White Matter Diseases

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Thanks to LTC Alice Smith (retired)
Disclosures: None.

This presentation reflects the personal views of the speaker and not of the US government or Department of Defense.
Unknown Case 1

22 year old female was found unresponsive. Her roommate says patient had been vomiting all week.
What is the most likely etiology?

1. Vascular
2. Infectious
3. Traumatic
4. Autoimmune
5. Metabolic
Unknown Case 2

68 year old with Waldenstrom’s macroglobulinemia who is presenting with altered mental status.
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Myelin – the dielectric insulation

Normal white matter is hyperintense on T1 and hypointense on T2 compared with gray matter because myelin is 80% lipid and 20% protein. White matter diseases are often T2 hyperintense because of myelin loss (decreased lipid and increased water).
Approach to White Matter Lesions

History & distribution

Common diseases
- MS, SVID

Uncommon diseases
- PML, CPM

No specific pattern
- VITAMIN C
Primary: Multiple Sclerosis

- Etiology: Unknown
- Peak age: 20-40 years
- Diagnosis: Clinical & paraclinical criteria  
  - CSF oligoclonal bands
Perivenular Inflammation: “Dawson’s Fingers”

Courtesy of Robert E. Schmidt, MD, PhD
FLAIR does not detect lesions in posterior fossa, brain stem, & spinal cord as well as T2
MS: Imaging

- MR spectroscopy:
  - Decreased N-acetyl aspartate (NAA)
  - Increased choline, lipids, & lactate (nonspecific)

32 Year Old
Cord lesions can be small and subtle (more conspicuous on sagittal STIR).
Revised McDonald Criteria

**SPACE**

- Three of the following:
  - ≥ 1 gadolinium-enhancing lesion or 9 T2 hyperintense lesions if there is no gadolinium enhancing lesion
  - ≥ 1 infratentorial lesion
  - ≥ 1 juxtacortical lesion
  - ≥ 3 periventricular lesions

**TIME**

- Detection of gadolinium enhancement ≥ 3 mos after onset of initial clinical event, if not at site corresponding to initial event.
- Detection of new T2 lesion if it appears at any time compared with reference scan done ≥ 30 days after onset of initial clinical event
Teaching Point:
Multiple Sclerosis

Dissemination in space:
1. Periventricular – radiating
2. Callosal – inferior margin
3. Infratentorial – peripheral

Dissemination in time:
New or enhancing lesions
Tumefactive Demyelination
Tumefactive Demyelinating Lesion (TDL)
Tumefactive Demyelinating Lesion (TDL)
Tumefactive Demyelination

- Difficulty in diagnosing TDLs often leads to surgical biopsy

- Histopathologic findings can be misleading
  - Hypercellularity
  - Atypical reactive astrocytes
  - Mitotic figures

- Unnecessary & potentially harmful surgical resection or radiation therapy
Teaching Point: Tumefactive Demyelination

"open ring sign"

Signal abnormality ends at edge of enhancement!
Neuromyelitis Optica (Devic's Disease)
Rare Multiple Sclerosis Variants

- Balo
- Schilder
- Marburg

Balo’s
Balo’s Concentric Sclerosis
## Primary Demyelinating Diseases = Autoimmune

<table>
<thead>
<tr>
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<th>CNS</th>
<th>PNS</th>
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<tr>
<td>Acute / Monophasic</td>
<td>ADEM</td>
<td>Guillain-Barre</td>
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<tr>
<td>Chronic / Multiphasic</td>
<td>MS</td>
<td>CIDP</td>
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Acute Disseminated Encephalomyelitis

- Diffuse perivenous inflammatory process
  - Results in confluent areas of demyelination
- Cortical & deep gray matter also involved
ADEM: Imaging

- Multiple lesions, may be large
- No new lesions after 6 months
- May be incomplete resolution of lesions
- Periventricular: 50%
ADEM: Imaging

- Brainstem, spinal cord, & cerebellar white matter: 30-50%
Demyelinating Lesions: Imaging

DWI
Acute Disseminated Encephalomyelitis

ADC
ADEM

- Etiology: Allergic or autoimmune reaction with viral protein
- 10-30% neurologic sequelae
  - Acute hemorrhagic leukoencephalitis (Hurst disease)
Acute Hemorrhagic Leukoencephalitis
White Matter Diseases

- V
- I
- T
- Autoimmune: MS, NMO, ADEM
- M
- I
- N
- C
Infectious

- HIV-associated encephalitis
- Progressive multifocal leukoencephalopathy
- Lyme disease
HIV Encephalopathy

- HIV-associated chronic, neurodegenerative syndrome
- 15-20% of AIDS patients
- Diagnosis: Clinical
- Pre highly active antiretroviral therapy (HAART) median survival after onset of dementia: 6 months
HIV Encephalopathy

27 year old
HIV Encephalopathy: Imaging

42 Year Old Male
HIV Encephalopathy

No enhancement, no mass effect
Progressive Multifocal Leukoencephalopathy (PML)

• Progressive demyelinating disorder

• Results from CNS infection with JC papovavirus
  – Up to 80% of people infected prior to adulthood without producing illness
  – Latent in CNS - reactivates in setting of immune compromise

• Found in 5% of autopsies in patients with AIDS

• AIDS patients with very low CD4 counts
  – 50-100 cells/mm³

• Oligodendrocytes infected unable to maintain myelin: Focal demyelination
Progressive Multifocal Leukoencephalopathy (PML)

- CNS infection with JC papovavirus
  - Up to 80% of people infected prior to adulthood
  - Latent in CNS - reactivates in setting of immune compromise
PML: Confluent Asymmetrical White Matter Lesion (subcortical U-fibers)
Lyme disease: CNS 10-15%
White Matter Diseases

- V
- Infectious: HIV, PML, Lyme
- T
- Autoimmune: MS, NMO, ADEM
- M
- I
- N
- C
Vascular White Matter Disease

- Senescent or chronic small vessel ischemic changes
- Cerebral autosomal dominant arteriopathy with subcortical infarction & leukoencephalopathy (CADASIL)
- Vasculitis
CADASIL

- Familial, non-amyloid microangiopathy
  - Mutation of Notch 3 gene on chromosome 19

- Early onset ischemic stroke (40-50s)
  - Migraine in younger patients

- Multi-infarct dementia
CADASIL

40 Year Old
Vasculitis / Vasculopathies

• Etiologies:
  – Primary: PACNS
  – Autoimmune: SLE
  – Infection: Syphilis, TB, HIV
  – Drugs: Cocaine, methamphetamine
  – Radiation
Vasculitis: Imaging

Methamphetamine
White Matter Diseases

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- Infectious: HIV, PML, Lyme
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Metabolic/Nutritional

- Osmotic demyelination
- Alcoholism
- B12 deficiency

Central Pontine Myelinolysis
Osmotic Myelinolysis

T2 FLAIR

DWI
Osmotic Myelinolysis

- Sparing of blood vessels, most nerve cells, & axons
Osmotic Myelinolysis

Stroke
Alcohol

- Atrophy: Cerebral hemispheres, superior vermis
- Marchiafava-Bignami (rare)
  - Type A: swelling of corpus, poor outcome
  - Type B: Partial callosal lesions, better outcome
- Wernicke encephalopathy
  - Thiamine deficiency
  - Severe memory impairment
  - Mamillary bodies & periaqueductal gray (around 3rd to 4th ventricles)
Wernicke Encephalopathy
B12 Deficiency

- Most common cause in US: Pernicious anemia
- Subacute combined degeneration
  - Loss of position & vibration, paresthesias of hands & feet, lower extremity weakness
  - Can affect brain, optic tracts, & peripheral nerves
  - Demyelination & axonal loss posterior & lateral spinal cord columns
  - MR: T2 hyperintensity posterior columns
Whippet Abuse

N2O CARTRIDGES ARE TO BE USED FOR FOOD CONSUMPTION ONLY AND NOT FOR SALE TO MINORS UNDER THE AGE OF 10. DO NOT INHALE CONTENTS. MISUSE CAN BE DANGEROUS TO YOUR HEALTH.
White Matter Diseases

- Vascular: SVID, CADASIL, vasculitis
- Infectious: HIV, PML, Lyme
- Autoimmune: MS, NMO, ADEM
- Metabolic: CPM/EPM, WE, SCD
Iatrogenic / Toxic

• Radiation

• Drugs

13 year old on methotrexate, vincristine, pegasparaginase
Radiation

- Can produce demyelination
- May cause mineralizing microangiopathy
- Delayed radionecrosis can occur as late as 20 years after radiation.
Radiation

Images Courtesy Steven Goldstein, MD
Radiation
Toxins/Drugs

- Drug abuse
- Chemotherapy
- Methanol: Optic nerve atrophy with necrosis of putamen & subcortical white matter
Methotrexate

- Major cause of acute neurotoxicity
  - Leukoencephalopathy
  - Incidence: 9-35%
- Pathophysiology: Unclear
Heroin

- Leukoencephalopathy
- Inhalation of heroin vapor
  - Drug heated on tinfoil – ”chasing the dragon”
- Cerebellar or extrapyramidal syndromes
Inhaled Heroin

Spongiform degeneration of these regions on histology

Central Tegmental Tracts
Delayed Hypoxic-Ischemic Leukoencephalopathy

Carbon Monoxide

Images courtesy Howard Rowley, MD
Delayed Hypoxic-Ischemic Leukoencephalopathy

Images courtesy Steven Goldstein, MD
Delayed Post-Hypoxic Leukoencephalopathy

- Rare demyelinating syndrome
  - Acute onset neuropsychiatric symptoms days to weeks after recovery from coma after period of prolonged cerebral hypo-oxygenation
  - Carbon monoxide poisoning, narcotic overdose, myocardial infarction, other global cerebral hypoxic event.

- Imaging: Diffuse hemispheric increased T2 sparing cerebellar & brainstem tracts
White Matter Diseases

• Vascular: SVID, CADASIL, vasculitis
• Infectious: HIV, PML, Lyme
• Toxic: Methanol, heroin, anoxia
• Autoimmune: MS, NMO, ADEM
• Metabolic: CPM/EPM, WE, SCD
• Iatrogenic: methotrexate, radiation
• N
• C
Conclusions

• White matter and demyelinating diseases can have similar imaging appearances
  – Patient demographics, clinical history, and lesion distribution may be helpful
  – When not helpful, consider lumbar puncture and followup imaging with gadolinium

• May mimic neoplasm – keep in back of mind
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The End
Thank you!