Radiologic Findings in Alzheimer’s Disease

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Overview

- Pathology of Alzheimer’s
- Clinical presentation
- CT/MRI presentation
- Nuclear medicine presentation
- Differential diagnosis
Pathology of Alzheimer's

- **Amyloid plaques**
  Comprised of amyloid beta proteins that have aggregated into plaques in the intercellular space between neurons. Misfolded amyloid beta oligomers are thought to be cytotoxic and thus causative of Alzheimer’s disease.

- **Neurofibrillary tangles**
  Comprised of tau, a protein that normally serves to stabilize the microtubules in neurons. Hyperphosphorylated tau accumulates into insoluble tangles within the neuron, as opposed to their normal straight, “train track” shape. The presence of these tangles has a strong correlation with Alzheimer’s, although it is not definitive if they are directly causative.
Pathology of Alzheimer's

- **Amyloid plaques**
  
  John Gever, MedPage Today
  http://www.medpagetoday.com/Geriatrics/AlzheimersDisease/15322

- **Neurofibrillary tangles**
  
  University of Utah,
  Spencer J Eccles Health Sciences Library
  http://library.med.utah.edu/WebPath/CINJHTML/CINJ034.html
Clinical Presentation of Alzheimer's

In the prodromal stages of Alzheimer's, symptoms may resemble normal changes due to aging. Minor loss of recent memory, confusion in unfamiliar situations, and difficulty finding words are typically the first changes to be observed.
Clinical Presentation of Alzheimer's

As the disease progresses, more marked decline in function is seen. Memory loss extends to more distant memories, and increasing difficulty in finding words may lead to speech impairment or poverty of speech. There may be motor impairment starting with small, complex motions such as writing. The ability for abstract thinking and executive planning wanes, and psychotic symptoms become progressively more severe, leading to personality and behavioral changes.
● Pathology of Alzheimer’s

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● Differential diagnosis
59 year old man with clinical diagnosis of early onset Alzheimer’s disease
Coronal T1 weighted MRI image with gadolinium contrast

- Increased ventricle size
- Atrophy of hippocampal area in temporal lobes
Cortical atrophy in frontal and parietal lobes

Sagittal T1 weighted MRI image with gadolinium contrast
70 year old female with loss of recent memory but preservation of distant, long term memory
Patient 2

Enlarged temporal horns of lateral ventricles

Axial T1 weighted MRI image
Patient 2

Markedly increased size of lateral ventricle
Decreased hippocampus volume
Decreased amygdala volume

Sagittal T1 weighted MRI image
Patient 2

Coronal T1 weighted MRI image

- Increased ventricle size
- Atrophy of hippocampal area in temporal lobes
Patient 2 vs. Normal Brain

Amygdala in yellow
Hippocampus in red

Hippocampus and amygdala volumes are visibly decreased compared to non-Alzheimer’s brain (below)

Dr. Pedro Oliveira Jr., developer of BrainView iOS app, and the FreeSurfer team
Patient 2 vs. Normal Brain

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Generalized Anatomic Changes

Dilated temporal horns and sulci
Decreased hippocampal, parahippocampal, and amygdala volume
Temporal and parietal lobe atrophy

Image courtesy of Dr. Rafeeqe Bhadelia, Beth Israel Deaconess Medical Center
Generalized Anatomic Changes

Various Alzheimer’s patients, CT (below) and T1 MRI images (above)

Images courtesy of Dr. Rafeeqe Bhadelia, Beth Israel Deaconess Medical Center
Assessing Degree of Atrophy

MTA-Scale (Scheltens)

Scheltens score for Alzheimer Disease on MRI - MTA-scale for Medial Temporal lobe Atrophy,
Dr. Antoine Micheau
**Assessing Degree of Atrophy**

<table>
<thead>
<tr>
<th>Grade 0</th>
<th>no cortical atrophy</th>
<th>closed sulci of parietal lobes and cuneus</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1</td>
<td>mild parietal cortical atrophy</td>
<td>mild widening of posterior cingulate and parieto-occipital sulci</td>
</tr>
<tr>
<td>Grade 2</td>
<td>substantial parietal atrophy</td>
<td>substantial widening of the sulci</td>
</tr>
<tr>
<td>Grade 3</td>
<td>end-stage ‘knife-blade’ atrophy</td>
<td>extreme widening of the posterior cingulate and parieto-occipital sulci</td>
</tr>
</tbody>
</table>

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Dementia: Role of MRI, Frederik Barkhof
Dutch Radiological Society
Adapted by Robin Smithius
Assessing Degree of Atrophy

Sagittal T1 weighted MRI images

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Positron Emission Tomography (PET)

A biologically active molecule (glucose, for example) is introduced into the patient’s body. The molecule is tagged with a radioactive isotope which undergoes proton decay and releases positrons. The positrons collide with electrons and releases gamma radiation from antimatter-matter annihilation. The PET scanner then detects the point of origin and amount of gamma radiation, thus pinpointing the location of radiotracer uptake.
Positron Emission Tomography (PET)

For imaging of Alzheimer’s, the radiotracers of choice are fluoro-deoxy-glucose (FDG) and Pittsburgh Compound B (thioflavain analogue).

FDG uptake is a general marker for metabolism and function. Normally, grey matter (cortices, basal ganglia) should exhibit high FDG uptake.

Pittsburgh Compound B has an affinity for amyloid deposits. Uptake in other brain tissue should be minimal.
Normal brains
Note the widening of sulci and fissures, as well as generalized decrease in uptake in all cortices and basal ganglia as age increases.

Brain 18F-FDG PET in the Diagnosis of Neurodegenerative Dementias: Comparison with Perfusion SPECT and with Clinical Evaluations Lacking Nuclear Imaging,
Daniel Silverman, MD, PhD
Journal of Nuclear Medicine, April 1, 2004, Volume 45 no. 4, 594-607
http://jnm.snmjournals.org/content/45/4/594.figures-only
Two patients, top and bottom, with Lewy body dementia, displaying similar pattern as AD

Note decreased FDG uptake in parietal and temporal cortices out of proportion with basal ganglia and visual cortex uptake.

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Pittsburgh Compound B

Note increased uptake of compound in AD and mild cognitive impairment-4 patients compared to normal control.

Kinetic modeling of amyloid binding in humans using PET imaging and Pittsburgh Compound-B, Price et al.
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Differential Dx

What is not seen is important too

- Hemorrhage
- Vascular (multiple infarct) dementia
- Intracerebral masses
- Hydrocephalus
- Infection
- Huntington's Disease
- Creutzfeld-Jakob Disease
- Wilson’s Disease
Patient 2, revisited

Overall no gross abnormalities in the anatomy are seen

Rule out
- Intra-axial mass
- Acute hemorrhage

Sulci and Sylvian fissure are preserved, grey/white matter are easily differentiated

Rule out increased intracranial pressure from hydrocephalus

Axial T1 weighted MRI image

Caudate

Putamen

Thalamus
Patient 2, revisited

Axial T2 weighted MRI image

Hyperintense areas are likely microvascular ischemic changes in bilateral putamen, but basal ganglia otherwise look normal.

Rule out
Wilson’s Disease
Huntington’s Disease
Creutzfeld-Jakob’s Disease
Patient 2, revisited

Other than highlighted area, no hyperintense lesions that represent restricted diffusion are seen in the brain parenchyma.

Rule out
Infectious lesions
Infarction

Hyperintense areas in external capsule and periventricular area are again likely microvascular ischemic changes, a common and relatively benign finding in elderly patients.
Differential Dx, continued

Some other diseases and conditions may have similar radiologic presentation as Alzheimer's. Clinical history and presentation are important to make the distinction.
Mystery Patient 1: Alzheimer’s?

Axial T1 weighted MRI image

Dilated ventricle and severe atrophy of hippocampus and amygdala

Cortical atrophy in temporal lobe
Mystery Patient 2: Alzheimer’s?

Axial FLAIR MRI image

Dilated ventricle and atrophy of hippocampus and amygdala

Dr. Frank Gaillard, Radiopaedia.org
Mystery Patient 2: Alzheimer’s?

Enlarged Sylvian fissures and sulci

- Enlarged ventricles
- Periventricular white matter changes
- Microvascular ischemic changes in external capsule

Axial FLAIR MRI images

Dr. Frank Gaillard, Radiopaedia.org
Differential Dx, continued

Previous two mystery patients were frontal temporal dementia and normal pressure hydrocephalus, respectively.

Clinical history can help to make the distinction. FTD is more likely to present with personality and behavioral changes rather than memory loss in its early stages.

NPH causes triad of “wet, wacky, wobbly” – urinary incontinence, dementia, ataxia.
Summary

Amyloid plaques and neurofibrillary tangles are histological markers for Alzheimer’s.

Early clinical manifestations are recent memory and vocabulary loss.

Later manifestations include loss of executive function, long term memory loss, dementia, and psychosis.

CT/MRI findings include loss of amygdala and hippocampal volume, temporal and parietal cortex atrophy, and enlarged ventricles.

CT/MRI findings are not definitive in and of themselves, thus clinical history is key.

FDG PET is an analogue for function vis a vis glucose metabolism, and AD patients show disproportionately decreased uptake in the parietal and temporal lobes.

Pittsburgh Compound B accumulates in amyloid deposits, thus increased uptake is suspicious for Alzheimer’s.
References

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http://www.medpagetoday.com/Geriatrics/AlzheimersDisease/15322

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Behavioural Variant of Fronto-Temporal Lobar Degeneration, August 13, 2013
Dr. Brad Hayhow
http://radiopaedia.org/cases/behavioural-variant-of-fronto-temporal-lobar-degeneration

Normal Pressure Hydrocephalus, November 26, 2013
Dr. Frank Gaillard
http://radiopaedia.org/cases/normal-pressure-hydrocephalus-8

Dementia: Role of MRI, Frederik Barkhof, Dutch Radiological Society

Brain 18F-FDG PET in the Diagnosis of Neurodegenerative Dementias: Comparison with Perfusion SPECT and with Clinical Evaluations Lacking Nuclear Imaging, Daniel Silverman, MD, PhD
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