NOTES
CNS DEMYELINATING DISORDERS

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

- Disorders affecting brain, spinal cord; damage to oligodendrocytes → loss of myelin, axons
- Damage mostly caused by autoimmune reaction
  - Inflammatory cells release cytotoxic molecules/engulf cells
- Trigger unknown

RISK FACTORS

- Genetic predisposition
- Environmental factors (e.g. infections)

SIGNS & SYMPTOMS

- *Motor:* weakness, tremors, paraparesis/quadriparesis
- *Sensory:* abnormal sensations, numbness, visual problems
- *Autonomic:* sphincter, sexual dysfunction

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan, MRI

- Abnormal signals in white matter regions

LAB RESULTS

- Cerebrospinal fluid (CSF)
  - ↑ cell count, ↑ protein level

OTHER DIAGNOSTICS

- Neurologic symptoms

TREATMENT

MEDICATIONS

- Reduce inflammation (e.g. corticosteroids)

OTHER INTERVENTIONS

- Plasma exchange
- Manage symptoms

ACUTE DISSEMINATED ENCEPHALOMYELITIS

osms.it/acute-diss-encephalomyelitis

PATHOLOGY & CAUSES

- Autoimmune disease characterized by sudden inflammation of brain, spine; destruction of myelin sheath at multiple locations

Type IV hypersensitivity reaction

- Cell-mediated
- T-cells penetrate blood brain barrier, activated by myelin antigens (myelin basic protein, proteolipid protein, myelin oligodendrocyte protein) → release of cytokines (IL-1, IL-6, TNF-alpha, interferon-gamma)
  - Direct damage to oligodendrocytes, myelin
  - Blood brain barrier expresses more receptors → attracts more immune cells (B-cells, macrophages) → blood vessel dilatation
- B-cell activation → production of autoantibodies against myelin proteins
- Macrophages look for antibody marked oligodendrocytes, destroy them

CAUSES

- Antigen mimicry
  - Antibodies aimed against pathogen antigens bind to myelin proteins

RISK FACTORS

- Genetic predisposition
- Infections
  - Viral (measles, mumps, rubella); bacterial (*Mycoplasma pneumoniae*, beta-hemolytic *Streptococci*)
- Vaccination
  - Measles-mumps-rubella (MMR) vaccination
- Usually affects children

SIGNS & SYMPTOMS

- Sudden onset of symptoms 1–3 weeks after interaction with pathogen
- Systemic inflammation (fever, headache, nausea, vomiting)
- Sensory, visual deficits
- Seizures, confusion, drowsiness
- Motor deficits, weakness, ataxia
- Oculomotor deficits, nystagmus, dysarthria
- Coma

DIAGNOSIS

DIAGNOSTIC IMAGING

MRI

- Multiple lesions in white matter regions of central nervous system (CNS)
- Open ring sign with contrast enhancement
- Edema

CT scan

- Emergency cases
- Low density lesions in white matter region

LAB RESULTS

- Lumbar puncture
  - ↑ protein, ↑ cell count (lymphocytes), high level of antibodies, CSF culture

OTHER DIAGNOSTICS

- Clinical
  - Polyfocal neurologic symptoms, encephalopathy
- Microscopically
  - All lesions similar, preserved axons with myelin loss, mononuclear infiltration, foamy macrophages

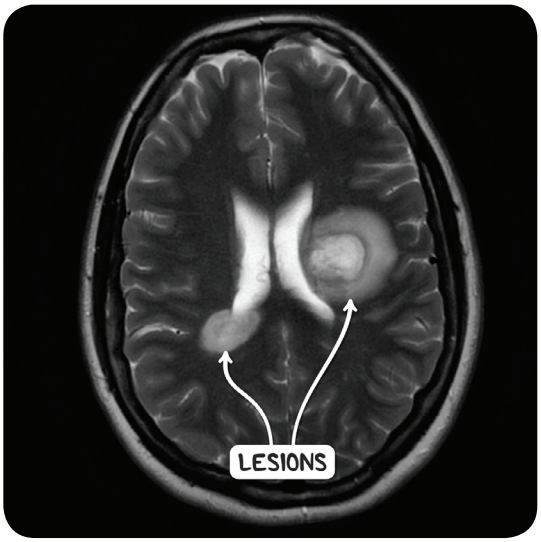

Figure 68.1 An MRI scan of the head of an individual with acute disseminated encaphalomyelitis. There are bilateral, asymmetrical, tumefactive lesions of the cerebral white matter.

TREATMENT

MEDICATIONS

- Corticosteroids
  - Reduce inflammation
  - E.g. glucocorticoids
- Cyclophosphamide
  - Cell cycle inhibition

OTHER INTERVENTIONS

- Intravenous immune globulins
  - Neutralize antibodies
- Plasma exchange

CENTRAL PONTINE MYELINOLYSIS

osms.it/central-pontine-myelinolysis

PATHOLOGY & CAUSES

- Destruction of myelin sheath around nerve cells in pons due to rapid osmotic changes (osmotic demyelination syndrome)
- ↓ sodium level in serum → water leakage through blood brain barrier → ↑ brain volume
- Activation of defense mechanisms
  - *After few minutes:* ↑ intracranial pressure pushes excess water, sodium into CSF → ↓ brain volume
  - *After few hours:* astrocytes release organic solutes → release of excess intracellular water → evening osmolarity with serum
  - *After two days:* fully adapted to altered osmolarity
- Sudden correction of hyponatremia in already adapted brain
  - Potassium, sodium surge back into astrocytes → ↑ cation concentracion
  - Shrinkage of endothelial cells → distortion of blood brain barrier → complements, cytotoxic elements form blood leak into brain
- Damage astrocytes, induce apoptosis
  - Interruption of myelin-making process in oligodendrocytes
  - Release of cytokines
  - Activation of microglia

RISK FACTORS

- Sodium level < 120meq/L
- Hyponatremia lasts > two days
- Syndrome of inappropriate diuretic hormone (SIADH)
  - Kidneys retain too much water
- Alcoholism, malnutrition

COMPLICATIONS

- Respiratory failure, aspiration pneumonia, coma, death

SIGNS & SYMPTOMS

- Movement disorders
- Paraparesis/quadriparesis
- Severe cases
  - "Locked-in" syndrome (conscious, paralyzed; can only move eyes, blink)
- Dysarthria, dysphagia, diplopia
- Seizures, confusion, lethargy, coma

DIAGNOSIS

DIAGNOSTIC IMAGING

MRI

- Earliest changes seen in diffusion weighted imaging (DWI)
  - Restriction in pons region
- Later changes
  - High T2, low T1 signal
  - "Trident sign" (trident spear-shaped lesion in pons)

CT scan

- Low sensitivity; low attenuation signal in pons

PET

- Initial high uptake

TREATMENT

OTHER INTERVENTIONS

- Correcting serum sodium slowly
- 6–8 weeks; endotracheal intubation, ventilator support

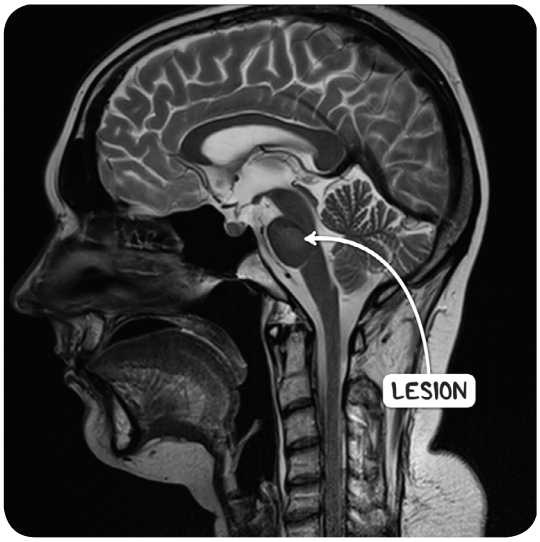

Figure 68.2 An MRI scan of the head and neck in the sagittal plane demonstrating a hypointense lesion in the pons of an individual with central pontine myelinolysis.

MULTIPLE SCLEROSIS (MS)

osms.it/multiple-sclerosis

PATHOLOGY & CAUSES

- Autoimmune demyelinating disease of nerve cells in brain, spinal cord characterized by various neurological disorders
- Cell-mediated (Type IV) hypersensitivity reaction
  - T cells, B cells, macrophages

T cells

- Break through blood brain barrier → activated by myelin proteins (myelin basic protein)
- Th17 cells produce cytokines → attract other leukocytes
- Th1 cells produce interferon gamma → activation of macrophages
- Produce cytokines (IL-1, IL-6, TNF-alpha)
  - Oligodendrocytes damaged
  - Blood brain barrier expresses more receptors for other leukocytes
  - Blood vessels dilate; easier passage for other leukocytes

B cells

- Produce antibodies that bind to myelin proteins, mark them

Macrophages

- Recognize marked oligodendrocytes, engulf them
- Attacks
  - *Early:* regulatory T cells reduce inflammation → oligodendrocytes heal, renew myelin (remyelination)
  - *Later:* repetitive extensive damage → death of oligodendrocytes → loss of myelin → damage, loss of axons

TYPES

- Relapsing-remitting multiple sclerosis (RRMS)
  - Bouts of autoimmune attacks, months/years apart
  - Improvement after attack
  - Residual permanent damage accumulates
  - Disabilities do not increase between bouts
- Secondary progressive multiple sclerosis (SPMS)
  - Starts as RRMS
  - Over time attacks become constant → progression of disabilities
- Primary progressive multiple sclerosis (PPMS)
  - One constant attack → progression of disabilities over lifetime
- Progressive-relapsing multiple sclerosis (PRMS)
  - One constant attack
  - Superimposed bouts → faster progression of disabilities

RISK FACTORS

- Genetic
  - Individuals who are biologically female twice as susceptible
  - Polymorphisms of certain alleles of major histocompatibility complex (e.g. HLA-DR2; identifying, binding of foreign molecules)
- Environmental
  - Infections (e.g. Epstein–Barr virus infection)
  - Vitamin D deficiency
- Usually affects young adults

MNEMONIC: MS MS

Pathology of multiple sclerosis

Multiple **S**clerosis affects **M**yelin **S**heath

SIGNS & SYMPTOMS

- Charcot's neurologic triad
  - Dysarthria, nystagmus, intention tremor
- Lhermitte's sign
  - Bending neck forward → electric shock runs down back, radiates to limbs
- Higher order activities
  - Poor concentration, critical thinking; depression, anxiety

Plaque location

- Brainstem
  - Conscious movements (e.g. difficulty talking/eating)
  - Unconscious movements (e.g. difficulty swallowing)
- Eye nerves
  - Optic neuritis (e.g. loss of vision)
  - Eye movement nerves (e.g. double vision)
- Motor pathways
  - Muscle weakness, spasms, tremors, ataxia, paralysis
- Sensory pathways
  - Numbness; pins, needles; paresthesias (tingling, itching, burning)
- Autonomic nervous system
  - Constipation, urinary incontinence, sexual dysfunction

DIAGNOSIS

DIAGNOSTIC IMAGING

MRI

- Hypointense T1, hyperintense T2 lesions
- ≥ one lesions in periventricular, juxtacortical, infratentorial, spinal cord
- Gadolinium-enhanced, nonenhanced lesions simultaneously
- Dawson's fingers
  - Plaques radiating outwards from corpus callosum in sagittal images

LAB RESULTS

- CSF
  - High levels of antibodies

OTHER DIAGNOSTICS

- Clinical
  - Neurologic symptoms with relapsing-remitting course
- Visual evoked potential
  - Measure response to visual stimuli

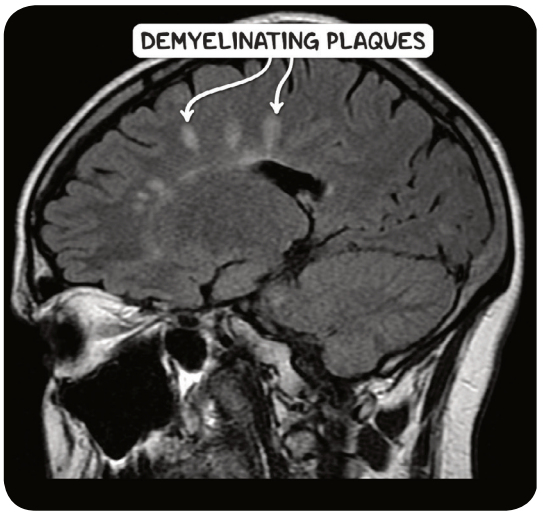

Figure 68.3 An MRI scan of the head in the sagittal plane demonstrating multiple demyelinating plaques adjacent to the corpus callosum. This radiological sign is known as Dawson's fingers and is specific for multiple sclerosis.

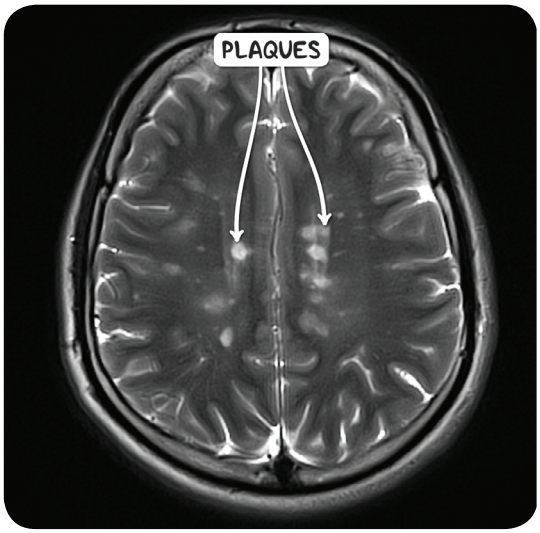

Figure 68.4 An MRI scan of the head in the axial plane demonstrating the multiple demyelinating plaques present in the brain of an individual with multiple sclerosis.

TREATMENT

MEDICATIONS

- RRMS
  - Corticosteroids, cyclophosphamide, intravenous immunoglobulin

OTHER INTERVENTIONS

- RRMS
  - *Plasmapheresis:* removing antibodies
  - Immunosuppressants
- Progressive MS
  - Manage symptoms (e.g. urinary incontinence), physical therapy, cognitive rehabilitation therapy, vitamin D

TRANSVERSE MYELITIS

osms.it/transverse-myelitis

PATHOLOGY & CAUSES

- Rare immune disorder affecting spinal cord; causes acute motor, sensory, autonomic defects
- Perivascular inflammation (monocytes, lymphocytes) → damage to oligodendrocytes → loss of myelin sheath around axons → loss of axons, neurons

TYPES

- Acute partial
  - Asymmetric dysfunctions
  - 1–2 segments involved
- Acute complete
  - Symmetric dysfunctions
  - 1–2 segments involved
- Longitudinally extensive
  - Symmetric/asymmetric dysfunctions
  - > two segments involved

RISK FACTORS

- CNS, systemic infections
- CNS disease (e.g. multiple sclerosis)

SIGNS & SYMPTOMS

- *Motor:* extremity weakness → paraparesis
- *Sensory:* abnormal sensations, numbness, pain
- *Autonomic:* sphincter, sexual dysfunction

DIAGNOSIS

DIAGNOSTIC IMAGING

MRI

- Hypointense/isointense T1, hyperintense T2 signal
- Abnormal contrast enhanced signal on ≥ one segment
- Spinal cord swelling

LAB RESULTS

- CSF
  - ↑ cell count (lymphocytes), ↑ protein level

OTHER DIAGNOSTICS

- Clinical
  - Motor, sensory, autonomic defects

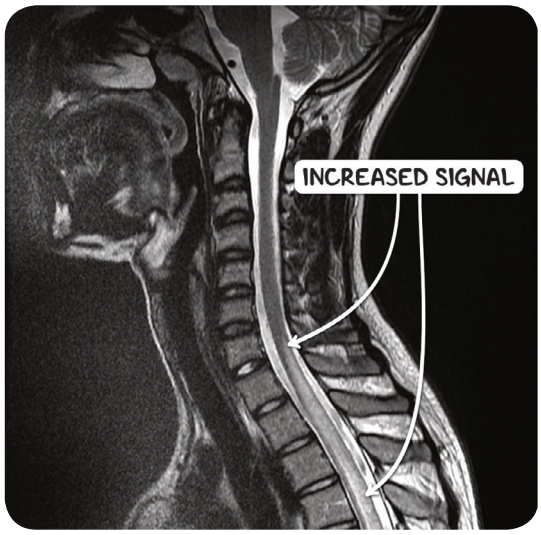

Figure 68.5 An MRI scan of the spine in the sagittal plane demonstrating increased T2 signal uptake in the spinal cord, typical of transverse myelitis, extending from C7 downwards and ending at T12 (not shown).

TREATMENT

OTHER INTERVENTIONS

- Intravenous glucocorticoids
- Plasma exchange