically considered to have Alzheimer’s disease, Alzheimer’s disease can be differentiated from vascular dementia on the basis of the pattern of occurrence of the symptoms of dementia, the course of the dementia, and of whether the site of lesion is related to higher brain functions. In Pick’s disease and fronto-temporal lobar degeneration (FTLD), dilatation of the anterior horn of the lateral ventricle is marked even in the early stages, and atrophy of these lobes is observed. These findings are useful for differentiating these diseases from Alzheimer’s disease. Alzheimer’s disease can, however, hardly be differentiated by X-CT from dementia with Lewy bodies, or Parkinson’s disease with dementia (parkinsonism-dementia complex).

As to the usefulness of X-CT in making an early diagnosis of Alzheimer’s disease, there are no characteristic findings on X-CT in the early stages of Alzheimer’s disease, and only nonspecific findings, such as cerebral atrophy mentioned above, which cannot be easily differentiated from that associated with normal ageing, are observed. Thus, X-CT cannot be considered useful for making an early diagnosis of Alzheimer’s disease.

**MRI**

Cerebral atrophy, similar to that observed by X-CT, is also observed in MR images. Since MRI can provide images of slices parallel to the long axis of the hippocampus and of coronal sections, atrophy of the medial temporal lobe including the hippocampus related to memory.
can be evaluated (Fig. 2). In its usefulness in this regard, MRI differs from X-CT. When the diagnosis of Alzheimer’s disease on MR images was attempted by visually evaluating the atrophy of the hippocampus and amygdala on T1-enhanced images of coronal sections, it was found that observation of atrophy of the anterior portion of the hippocampus was the most useful feature, with a sensitivity of 83%, and specificity of 80% in healthy individuals and 87% in depressed patients.\textsuperscript{1)}

While atrophy of the hippocampus can be seen more distinctly in patients with advanced dementia than in normal persons, it may be visually obscure in patients with early-stage dementia. However, some reports have shown that the differences in the extent of atrophy between patients with Alzheimer’s disease and normal persons can be appreciated by determination of the area and volume of the hippocampal region. A volumetric evaluation indicated that the volume of the hippocampus was 39.4% lesser in Alzheimer’s disease patients than in controls, and that the sensitivity and specificity of this measurement, which were 95% and 92%, respectively, are useful for making the diagnosis of Alzheimer’s disease; Alzheimer’s disease is diagnosed when the volume of the hippocampus is less than 2.2 cm\textsuperscript{3}.\textsuperscript{2)}

However, in the clinical setting, volumetric evaluation is not very practical, since the procedure for determination of the volume and area of the hippocampus is not a simple or easy one.

Besides PVL, a high-intensity area sur-

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**Fig. 3** Images of cerebral blood flow taken by \textsuperscript{123}I-IMP SPECT autoradiographic method in dementias of varied causation

Multiple areas of reduced cerebral blood flow are observed in vascular dementia, according to the sites of the lesions. The areas of reduced cerebral blood flow differed according to the stage of Alzheimer’s disease. The image on the extreme left shows the findings in the mild stage, followed by those in moderate and severe stages, in that order. Cases with moderate dementia show progressively more marked reduction in blood flow in the temporal and parietal lobes. In cases of severe dementia, reduced blood flow is observed in the frontal lobe as well, but the primary sensori-motor area is relatively spared. Pick’s disease is characterized by reduced blood flow in the frontal lobe, and corticobasal degeneration is characterized by asymmetric reduction in blood flow in the parietal lobe.
rounding the ventricle, i.e., periventricular high intensity (PVH), is also frequently observed in cases of vascular dementia; PVH may be observed in patients with Alzheimer’s disease as well. It is usually mild to moderate, and is frequently observed in cases with advanced dementia.

**SPECT**

While mainly the morphological changes are detected by X-CT and MRI, PET and SPECT images reflect the cerebral blood flow and metabolism. Thus, functional changes in the brain can be determined by PET and SPECT, because both cerebral blood flow and metabolic rate are correlated with the function of nerve cells. For this reason, PET and SPECT images have come to be called functional images of the brain.

SPECT allows imaging of the cerebral blood flow and measurement of the cerebral blood flow. Areas of reduced blood flow, depending on the pathological stage of the disease are detected by SPECT, while only nonspecific findings of atrophy are observed by X-CT and MRI. Typically, reduced cerebral blood flow is observed in the temporal and parietal lobes in the early stage of the disease, and in the terminal stage, reduced cerebral blood flow in the frontal lobe is observed in addition. Blood flow in the cerebellum and primary sensori-motor area is relatively well maintained until the very late stage (Fig. 3).

Reduction of cerebral blood flow in an area extending from the temporal lobe to the parietal lobe is a characteristic finding that supports the diagnosis of Alzheimer’s disease. In vascular dementia, reduced blood flow may be observed by SPECT in areas distant from the
lesion, in addition to local areas of reduced blood flow consistent with hemorrhagic lesions and infarcts as revealed by X-CT and MRI. SPECT may reveal relatively more severe reduction in blood flow in the frontal lobe in cases of vascular dementia. In Pick’s disease and dementia due to degeneration of the frontal and temporal lobes, reduced blood flow in the anterior parts of the brain, i.e. the frontal and temporal lobes, is commonly observed, while in Alzheimer’s disease, reduced blood flow is observed in more posterior parts of the brain. Diseases associated with dementia thus show characteristic patterns of reduced blood flow; e.g., progressive supranuclear palsy is characterized by reduced blood flow in the cingulate gyrus and Huntington’s disease is characterized by reduced blood flow in the caudate nucleus. These findings are useful for differential diagnosis.

The methods for the diagnosis of Alzheimer’s disease from SPECT images include the visual evaluation method, and evaluation of the values obtained in set regions of interest (ROI) on the image. The statistical analysis methods include statistical parametric mapping (SPM) and three-dimensional stereotactic surface projections (3D-SSP).

Each method has its own merits and demerits. The visual evaluation method needs experience. In the method where cerebral blood flow is calculated in ROI, it is difficult to compare all the areas. In 3D-SSP, functional images of the brain are evolved into a standard stereotactic brain coordinate system, and cerebral cortical blood flow is extracted three-dimensionally for reconstruction. The data are statistically compared with the database composed of many images taken in normal subjects processed in a way similar to that of the relevant data, and the sites of reduced blood flow are three-dimensionally displayed as a statistical image. Since the areas of reduced cerebral blood flow are displayed on the images, it becomes easy to make a diagnosis even if the physician is inexperienced.

3D-SSP analysis allows visual evaluation of areas of reduced blood flow; Alzheimer’s disease shows reduced blood flow in the posterior cingulate gyrus, in addition to reduced blood flow in the parietal lobe and lateral temporal lobe (Fig. 4). Reduced blood flow in the posterior cingulate gyrus, which can scarcely be determined on usual axial images, is a characteristic finding of Alzheimer’s disease. SPM analysis results are also similar to the findings of 3D-SSP.

PET

PET images reflect the cerebral oxygen consumption rate and cerebral glucose metabolic rate, in addition to the cerebral blood flow. Similar to the findings in SPECT images, areas of reduced cerebral blood flow and metabolism can be observed, depending on the pathological stage of the disease. Since blood flow is correlated with metabolism, a similar pattern of reduction of metabolism is noted in PET images to that in SPECT images.

It has been indicated that $^{18}$F-fluorodeoxyglucose-PET ($^{18}$FDG-PET) is useful for differentiation of Alzheimer’s disease from diffuse Lewy-body disease, the incidence of which has been believed to be only second to that of Alzheimer’s disease. When the findings in Alzheimer’s disease and diffuse Lewy-body disease were compared, it was found that the decrease in the cerebral glucose metabolic rate was more marked in diffuse Lewy-body disease, and was more clearly observed in the lateral and medial occipital lobe. Alzheimer’s disease was differentiated from diffuse Lewy-body disease based on the minimum relative values of cerebral glucose metabolic rate in the occipital cortex in the healthy group, relative to the values in the primary sensori-motor area as reference. This PET method of diagnosis showed a sensitivity of 92% and specificity of 92%, for the differential diagnosis of the two diseases. 


Early Diagnosis of Alzheimer’s Disease

Functional images of the brain obtained by PET and SPECT, rather than images obtained by X-CT and MRI, may be more useful to detect earlier functional changes in the brain.

The following are the characteristic findings of early-stage Alzheimer’s disease:

1. Decrease in the cerebral oxygen metabolic rate in the medial and lateral temporal lobe and parietal lobe in $^{15}$O PET studies.\(^5\)

2. Early decrease of cerebral glucose metabolism in the posterior cingulate gyrus as revealed by 3D-SSP.\(^6\)

3. In patients at high risk of developing Alzheimer’s disease based on the family history and the presence of ApoE $e_4$, the cerebral glucose metabolism is decreased in the temporal and parietal lobes and in the posterior cingulate gyrus.\(^7,8\)

SPECT images before the occurrence of Alzheimer’s disease and in cases with mild dementia were investigated, and the following were found to be useful findings for making an early diagnosis:

1. Assessment of the time-course of changes in the findings in patients with amnesia due to aging revealed that the reduction in blood flow in the medial temporal lobe became progressively more marked in patients who started to show disturbances in daily living because of memory impairment.\(^9\)

2. Assessment of the course in mild Alzheimer’s disease revealed that selectively reduced blood flow is observed in the posterior cingulate gyrus, and with time, reduction of blood flow was also noted in the left hippocampus, left parahippocampal gyrus, left amygdala, and the basal forebrain.\(^10\)

3. In patients who were suspected to have Alzheimer’s disease and who could almost definitively be diagnosed to have the disease after 2 years’ observation, the cerebral blood flow was demonstrated to be decreased in the hippocampus, amygdaloid nucleus, posterior cingulate gyrus, anterior part of thalamus, and anterior cingulate gyrus, as compared to that in the controls, suggesting that the occurrence of Alzheimer’s disease can be predicted from SPECT findings.\(^11\)

Although there may be some differences in findings due to differences in the test procedures and analysis methods, decrease in cerebral blood flow and reduced metabolism in the medial temporal lobe including the hippocampus and the posterior cingulate gyrus, detected by PET and SPECT, is considered to be an early diagnostic indicator of Alzheimer’s disease.

Conclusions

As described above, differential diagnosis and early diagnosis of Alzheimer’s disease can be made based on characteristic morphological and functional imaging findings. Functional images may be extremely useful for the early diagnosis of Alzheimer’s disease.

REFERENCES


