MS-related Disorders

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NEUROMYELITIS OPTICA (s. DEVIC'S DISEASE)

- acute onset of OPTIC NEURITIS and TRANSVERSE MYELITIS in ***close temporal relationship*** (interval < 1 month).

ETIOLOGY

1) MS (whether Devic disease differs from MS is controversial)
2) ADEM
3) viral infections
4) autoimmune disorders (e.g. SLE)

PATHOPHYSIOLOGY

Lesion histology ≈ MS, although considerably more destructive with striking spinal gray matter involvement

Acute spinal lesion

- diffuse spinal cord ***swelling & softening*** (extends over several levels ÷ nearly entire cord in continuous or patchy distribution).
- white and gray matter destruction with dense macrophage infiltration, perivascular lymphocytic cuffing, loss of myelin and axons.
- prominent spinal cord swelling in confines of restrictive pia → intramedullary pressure↑ → collapse of small parenchymal vessels → further tissue injury.

Chronic spinal lesions

- cord is ***atrophic*** and ***necrotic***, with ***cystic degeneration*** and ***gliosis***.
- absence of perivascular cuffing.
- proliferation of thickened hyalinized vessels similar to that seen after infarction (so lesions resemble infarctions).

Optic nerves, chiasm, and occasionally cerebral hemispheres are involved in similar fashion (demyelinating, necrotizing lesions).

EPIDEMIOLOGY

- more common in Japan and East Asia, although even there it is uncommon (< 5 per 100,000).
- mean age at onset is 27 yrs (1-73 yrs).
- males = females (but in relapsing NMO, F:M = 3.8:1).
- 1/3 patients have ***preceding infection*** within few weeks (e.g. nonspecific upper respiratory tract infection, flu, gastroenteritis, chickenpox, pulmonary tuberculosis).

CLINICAL FEATURES

- symptoms of OPTIC NEURITIS and MYELITIS.

- no cortical, brainstem, cerebellar features at any time!
- develop over hours ÷ days (occasionally, progression over weeks ÷ months).
- preceded / accompanied by headache, nausea, somnolence, fever, myalgias.
- > 80% optic neuritis **bilateral**.
- Lhermitte sign is common.
- *severe neurological deficits* are usual.

Possible courses:
35% - **monophasic** illness; rarely fulminantly progressive course.
55% - **relapses** limited to OPTIC NERVES and SPINAL CORD (**relapsing NMO**, s. **opticospinal MS**);
  – often associated with autoimmune disorders (most commonly SLE).

Recovery is variable;
  – many recover remarkably.
  – prognosis is worse for relapsing NMO.

DIAGNOSIS

MRI (excludes structural lesions)

- **optic nerve / chiasm** enlargement, T2-signal enhancement during acute phase.
- T2-signal↑ in **medulla** represents extension of high cervical lesions.
- **cerebral** white matter lesions seen in 25% cases.
- **spine** - cord swelling, signal changes extending over several levels (appearance may resemble spinal cord tumor → biopsy).

CSF examination is essential (repeated studies ensure that there is no infection)

- ***marked pleocytosis*** during acute phase (17% patients have normocellular CSF); ***neutrophils*** may predominate!!!
- ***protein***↑↑↑
- oligoclonal bands are conspicuously absent in 80% patients.

Laboratory - ESR↑ (33%), positive antinuclear antibodies (50%).

Mayo Clinic criteria for diagnosis of Devic's disease (2006)
- both absolute criteria + at least two supportive criteria:

Absolute criteria:
1. Optic neuritis
2. Acute myelitis

Supportive criteria:
1. Brain MRI not meeting criteria for MS at disease onset
2. Spinal cord MRI with contiguous T2-weighted signal abnormality extending over ≥ 3 vertebral segments (indicating relatively large cord lesion)
3. NMO-IgG seropositive status (existence of antibodies against aquaporin 4 antigen)

MANAGEMENT

- SUPPORTIVE CARE is mainstay!
- patients often respond to **corticosteroids** (e.g. IV METHYLPREDNISOLONE).
- may respond to **plasma exchange** even when IV METHYLPREDNISOLONE does not produce improvement.

- *preventing relapses is disappointing* even with immunosuppressive agents (e.g. AZATHIOPRINE, CYCLOPHOSPHAMIDE).

  RITUXIMAB reduces frequency of attacks, with subsequent stabilization / improvement in disability!

CONCENTRIC SCLEROSIS (s. BALÓ DISEASE, ENCEPHALITIS PERIAXIALIS CONCENTRICA)

- rare rapidly progressive variant of MS (**histologic diagnosis** without recognizable clinical syndrome).

- cannot be differentiated clinically from MS.
- CSF is normal or more inflammatory than MS.
- MRI - extensive lesions in cerebral white matter.
- diagnosis is made pathologically - concentric zones of **myelinated** and **demyelinated** white matter;
  - pattern suggests disease progression from ventricles outward.
  - demyelinated zones are hypercellular, contain macrophages.
  - cause of this pattern is unknown (myelinated zones are formed by remyelination at edges of demyelinated foci).
  - this concentric pattern has also been found in typical leukoencephalopathy (diffuse sclerosis).
- treatment - PREDNISONE therapy.
- prognosis is poor - most patients survive < 1 year.

SCHILDER DISEASE (s. ENCEPHALITIS PERIAXIALIS DIFFUSA, DIFFUSE SCLEROSIS)

- nonfamilial disorder affecting primarily **children & young adults**.

- pathology - massive asymmetric area of demyelination (may involve entire cerebral hemisphere), typically with extension across corpus callosum.
  - subcortical U-fibers are often spared.
  - perivascular infiltration by lymphocytes and giant cells → actual necrosis.
  - lesions are similar to MS (small lesions coalesce to form large ones).
- clinical syndrome is one of leukoencephalopathy - progressive dementia, aphasia, blindness (cortical or optic neuritis), deafness, pseudobulbar palsy, hemiplegia / quadriplegia.
- **CSF** – pleocytosis, ± oligoclonal bands.
- main differential – adrenoleukodystrophy.
- only some patients respond to **steroids** and **immunosuppressive** therapy.
- *malignant course* - most patients die within few years of onset (average – 6 yrs).

EXPERIMENTAL ALLERGIC ENCEPHALOMYELITIS (EAE)

- most widely studied animal model of MS.

- EAE is antigen-specific, T-cell-mediated autoimmune disease that can be induced in many species.
- induced by injection of brain or spinal cord extracts emulsified in complete Freund adjuvant (encephalitogenic factor is certain polypeptide sequences of ***myelin basic protein***).
- animals demonstrate classic cutaneous delayed hypersensitivity to ***myelin basic protein***.
- ***lymphoid cells*** can passively transfer disease to other animal; ***antibodies*** poorly correlate with disease and cannot passively transfer it.
- HISTOLOGY closely parallels pathological picture of MS.
- **acute EAE** is monophasic illness that more closely resembles ADEM.
- **chronic-relapsing EAE** closely mimics clinical course of MS.

BIBLIOGRAPHY for ch. "Demyelinating Disorders" → follow this LINK >>