Metabolic Demyelinations

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DEMYELINATION OF CORPUS CALLOSUM (MARCHIAFAVA-BIGNAMI DISEASE)

- primary regeneration of corpus callosum
  - first described by Marchiafava and Bignami in 1903.
  - > 100 cases have been reported.
  - frequent reports in Italian men (genetic predisposition?).

ETIOLOGY
- not known, possible causes / risk factors:
  a) long-standing alcoholism (may have common pathogenesis with central pontine myelinolysis or Wernicke encephalopathy)
  b) nutritional deficiencies
  c) toxic factors

PATHOPHYSIOLOGY

Noninflammatory demyelination → necrosis of middle lamina of corpus callosum (dorsal and ventral rims are spared!!!)
- Constant bilateral symmetry!
- other CNS areas may be involved: anterior commissure, posterior commissure, centrum semiovale, subcortical white matter, long association bundles, middle cerebellar peduncles.
- spared structures: internal capsule, corona radiata, subgyral arcuate fibers, gray matter.
- Microscopy - sharply defined necrotic process with myelin loss; relative preservation of axis cylinders in periphery of lesions;
  - no inflammation!
  - fat-filled phagocytes are common.
  - gliosis is not well advanced.

MEDIAL NECROSIS OF CORPUS CALLOSUM AND ANTERIOR COMMISSURE WITH SPARING OF MARGINS:

MEDICAL FEATURES
- onset - middle age or elderly.
- symptoms are insidious & nonspecific (only scarcely explained by callosal lesions) - multifocal & diffuse neurologic signs:
  1) transient focal neurological deficits (frontal release signs)
  2) cognitive and behavioral (progressive dementia, depression and extreme apathy, confusion, mania, paranoid, or delusional states).
  3) seizures
  4) altered mental status (stupor → coma → death).
- slowly progressive → death within 3-6 years.

DIAGNOSIS
CT / MRI - typical symmetric demyelinating callosal lesions.

TREATMENT
- no known therapy.

CENTRAL PONTINE MYELINOLYSIS

PATHOPHYSIOLOGY
- acute symmetric, noninflammatory demyelination in central basis pontis.
  - demyelination and associated reduction in oligodendroglia; relative preservation of axons and surrounding neurons (lesions resemble Marchiafava-Bignami disease).
  - in 10% cases, demyelination also occurs in extrapontine regions (midbrain, thalamus, basal nuclei, cerebellum; never below pontomedullary junction; rarely supratentorially).
  - hypothesis - in regions of compact interdigitation of white and gray matter, cellula redem (caused by fluctuating osmotic forces) compresses fiber tracts → demyelination.
    - during prolonged hyponatremia, concentration of intracellular charged protein moieties is altered; reversal cannot parallel rapid correction of electrolyte status.

ETIOLOGY
Predisposing conditions:
1) alcoholism
2) liver disease, orthotopic liver transplantation surgery
3) malnutrition (esp. after burns)

Cause - too rapidly corrected severe and prolonged (< 120 mEq/L for > 48 hours) hyponatremia (osmotic myelinolysis).

CLINICAL FEATURES
1. Locked-in (horizontal gaze paralysis + pseudobulbar palsy + spastic quadriplegia)
2. Preserved functions: sensory modalities, vertical eye movements, blinking, breathing, alertness.
   - if demyelination extends through midbrain → vertical ophthalmoplegia.
   - if demyelination extends to pontine tegmentum and/or thalamus → delirium, coma.

Typical scenario:
**METABOLIC DEMYELINATIONS**

- severe hyponatremia is diagnosed in person with delirium.
- IV fluid therapy is administered, and serum \( \text{[Na}^+ \] ) is normal by next day.
- mental status improves, but is followed by neurologic deterioration 48-72 hours later.
- maximum recovery may require several months; full recovery has been reported.

**DIAGNOSIS**
- **CSF** - increased opening pressure, protein↑, mononuclear pleocytosis.
- **EEG** - diffuse bihemispheric slowing.
- **T2-MRI** (imaging modality of choice) - hyperintense bright areas (water content↑) in central pons, sparing peripheral rim; later central lesion diminishes in size and signal, and mild pontine atrophy may result.

**TREATMENT**
- supportive only:
  - correct hyponatremia at 10 mmol/L/24 h + free water restriction.
  - vitamin supplementation for alcoholic patients.

**BIBLIOGRAPHY** for ch. “Demyelinating Disorders” → follow this LINK >>