5.14.3. Systemic Conditions (III): Immunologic Disorders (III): Multiple Sclerosis (II)

- Chiasmal and retrochiasmal abnormalities
  - white matter within the optic chiasm, optic tracts, and optic radiations is frequently involved
    - 13.2% after 1 year of follow-up
    - recovery pattern similar to that of optic neuritis
- Ocular motility disturbances
  - symptoms
    - diplopia
    - blurred vision
    - oscillopsia
  - localized to supranuclear, nuclear, and fascicular portions of ocular motor system
  - bilateral internuclear ophthalmoplegia
    - exotropia in primary position
    - bilaterally impaired adduction
    - wall-eyed, bilateral internuclear ophthalmoplegia, WEBINO
      - ★ highly suggestive of MS < 50 years
  - horizontal or vertical gaze paralysis
    - complete or partial
  - skew deviation
    - vertical misalignment not attributable to single nerve or muscle dysfunction
  - isolated ocular motor cranial nerve palsy
    - MS must be considered in a young adult with an isolated ocular motor cranial nerve palsy and no history of trauma
    - most likely reflect fascicular involvement and are frequently accompanied by other brainstem findings
    - ★ sixth nerve involvement is most common
  - nystagmus
    - horizontal, rotary, or vertical
    - both pendular and jerk types may occur
    - concomitant vertical and horizontal nystagmus (out of phase)
      - circular or elliptical eye movements
        - ★ highly suggestive of MS
  - common cerebellar eye findings
    - rebound nystagmus
    - fixation instability (macrosaccadic oscillations)
    - saccadic dysmetria
    - abnormal pursuit movements
  - dorsal midbrain (Parinaud) syndrome
- Laboratory evaluation
  - MS is a clinical diagnosis
  - CSF in patients with definite MS is abnormal in >90%
    - elevation of immunoglobulin G (IgG)
    - elevation of the IgG/albumin index
    - oligoclonal IgG bands
      - in CSF but not in serum
    - ✗ none of these findings is specific for demyelinating disease
- Neuroimaging
  - MRI with fluid-attenuated inversion recovery (FLAIR) sequencing + gadolinium
    - neuroimaging study of choice
  - sensitive for the identification of white matter plaques
  - far superior to CT scan for visualizing the posterior fossa and spinal cord
  - shows multiple lesions in
    - 85%–95% of patients with clinically definite MS
    - 66%–76% of patients with suspected MS
  - ✗ MRI findings are not specific for MS
  - lesions fluctuate over time
  - lesions most consistent with MS
    - ✓ multifocal
    - ✓ periventricular
    - ✓ ovoid
  - active lesions will enhance with gadolinium-DTPA
  - hypointense regions on postcontrast T1-weighted scans (black holes)
    - ★ marker of progressive disease
  - symptomatic optic neuritis
    - best visualized on MRI with fat-suppression and gadolinium
- Diagnosis of multiple sclerosis
  - modified McDonald criteria
    - based on the combination of clinical history and presentation along with neuroradiologic imaging, with or without CSF abnormality or an abnormal visual evoked response
  - recurrent optic neuritis, in the absence of other clinical or laboratory manifestations, is not sufficient for diagnosis of MS ✗
- Treatment
  - there is no cure for MS
  - several therapies slow the disease and assist specific symptoms
  - intravenous high-dose corticosteroids
    - for acute exacerbations
  - disease-modifying drugs
    - for long-term treatment
    - drugs
      - Interferon beta-1b
      - subcutaneous interferon beta-1a
      - intramuscular interferon beta-1a
      - glatiramer acetate
    - reduce MS exacerbations by ≈1/3
    - show positive effect on MRI changes in patients with relapsing-remitting disease
    - early diagnosis and therapy are advantageous ★
      - disease-modifying injectable drugs
        - delay the development of clinically definite MS ✓
        - ± reduce risk of disability progression compared with placebo ✓
    - adverse effects
      - interferon
        - injection site reactions
        - flulike symptoms
        - abnormal results for blood count or liver function tests
      - glatiramer acetate
        - injection site reactions
        - lipoatrophy
        - immediate postinjection reactions
    - should be managed by specialists
  - mitoxantrone
    - for worsening forms of relapsing-remitting and secondary progressive MS
  - fingolimod
    - once-daily oral medication
    - for relapsing MS
    - associated with risks including
      - cystoid macular edema ✓
        - 0.4%
      - cardiac symptoms ✓
      - hepatic toxicity ✓
      - increased susceptibility to serious viral infections ✓
  - natalizumab
    - recombinant monoclonal antibody
    - prevents transmigration of leukocytes from the vasculature across the endothelium into the CNS
    - associated with progressive multifocal leukoencephalopathy (viral infection)
      - ≤ 1.8 cases per 1000 patients
    - liver damage
  - additional drugs
    - low-dose oral methotrexate
    - pulsed corticosteroids
    - cyclophosphamide
  - these drugs should be used with caution by physicians experienced in MS therapy.
  - references

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