Pathology of Primary Demyelinating Diseases

GENERAL PROPERTIES OF MYELIN

Normal Myelin

- enhances conduction velocity
- oligodendocytes – 4-50 internodes – loss causes plaque
- Schwann Cells – 1 internode – loss causes segmental demyelination in the PNS
- Development
  - PNS 1st, then spinal cord, then brain
  - myelination occurs at different rates in different areas
  - complete by end of 2nd year of life
- CNS myelin contains more lipid than any other cell membrane

Pathological Myelin

- influx of “foamy” lipid-laden macrophages
- associated with myelin pallor and preservation of axons
- Luxol fast blue – myelin stain used to confirm myelin loss
- Silver Stain – shows integrity of axons
- 1st demyelination – demyelination occurring by itself
- 2nd demyelination – loss of myelin at the same time as axonal loss and destruction

PATTERN OF DISSEMINATED PERIVENOUS DEMYELINATION

Acute disseminated encephalomyelitis (ADEM)

- very rare, autoimmune
- usually children (6-10 years of age)
- headache, vomiting, fever, stupor, flaccid paraplegia, and incontinence
- widespread perivenous demyelination and mononuclear inflammatory infiltrates

Acute necrotizing hemorrhagic leukoencephalopathy (Weston-Hurst Disease)

- hyperacute form of ADEM
- in most instance has a fatal outcome in 1-6 days
- perivenous demyelination, vascular fibrinoid necrosis with hemorrhages, inflammatory infiltrate, high PMNs
- DIFFERENCE FROM ADEM – vascular wall necrosis

Guillain – Barre syndrome

- peripheral nerve segmental degeneration
- severe paralytic illness of short duration
- occurs 1-2 weeks after a banal respiratory infection, flu, or immunization
- rapid onset of flaccidity, areflexic weakness, sometimes with respiratory compromise
- There is a chronic form – chronic inflammatory demyelinating polyneuropathy
PATTERN OF IRREGULAR PATCHES OF DEMYELINATION

Multiple Sclerosis – Chronic Multiple Sclerosis (Classic Type)
- Clinical features
  - DISTINCT EPISODES OF NEUROLOGIC DEFICITS, SEPARATED IN TIME, ATTRIBUTABLE TO WHITE MATTER LESIONS THAT ARE SEPARATED IN SPACE.
  - optic neuritis
- Most common demyelinating disorder
- One in 1000 in US
- Most common in young adults < 50 years of age
- CSF: MILDLY INC PROTEIN, OLIGOCLONAL BANDS, MILD LYMPHOCYTIC PLEOCYTOSIS
- Risk factors:
  - Women > men
  - frequency increases with distance from equator and one takes on the relative risk of the environment of which they spent the first 15 years of life
  - familial
- cellular immunity against myelin components is supported by the presence of CD4+ and CD8+ lymphs in active lesions
- autoimmune mechanisms
- Gross:
  - scattered well-circumscribed “plaques” of gray discoloration of white matter
  - particularly in the white matter adjacent to the lateral ventricles, optic nerves, spinal cord, and brainstem
- In active plaque
  - perivascular and parenchymal inflammation
  - diffuse ongoing demyelination
  - gliosis
- Prognosis: variable

Variants of Multiple Sclerosis

1. Acute multiple sclerosis
   - fatal in < 10 months
   - resembles ADEM, no evidence of antecedent infection

2. Concentric sclerosis (Balo’s disease)
   - rings around BVs
   - seen mainly in Asian countries
   - seen in young individuals
   - death in 3-5 years

3. Neuromyelitis optica (Devic’s disease)
   - involves the optic nerves and spinal cord
DIFFUSE CONTINUOUS PATTERN OF DEMYELINATION

Leukodystrophies
• Dysmyelinating diseases because they are characterized by abnormal formation of myelin
• almost exclusively occur in children or infants
• the earlier the age of onset, the more likely the severity of the illness
• This group share the following features
  1. symmetric degeneration or failure of myelin formation
  2. lack of inflammation
  3. minimal to mild axonal destruction

Krabbe’s Disease
• autosomal recessive
• results from deficiency of galactocerebroside B-galactosidase
• does not result in accumulation of psychosine (a metabolite of galactocerebroside that is toxic to oligodendrocytes)
• Clinical Features
  ➢ rapidly progressing
  ➢ 3-6 mths of age
  ➢ motor signs are chief manifestations
  ➢ 90% of patients die or are chronically vegetative before the age of one year
  ➢ HYPERIRRITABLE!!
  ➢ Exaggerated startle response
• Gradual loss of myelin and oligodendrocytes in white matter, as well as myelin loss in peripheral nerves
• Aggregation of multinucleated GLOBOID CELLS around BVs
• spares cortex neurons and axons

Metachromatic Leukodystrophy
• arylsulfatase deficiency
• autosomal recessive
• cerebroside sulfate accumulates (as does other sulfatides)
• Four clinical syndromes: congenital, late infantile, juvenile, and adult
  ➢ Juvenile: affects brain primarily
  ➢ late infantile: peripheral nerves
• Myelin loss with sparing of subcortical U fibers
• name of disease derived from the ability of the sulfatides to bind dyes and shift their color

REVIEW

Disseminated perivascular demyelination
1. Acute Disseminated Encephalomyelitis (ADEM) – Central
2. Acute Necrotizing hemorrhagic leukoencephalopathy (AHEM) – Central
3. Guillain-Barre syndrome – Peripheral
4. Chronic inflammatory demyelinating polyneuropathy (CIDP) – peripheral

Pattern of Irregular, patchy demyelination
Chronic and acute relapsing multiple sclerosis

Pattern of diffuse continuous demyelination
1. Krabbe’s Disease
2. Metachromatic leukodystrophy