

# MS-related Disorders

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|---|---|
| NEUROMYELITIS OPTICA (S. DEVIC'S DISEASE) .....                                   | 1 |
| CONCENTRIC SCLEROSIS (S. BALÓ DISEASE, ENCEPHALITIS PERIAXIALIS CONCENTRICA)..... | 1 |
| SCHILDER DISEASE (S. ENCEPHALITIS PERIAXIALIS DIFFUSA, DIFFUSE SCLEROSIS).....    | 2 |
| EXPERIMENTAL ALLERGIC ENCEPHALOMYELITIS (EAE) .....                               | 2 |

## 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  $\approx$  MS, although considerably more destructive with striking spinal gray matter involvement

#### Acute spinal lesion

- diffuse spinal cord *swelling & softening* (extends over several levels  $\div$  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  $\rightarrow$  intramedullary pressure  $\uparrow$   $\rightarrow$  collapse of small parenchymal vessels  $\rightarrow$  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  $\div$  days (occasionally, progression over weeks  $\div$  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  $\uparrow$  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  $\rightarrow$  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*  $\uparrow\uparrow\uparrow$
- oligoclonal bands are conspicuously absent in 80% patients.

**Laboratory** - ESR  $\uparrow$  (33%), positive antinuclear antibodies (50%).

### 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 >>](#)