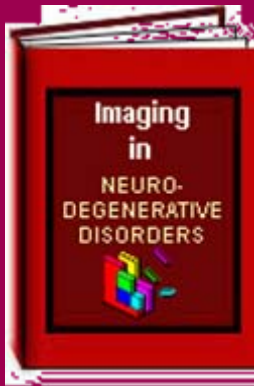




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IMAGING IN NEURODEGENERATIVE DISORDERS

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Neurodegenerative Diseases

- Programmed cell death
 - part of normal early development of brain
 - normal component of senescence.

- Neurodegenerative disorders
 - occurs prematurely
 - leads to focal and/or diffuse atrophy
 - white matter changes
 - spectroscopic abnormality.

Neurodegenerative Diseases

It is important to be aware of

- ❑ Wide range of "normal" changes in older patients,
- ❑ Differentiate normal and abnormal aging,
- ❑ Findings in neurodegenerative disorders

Neurodegenerative Diseases

Why imaging

- ❑ Not necessary when diagnosis & underlying etiology is certain
- ❑ When there is uncertainty regarding the diagnosis.
- ❑ To identify additional or superimposed treatable conditions (hemorrhage, neoplasm, and hydrocephalus) are not overlooked

OPTIMAL IMAGING

SPIN ECHO SEQUENCES

GRADIENT ECHO SEQUENCES

DIFFUSION

MAGNETIZATION TRANSFER

MR SPECTROSCOPY



High Signal on Long TR/TE Images

Normal conditions

Terminal Areas of Myelination

- ❑ Trigone
- ❑ frontal Horns (Ependymitis Granularis)
- ❑ Posterior Limb of Internal Capsule

High Signal on Long TR/TE Images

Normal conditions

Perivascular VR Spaces extension of the subarachnoid space into brain to the level of the capillaries

round, very regular cavities

always contain one or two sections of an artery with a patent lumen



High Signal on Long TR/TE Images

Normal conditions

Perivascular VR Spaces four varieties exist

- 3a Numerous small round perivascular spaces
- 3b Perivascular dilatation destroying the adjacent brain
- 3c Solitary subputaminal cavities surrounding lenticulostriate arteries
- 3d Expanding perivascular spaces that cause mass effect myelin loss with edema

High Signal on Long TR/TE Images

Normal conditions

Periventricular Hyperintense White Matter Lesions

- contiguous with the margins of the lateral ventricles
- PVH increases with increasing age and in patients with a variety of cerebral pathologies

High Signal on Long TR/TE Images

Normal conditions

Deep White Matter

- Hyperintense white matter lesions seen in
 - corona radiata,
 - centrum semiovale
 - subcortical regions
- distinct sparing of the subcortical arcuate U fibers

High Signal on Long TR/TE Images

Normal conditions

Hypointensity of Extrapyramidal Nuclei Due to Iron / mineral Deposition

- ❑ < 10 yrs: isointense to cortical GM
- ❑ > 25 yrs
 - hypointensity
 - globus pallidus, red nucleus
 - pars reticulata
- ❑ further aging
 - hypointensity in
 - caudate putamen progresses

DEFINITION OF DEMENTIA

CLINICAL PRESENTATION



Dementias

A. Primary neurodegenerative disorders

1. Alzheimer's disease
2. Pick's disease

B. Related disorders

1. Multi-infarct dementia
2. Normal pressure hydrocephalus
3. Creutzfeldt-Jacob disease



Degeneration of extrapyramidal nuclei

A. Primary neurodegenerative disorders

1. Huntington's disease
2. Hallervorden-Spatz disease
3. Leigh's syndrome

B. Related disorders

1. Mitochondrial encephalomyelopathies
2. Wilson's disease
3. Acquired hepatocerebral syndromes
4. Hypoxic-ischemic insults (e.g., carbon monoxide poisoning)



Degeneration of the substantia nigra and related systems

A. Primary neurodegenerative disorders

1. Parkinson's disease
2. Striatonigral degeneration
3. Shy-Drager syndrome
4. Progressive supranuclear palsy
5. Multiple system atrophy

B. Secondary parkinsonisms

1. Infarction
2. Infection
3. Trauma
4. Drug or toxin-induced



Degeneration of cerebellum, brainstem, and spinal cord

A. Primary neurodegenerative disorders

1. Olivopontocerebellar degeneration
2. Cerebellar-olivary degeneration
3. Infantile cerebellar ataxia
4. Acetazolamide-responsive familial ataxia
5. Friedreich's ataxia

B. Acquired cerebellar degenerations

1. Alcohol abuse
2. Paraneoplastic disorders
3. Drug toxicity
4. Following influenza vaccination (rare)



Degeneration of motor system

A. Primary neurodegenerative disorders

1. Amyotrophic lateral sclerosis
2. Progressive spinal muscular atrophy
3. Progressive bulbar palsy
4. Juvenile amyotrophy of distal upper extremity

B. Related disorders

Wallerian degeneration



Alzheimer's Disease

Routine Imaging features

Signal changes

- hyperintense sylvian and/or hippocampal-uncal cortex on long TR sequences
- WMH are usually periventricular and localised to ventricular caps similar to normal aging.

Alzheimer's Disease

Routine Imaging features

- ❑ Diffuse cerebral atrophy
 - ❑ Enlarged cortical sulci
- ❑ Focal cerebral atrophy; hippocampus
- ❑ symmetric /asymmetric enlargement
 - temporal horn
 - choroidal/hipocampal fissure
 - suprasellar cistern
 - sylvian fissure
- ❑ Interuncal distance > 30 mm



Alzheimer's Disease

Spectroscopy

□ P31 spectroscopy

↑ phosphomonoesters &
phosphodiester reflecting
hyperphosphorylation of neuronal
cytoskeletal components

□ proton spectroscopy

↑ myo-inositol & ↓ N-acetylaspartate in
patients with mild to moderate dementia
relative to healthy age-matched controls



Pick's Disease

(Lobar Atrophy, Lobar Sclerosis)

- ❑ Primary dementing illness, far less common than AD.
- ❑ F > M
- ❑ Reduction of affected gyri to a paper-thin edge "knife blade atrophy"

Pick's Disease

(Lobar Atrophy, Lobar Sclerosis)

- ❑ Circumscribed, lobar atrophy
 - frontal and/or temporal lobes,
 - left more frequently than right,
 - extrapyramidal nuclei, island of Reil,
 - amygdaloid-hippocampal
 - corpus callosum, anterior commissure.
- ❑ Sparing of
 - posterior two-thirds of STG,
 - occipital lobes, pre- and postcentral gyri,
 - parietal lobes,
- ❑ signal changes
 - mild hyperintensity on long TR sequences of cortex and
 - adjacent white matter

Multi-Infarct Dementia

- ❑ Dementia is a common sequelae of infarction in older people
- ❑ Infarction is the single most common risk factor for age-associated dementias
- ❑ Multiple small or large infarcts may result in dementia
 - multi-infarct dementia (MID)
 - état lacunaire
 - subcortical arteriosclerotic encephalopathy (SAE)
- ❑ MID can be prevented /arrested by preventing recurrent infarction

Multi-Infarct Dementia

Imaging

- ❑ Cortical infarcts,
- ❑ Basal ganglia lacunar infarcts
- ❑ Extensive WM lesions
- ❑ Absence or mild extent of these changes militates against diagnosis of MID

Normal Pressure Hydrocephalus

The classic clinical triad of NPH is dementia, gait disturbance, and urinary incontinence (236).



Huntington's Disease

- ❑ Occurs in approximately 4 to 5 per million
- ❑ Age of onset - fourth to fifth decades
- ❑ Atrophy
caudate, putamen, diffuse cerebral
- ❑ Signal changes
striatum - \uparrow / \downarrow intensity on long TR/TE images

Huntington's Disease

- Volumetric studies
 - reductions in volume of striatum, thalamus and mesial temporal lobes
- ^{31}P spectroscopy
 - \uparrow phosphomonoesters and phosphodiester

Hallervorden-Spatz Disease

- ❑ Familial autosomal recessive disease
- ❑ Onset - late adolescence
- ❑ Group 1 globus pallidus & pars reticulata of substantia nigra
- ❑ Group 2 involves only the globus pallidus
- ❑ Long TR/TE images extrapyramidal nuclei either hypointense , hyperintense, or mixed.
'Tiger eye appearance'

Wilson's Disease

(Hepatolenticular Degeneration)

- ❑ Deficiency of ceruloplasmin → copper is abnormally deposited in various tissues with resultant toxicity
- ❑ Pronounced involvement is in liver and brain
- ❑ Presents at 5-50yrs



Wilson's Disease

Imaging

- ❑ Diffuse / focal cortical atrophy
- ❑ Signal change
 - bilaterally symmetric ↑intensity
 - putamen, caudate,
 - thalamus, globus pallidus,
 - dentate nucleus, pons,
 - mesencephalon (substantia nigra,
 - periaqueductal gray matter,
 - tectum, red nucleus), WM

Parkinsonism

Idiopathic Parkinson's Disease

- ❑ Hyperintense foci on long TR sequences in substantia nigra
- ❑ ↓width of pars compacta (also found in PSP and SND).
- ❑ In contrast to other Parkinsonian syndromes, PD patients do not have putaminal hypointensity on long TR images greater than expected with normal aging

Striatonigral Degeneration

Is characterized clinically
parkinsonian symptoms
prominence of rigidity
absent or poor response to medication

imaging

- ❑ Atrophy of striatum, putamen > caudate
- ❑ Signal changes
 - on long TR/TE images
 - putaminal hypointense (high field)
 - putamina hyperintense (low field)

Progressive Supranuclear Palsy

usually begins in the sixth decade, with a range from the mid-40s to the mid-70s

Clinically characterized by

axial rigidity with neck extension,
supranuclear ophthalmoplegia
impairment of vertical eye movements,
pseudobulbar palsy, extrapyramidal symptoms,
occasional dementia



Progressive Supranuclear Palsy

Imaging

□ Focal atrophy

Midbrain

superior collicular

pars compacta of substantia nigra

□ Signal changes

↓ signal on long TR sequence

Midbrain

substantia nigra

superior collicular

↑ signal on long TR sequences

periaqueductal gray matter



Mytochondrial diseases

Leigh's Syndrome

(Subacute Necrotizing Encephalomyelopathy)

- ❑ Presents early in life with
psychomotor regression,
abnormal muscle tone,
weakness, dystonia,
brainstem and cerebellar dysfunction
- ❑ Clinical findings can be variable and nonspecific
- ❑ Presentation
 - infantile form (less than 2 years)
 - juvenile form

Leigh's Syndrome

imaging

❑ Bilateral areas of ↑ signal long TR/TE

images

basal ganglia,

periventricular white matter,

corpus callosum,

brainstem.

❑ Sparing of the mammillary bodies in SNE is an important differential feature from Wernicke's encephalopathy

Other Mitochondrial Encephalomyelopathies

structural or functional mitochondrial abnormalities → in multisystem disorders of central and peripheral nervous systems, skeletal muscles, heart, endocrine glands, gastrointestinal tract, hematopoietic system, and kidneys

- Mitochondrial cytopathy,
- Mitochondrial myopathy,
- Kearns-Sayre (K-S) syndrome,
- MERRLA (myoclonus, epilepsy, ragged red fibers&lacticacidosis),
- MELAS (mitochondrial myopathy, lactic acidosis, and stroke),
- Alpers'
- Menke's diseases

MELAS syndrome

- ❑ Bilateral symmetric & asymmetric infarct-like lesions
- ❑ Do not strictly correlate with vascular territories.
 - basal ganglia, parietal, occipital, temporal lobes, cerebellar hemispheres
 - peripheral and retrotrigonal white matter
- ❑ Frontal lobes and brainstem are typically spared
- ❑ With progression of disease, diffuse atrophy develops

Rett's Syndrome

□ Clinically

disease of young females
loss of language skills,
autistic behaviors,
stereotypical hand movements,
loss of motor skills.

□ MR & CT

Frontal atrophy

□ Quantitative MR analysis

global brain hypoplasia.

progressive atrophy

cerebellum

cerebral hemisphere

caudate nuclei



Cerebello-Olivary Degeneration

onset & progression

❑ Familial form

around age 35,

but can occur between infancy and old age

❑ Sporadic form

10-20 years later than inherited form

Progression is extremely slow

survival 15 to 20 years

❑ Selective cerebellar atrophy

❑ Vermis, particularly anterior vermis

↓ widening

Fissure separating anterior and posterior parts cerebellar vermis

Superior cerebellar cistern.



Causes of acquired cerebellar degeneration

alcohol abuse

paraneoplastic disorders

toxic effects of drugs

following influenza vaccination

Sparing of pontocerebellar tracts and vermian atrophy predominating over hemispheric involvement are useful in differentiating cerebellar cortical degenerations from OPCD



Friedreich's Ataxia

- ❑ Autosomal recessive (more common)
- ❑ Dominant inheritance patterns
- ❑ Onset is between 10 and 20 years

Neuroimaging

small spinal cord
cerebellar atrophy

- ❑ Absence or milder nature of cerebellar atrophy in Friedreich's ataxia useful differential feature from primary cerebellar degenerative processes

Diseases of the Motor System

motor neuron diseases

Degeneration of upper and/or lower motor neurons

□ Upper motor

Cortical motor neurons,
pyramidal Betz cells, neuron in the circuit

□ Descending pathways

corticospinal, indirect corticorubrospinal,
corticoreticulospinal, corticovestibulospinal,
corticotectospinal tracts.



Amyotrophic Lateral Sclerosis

- ❑ most frequent degenerative motor neuron disease
- ❑ 50 years and older at onset of symptoms,
❑ incidence increases with aging.
- ❑ clinical triad
 - atrophic weakness of the hands and forearms,
 - slight spasticity of the legs,
 - generalized hyper-reflexia
- ❑ The disorder progresses relentlessly
 - about half are dead within 3 years and 90% within 6 years

Amyotrophic Lateral Sclerosis

imaging

- ↑ signal on long TR sequences
corticospinal tract from precentral
gyrus to level of cord

- ↓ signal on long TR/TE sequence
in motor cortex

- Focal atrophy
along course of corticospinal tract.
anterior and lateral portions of spinal
cord

Juvenile amyotrophy (monomelic amyotrophy)

unilateral muscular atrophy in the hand and forearm

It occurs most commonly in young males

stabilizes after 1 to 3 years.

MR shows focal atrophy

lower cervical cord, often limited to the anterior horn region



Sensory Degeneration

Subacute combined degeneration

- ❑ Vitamin B12 deficiency → demyelination of the dorsal and lateral columns of the spinal cord
- ❑ ↑ signal on long TR/TE MR seen in spinal cord, limited to dorsolateral columns
these lesions may decrease in conspicuosity with treatment

Wallerian Degeneration

Degenerative changes in the distal axonal segment

- ❑ Separated from the proximal axon
- ❑ Neuronal cell body is damaged or killed.
- ❑ This occurs as a series of events

MR imaging

Before 4 weeks - no abnormality

□ At 4 weeks - ↓ on T2-weighted images,

□ At 10-14 weeks ↑ on T2, ↓ T1 imaging.

□ At 1.5 T

↓ intensity seen as early as 25 days (PD)

later normalizes at 70-80 days.

↑ intensity Beyond 80 days (T2)

□ Magnetization transfer techniques appear very promising for early detection

and separation of some of these changes.



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