Nervous System Pathology
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CNS Outline

• Introduction
• Increased intracranial pressure
• Vascular and circulatory disorders
• Trauma
• Infections
• Tumors
• Demyelinating diseases
• Degenerative diseases
CNS Outline

• Introduction
Gross anatomy of brain
Cells of the CNS

- Neurons – transmit impulses
- Astrocytes – part of blood brain barrier
- Oligodendrocytes – produce myelin
- Microglia – phagocytose intruders
- Ependymal cells – line ventricles
Astrocytes and oligodendrocytes
Microglial cells
Ependymal cells
Ependymal cells
Reactions of Cells to Injury

- Neurons: become “red” and degenerate
- Astrocytes: undergo hypertrophy, hyperplasia
- Microglia: proliferate
- Oligodendrocytes: don’t react much
- Ependymal cells: don’t react much
CNS Outline

• Introduction
• Increased intracranial pressure
Causes of Increased ICP

- Cerebral edema
  - Generalized (diffuse insult, like hypoxia, toxin exposure, encephalitis, trauma)
  - Focal (around focal lesions, like acute infarcts, contusions, penetrating injuries, mass lesions)
- Increased CSF volume (hydrocephalus)
- Expanding mass lesions
Hydrocephalus

• Definition: accumulation of excessive CSF within the ventricular system
• Usually due to impaired flow and resorption of CSF (rarely due to overproduction of CSF)
• If occurs in infancy, head enlarges
• If after infancy, ventricles expand, ICP increases
CSF circulation
Hydrocephalus ex vacuo
Types of Hydrocephalus

- Noncommunicating: block is in ventricular system; only a portion of the ventricular system is enlarged
- Communicating: block is in subarachnoid space; entire ventricular system is enlarged
- Ex vacuo: ventricular system is dilated due to brain atrophy (with compensatory increase in CSF volume)
Feared Outcome: Herniation

- One part of brain gets pushed into another compartment
- Symptoms:
  - Headache
  - Vomiting
  - Decreased level of consciousness
  - Papilledema
- Often fatal
Case: A Friday Night Football Problem

- A 17-year-old male was knocked unconscious while playing in a football game one Friday night
- A CT scan in the ER was normal
- During the following week, he appeared normal but was secretly suffering from headaches
- Played part of the game the following Friday before collapsing on the field
Case: A Friday Night Football Problem

- Rushed to ER again, where a CT scan showed a left subdural hematoma with a midline brain shift
- On exam, lethargic but awake
  - Decreased vision in part of visual field of right eye
  - Limited ocular motility
  - Ptosis of left eye
Ptosis of left eye

Impaired adduction of left eye

Somewhat limited elevation and depression of left eye
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Global Cerebral Ischemia

- Due to hypotension
- Outcome depends on severity of hypotension
  - Mild: transient confusion
  - Severe: persistent vegetative state or brain death
- “Watershed” infarcts
Global ischemia
Watershed infarcts

Anterior cerebral artery area

Middle cerebral artery area

Posterior cerebral artery area

Infarct at ACA/MCA watershed

Infarct at PCA/MCA watershed

Watershed infarcts
Focal Cerebral Ischemia

• Due to obstruction of blood flow

• Hemorrhagic (red) infarcts
  • due to emboli + reperfusion
  • often arise from heart

• Ischemic (pale) infarcts
  • due to thrombi
  • often arise from atherosclerotic plaques

• Transient ischemic attacks (TIAs) are often harbingers
Hemorrhagic (L) vs. ischemic (R) infarction
Recent hemorrhagic infarct
Old infarct
<table>
<thead>
<tr>
<th>ACT F.A.S.T.</th>
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<tbody>
<tr>
<td><strong>Face</strong></td>
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<tr>
<td>Ask the person to smile.</td>
</tr>
<tr>
<td>Does one side of the face droop?</td>
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<tr>
<td><strong>Arms</strong></td>
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<tr>
<td>Ask the person to raise both arms.</td>
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<tr>
<td>Does one arm drift downward?</td>
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<tr>
<td><strong>Speech</strong></td>
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<tr>
<td>Ask the person to repeat a simple sentence.</td>
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<tr>
<td>Are the words slurred, and can the person repeat the sentence correctly?</td>
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<tr>
<td><strong>Time</strong></td>
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<tr>
<td>If the person shows any of these symptoms,</td>
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<tr>
<td>call 911 or get to the hospital fast.</td>
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<tr>
<td>Time is important, because brain cells are dying.</td>
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</tbody>
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What if you think someone might have had a stroke?
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Skull Fractures

• “Displaced” if bone is depressed

• Falls while awake are usually occipital; falls with loss of consciousness are usually frontal.

• Basal skull fractures have unique symptoms:
  • lower cranial nerves affected
  • orbital or mastoid hematomas distant from impact site
  • CSF draining from ear or nose
Raccoon eyes following basal skull fracture
Raccoon eyes following basal skull fracture
Concussion

- Definition: Altered consciousness from head injury due to change in momentum of head (head hits rigid surface)
- Mechanism unknown
- Symptoms: amnesia, confusion, headache, visual disturbances, nausea, vomiting, dizziness
- Post-concussive neuropsychiatric syndromes exist (especially after repetitive injuries)
Diffuse Axonal Injury

• Injury of axons in deep white matter of brain
• Twisting/shearing of axons
• Can be caused by angular acceleration alone
• “Shaken baby” syndrome
• Common cause of coma after trauma
Axonal shearing

A. Trauma causes the axon to twist and tear

B. The result is permanent death of the brain cell
Traumatic Vascular Injury

Epidural hemorrhage
• Blood above dura
• Tear in middle meningeal artery
• Neurosurgical emergency

Subdural hemorrhage
• Blood between dura and arachnoid
• Shearing of bridging veins
• Acute (hours) or chronic (months)

Subarachnoid hemorrhage
• Blood in subarachnoid space
• Contusions, ruptured berry aneurysms
• Neurosurgical emergency
Epidural hematoma is usually above the dura mater. A common site for an epidural bleed is the meningeal artery which is behind the ear and very close to the surface.
Epidural hematoma
Subarachnoid hemorrhage from ruptured berry aneurysm
Huge berry aneurysm near basilar artery
Common sites for berry aneurysms
Treatment of aneurysm with coils
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Meningitis

• Inflammation of the meninges
• Symptoms: Fever, headache, stiff neck.
• Bacterial meningitis is dangerous!
  • Newborns: *E. coli, Strep agalactiae*
  • Young adults: *Neisseria meningitidis*
  • Elderly: *Strep pneumoniae*
• Viral meningitis is much less serious
Bacterial meningitis
Abscess

• Focal infectious lesion
• Routes of infection: direct implantation, local extension, hematogenous spread
• *Strep viridans, Staph aureus*
• Symptoms: progressive focal deficits plus signs of increased ICP
Purulent bacterial abscess
Prion diseases

- Prion = abnormal form of a cellular protein called prion protein (PrP)
- Weird: prions are infectious and transmissible
- Diseases: Creutzfeldt-Jakob disease, kuru, scrapie, mad cow disease
- Causes “spongiform change” (intracellular vacuoles) in neurons and glia
- Symptoms: progressive dementia
Creutzfeldt-Jakob disease
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Brain Tumors

- Most are primary; about 30% are metastatic
- Classified by cell of origin
- “Benign” and “malignant” have different implications when it comes to brain tumors
- Most brain tumors in children arise in the posterior fossa
- Most brain tumors in adults arise in the cerebral hemispheres
Gliomas

- Arise from astrocytes, oligodendrocytes, ependymal cells
- Often fatal (location and infiltrative borders prevent complete excision)
- Glioblastoma (highest-grade astrocytoma) is the most common and the most malignant
Glioblastoma (highest-grade astrocytoma)
Oligodendroglioma
Ependymoma
Medulloblastoma

- Tumor of primitive neurons
- Cerebellum
- Children
- Very radiosensitive!
Medulloblastoma
Medulloblastoma
Meningioma

- Encapsulated, benign tumor
- Surface of brain (no invasion)
- Symptoms caused by compression
- Cured by resection
Meningioma
Nerve Sheath Tumors

• Arise from cranial (esp. VIII) and spinal nerve roots, and peripheral nerves
• Derived from support cells of nerve
• Benign but may compress nerve
• Schwannoma ("acoustic neuroma" if involving VIII), neurofibroma
“Acoustic neuroma” (schwannoma)
Schwannoma: Antoni A and B areas
Schwannoma: Verocay body
Neurofibromas
Neurofibromatosis
Neurofibromatosis
Multiple Sclerosis

• Most common demyelinating disorder
• Etiology unknown; related to autoimmunity
• Variety of motor and sensory symptoms
• Relapsing-remitting course
• Plaques (areas of demyelination) in brain, cord
Multiple sclerosis
Multiple sclerosis plaques around ventricles
Guillain-Barré Syndrome

• Acute peripheral neuropathy
• Autoimmune attack on myelin
• Progressive, ascending weakness
• Usually self-limited (but may involve respiratory muscles, requiring respiratory intensive care)
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Alzheimer Disease

- Most common cause of dementia in the elderly
- Symptoms:
  - Early on: forgetfulness
  - Then: issues with language, motor skills, mood
  - Finally: profound disability, immobility
- Gross: Cortical atrophy, neuronal loss
- Microscopic: plaques and tangles
Alzheimer disease: brain atrophy
Alzheimer disease: progression
Plaques contain Aβ peptides (fragments of amyloid)
Tangles contain tau protein
Parkinson Disease

- Degeneration of pigmented neurons (containing dopamine) in the substantia nigra
- Cause unknown
- Early symptoms: tremor, rigidity, slow movement
- Later: cognitive problems, dementia, dyskinesia
- Gross: atrophy of substantia nigra
- Microscopic: Lewy bodies (inclusions in neurons)
Parkinson disease (R) : atrophy of substantia nigra
Parkinson disease: Lewy body
Michael J. Fox and Muhammad Ali
Huntington Disease

- Degeneration of basal ganglia and cerebral cortex
- Early symptoms: lack of coordination, unsteady gait
- Later: chorea (involuntary writhing), psychiatric symptoms, dementia
- Autosomal dominant mutation
- Begins in 30s-40s; slow progression over 10-20 years
Read this story about Katharine and her family:
Amyotrophic Lateral Sclerosis

- Degeneration of motor neurons
- Sensory and cognitive function are unaffected
- Rapidly progressive weakness, muscle atrophy, spasticity, dysphagia
- Early: arm or leg weakness, twitching, slurred speech
- Death within 2-3 years due to respiratory compromise
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