Metabolic Demyelinations

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DEMYELINATION OF CORPUS CALLOSUM (MARCHIAFAVA-BIGNAMI disease)

- primary degeneration 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) longstanding **alcoholism** (may have common pathogenesis with central pontine myelinolysis or Wernicke encephalopathy)
  b) nutritional deficiencies
  c) toxic factors

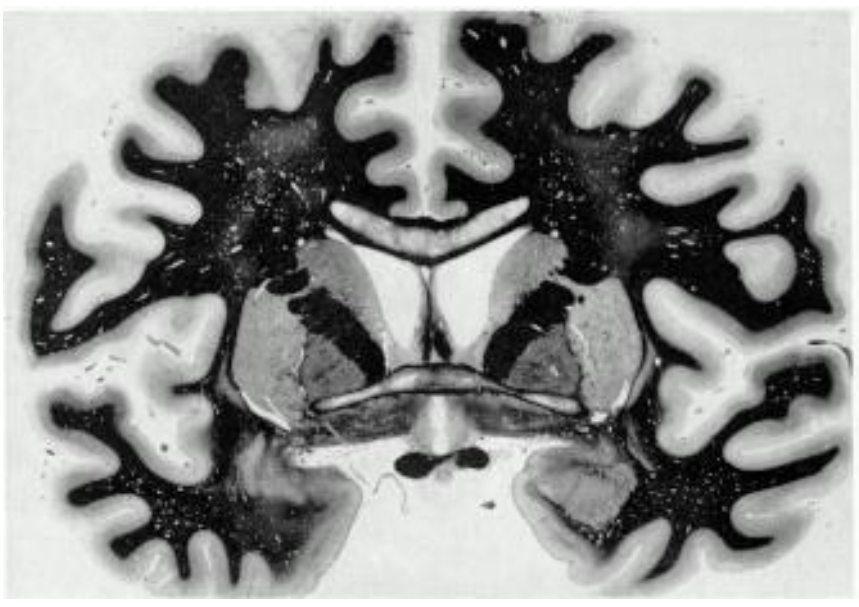
PATHOPHYSIOLOGY

Noninflammatory demyelination → **necrosis** of MIDDLE LAMINA OF CORPUS CALLOSUM (dorsal and ventral rims are spared!).

Constant bilateral symmetry!

- necrosis varies from softening & discoloration to cavitation & cyst formation.
- rostral position of corpus callosum is affected first.
- small symmetric lesions extend and become confluent.

- 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:

CLINICAL 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, manic, 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, **cellular edema** (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

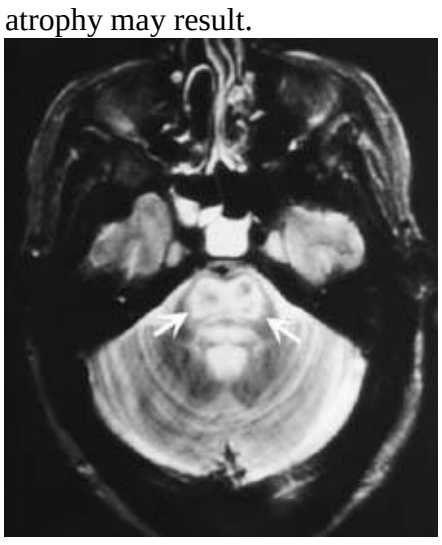
1. **Locked-in** (horizontal gaze paralysis + pseudobulbar palsy + spastic quadriplegia)
2. **Preserved functions**: sensory modalities, vertical eye movements, blinking, breathing, alertness.
   - if demyelination extends through midbrain → **vertical ophthalmoparesis**.
   - if demyelination extends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

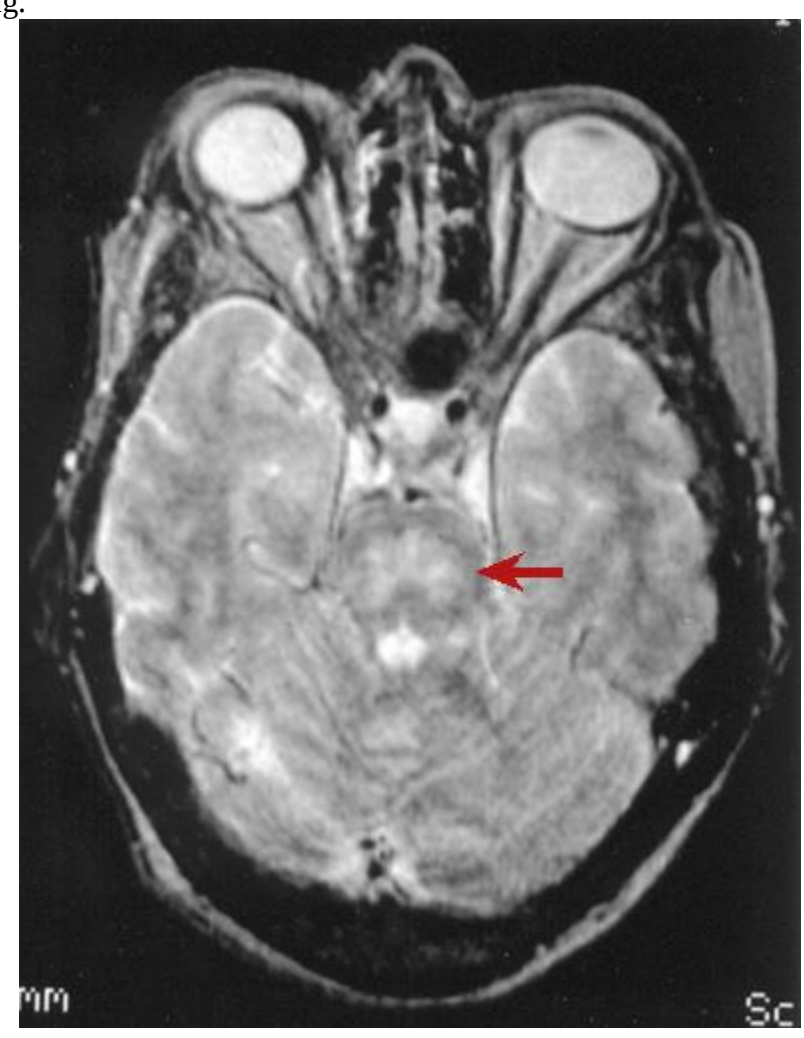
Typical scenario:

- severe hyponatremia is diagnosed in person with delirium.
- IV fluid therapy is administered, and serum [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.
- *death* is common within days or weeks.

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 >>