ACUTE DISSEMINATED ENCEPHALOMYELITIS (ADEM)

- monophasic inflammatory demyelinating disorder that begins within 6 weeks of antigenic challenge (infection or immunization).
- considerable overlap in epidemiological, pathological, pathophysiological, clinical, CSF, imaging features between ADEM and MS - difficult to distinguish between two when encountering patients with single demyelinating event.

PATHOPHYSIOLOGY

- transient cell-mediated autoimmune response toward myelin (e.g. myelin basic protein).
- infections and vaccinations induce ADEM by molecular mimicry or by nonspecific activation of autoreactive T-cell clones.
- Histology - perivascular inflammation - edema - demyelination with relative preservation of axons.
- PERIVENOUS DEMYELINATION !!!
- lesions commonly enlarge and coalesce, forming lesions pathologically indistinguishable from MS.
- repair occurs through remyelination.

ETIOLOGY

a) VACCINES - POSTVACCINAL ENCEPHALOMYELITIS (3-6% of all ADEM cases).
- only epidemiologically and pathologically proven association is with rabies vaccination.
- original Pasteur rabies vaccine (prepared in rabbit spinal cord - was contaminated with CNS tissue) had ADEM incidence 1 per 3,000-35,000 vaccinations.
- use of human diploid cell lines (contain no nervous system tissue) for production of rabies vaccine has virtually eliminated risk of ADEM.

b) INFECTIONS - POSTINFECTIOUS (S. PARAINFECTIOUS) ENCEPHALOMYELITIS
- most commonly nonspecific upper respiratory tract infection.
- measles carries highest risk (1 per 1,000 cases) for ADEM among specific infections; now measles-related ADEM is rare (ADEM is now most frequently associated with varicella-chickenpox infections).

CLINICAL FEATURES

- prodromal Viral syndrome (few days) - headache, low-grade fever, myalgias, malaise.
- Prodrome absent in MS! Also absent in 7-15% ADEM cases!
- hiatus between onset of viral prodrome and onset of ADEM may range 2-30 days.
- prodrome and ADEM are typically separated by phase of recovery from fever and other constitutional manifestations.

Viral Prodrome: (few days) - headache, low-grade fever, myalgias, malaise. Prodrome absent in MS! Also absent in 7-15% ADEM cases! hiatus between onset of viral prodrome and onset of ADEM may range 2-30 days. prodrome and ADEM are typically separated by phase of recovery from fever and other constitutional manifestations.

Neurological symptoms develop very rapidly (hours ÷ several days*) - irritability and lethargy, delirium (encephalopathy of varied degree), changes in mental status up to coma (88%), headache (55%), focal or generalized seizures (25%), meningoismus (25%). *rarely up to 6 weeks
**ACUTE NECROTIZING HEMORRHAGIC ENCEPHALOMYELITIS (ANHEM), s. Acute Hemorrhagic Leukoencephalitis of WESTON HURST**

- Hyperviscous variant of ADEM
- affects mainly children and young adults.
- almost invariably preceded by recent episode of upper respiratory infection.
- Immune neuroinflammation similar to ADEM (immune sensitization to MBP).
- Brain is swollen, with bilateral petechial hemorrhages throughout white matter (hemispheres, brainstem, and spinal cord).
- Microscopy: hyperacute EAE with perivascular demyelination and intense infiltration by mononuclear and especially polymorphonuclear cells!
- Necrosis of walls of venules → fibrin deposition, petechiae, disseminated necrosis of white and gray matter.
- Coalescence of smaller lesions → large necrotic foci.

**DIAGNOSIS**

- sudden headache → fever, various focal signs (seizures, quadriplegia) → rapid progression (few hours to several days) from lethargy to coma.
- > 80% cases are fatal (within 2-4 days).

**TREATMENT**

- supportive + METHYLPIREDNISOLONE-PREDNISONE regimens.

**BIBLIOGRAPHY**

For ch. “Demyelinating Disorders” → follow this [link] >>

---

**REFERENCES**

- CT – brain edema, diffuse areas of hypodensity in white matter.
- late MRI – evidence of blood products.
- blood – marked leukocytosis, ESR↑.
- CSF:
  1. marked pleocytosis up to 3000 cells/mm³ (predominance of POLYMORPHONUCLEATS!)
  2. evidence of hemorrhage
  3. total protein↑.

**PROGNOSIS**

- mortality < 2% (esp. measles-associated ADEM).
- 50-90% survivors have marked recovery (complete recovery may be observed even in children who become blind, comatose, and quadriparetic).
- risk factors for bad recovery: age < 2 yrs, transverse myelitis.
- long-term (10-y follow-up) risk for development of MS - 25%.

**TREATMENT**

- IV METHYLPIREDNISOLONE 20 mg/kg/d (maximum 1 g/d) for 3-5 days → oral taper for 3 weeks
- improvement usually requires several days.
- IVlg 2 g/kg for 2-3 days - preferable when meningo-encephalitis cannot be excluded.
- c) plasma exchange for severe deficits and little response to corticosteroids.

**DIAGNOSIS**

- CSF – although oligoclonal IgG bands occur transiently in 1/3 cases, their persistence implies diagnosis of MS!
- subsequent disappearance of bands is evidence against MS.
- myelin basic protein concentration? (reflects demyelination).
- mononuclear pleocytosis of 20-200 cells/mm³.
- MRI – identical to MS (basal ganglia or cortical lesions, large globular white matter lesions are more frequent in ADEM; 90% ADEM lesions disappear with time).
- characteristic centrifugal “cotton-ball” lesions at junction of deep cortical gray and subcortical white matter are found in 90% cases.
- classically all ADEM lesions develop simultaneously! (90% lesions enhance with gadolinium - i.e. all lesions are acute monomophic)
- Blood - platelet counts↑, ESR mildly elevated (greater elevation suggests vasculitis or infection).
- EEG - widespread slowing of background rhythms.
- EEg – widespread slowing of background rhythms.

**PROGNOSIS**

- mortality < 2% (esp. measles-associated ADEM).
- 50-90% survivors have marked recovery (complete recovery may be observed even in children who become blind, comatose, and quadriparetic).
- risk factors for bad recovery: age < 2 yrs, transverse myelitis.
- long-term (10-y follow-up) risk for development of MS - 25%.

**TREATMENT**

- IV METHYLPIREDNISOLONE 20 mg/kg/d (maximum 1 g/d) for 3-5 days → oral taper for 3 weeks
- improvement usually requires several days.
- IVlg 2 g/kg for 2-3 days - preferable when meningo-encephalitis cannot be excluded.
- c) plasma exchange for severe deficits and little response to corticosteroids.

**DIAGNOSIS**

- CSF – although oligoclonal IgG bands occur transiently in 1/3 cases, their persistence implies diagnosis of MS!
- subsequent disappearance of bands is evidence against MS.
- myelin basic protein concentration? (reflects demyelination).
- mononuclear pleocytosis of 20-200 cells/mm³.
- MRI – identical to MS (basal ganglia or cortical lesions, large globular white matter lesions are more frequent in ADEM; 90% ADEM lesions disappear with time).
- characteristic centrifugal “cotton-ball” lesions at junction of deep cortical gray and subcortical white matter are found in 90% cases.
- classically all ADEM lesions develop simultaneously! (90% lesions enhance with gadolinium - i.e. all lesions are acute monomophic)
- Blood - platelet counts↑, ESR mildly elevated (greater elevation suggests vasculitis or infection).
- EEG - widespread slowing of background rhythms.

**PROGNOSIS**

- mortality < 2% (esp. measles-associated ADEM).
- 50-90% survivors have marked recovery (complete recovery may be observed even in children who become blind, comatose, and quadriparetic).
- risk factors for bad recovery: age < 2 yrs, transverse myelitis.
- long-term (10-y follow-up) risk for development of MS - 25%.

**TREATMENT**

- IV METHYLPIREDNISOLONE 20 mg/kg/d (maximum 1 g/d) for 3-5 days → oral taper for 3 weeks
- improvement usually requires several days.
- IVlg 2 g/kg for 2-3 days - preferable when meningo-encephalitis cannot be excluded.
- c) plasma exchange for severe deficits and little response to corticosteroids.

**DIAGNOSIS**

- CSF – although oligoclonal IgG bands occur transiently in 1/3 cases, their persistence implies diagnosis of MS!
- subsequent disappearance of bands is evidence against MS.
- myelin basic protein concentration? (reflects demyelination).
- mononuclear pleocytosis of 20-200 cells/mm³.
- MRI – identical to MS (basal ganglia or cortical lesions, large globular white matter lesions are more frequent in ADEM; 90% ADEM lesions disappear with time).
- characteristic centrifugal “cotton-ball” lesions at junction of deep cortical gray and subcortical white matter are found in 90% cases.
- classically all ADEM lesions develop simultaneously! (90% lesions enhance with gadolinium - i.e. all lesions are acute monomophic)
- Blood - platelet counts↑, ESR mildly elevated (greater elevation suggests vasculitis or infection).
- EEG - widespread slowing of background rhythms.

**PROGNOSIS**

- mortality < 2% (esp. measles-associated ADEM).
- 50-90% survivors have marked recovery (complete recovery may be observed even in children who become blind, comatose, and quadriparetic).
- risk factors for bad recovery: age < 2 yrs, transverse myelitis.
- long-term (10-y follow-up) risk for development of MS - 25%.

**TREATMENT**

- IV METHYLPIREDNISOLONE 20 mg/kg/d (maximum 1 g/d) for 3-5 days → oral taper for 3 weeks
- improvement usually requires several days.
- IVlg 2 g/kg for 2-3 days - preferable when meningo-encephalitis cannot be excluded.
- c) plasma exchange for severe deficits and little response to corticosteroids.