Diseases of nervous system

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Part I

Infectious Diseases
Infectious Disease

- A group of diseases with infectivity and epidemic, caused by infectious agents that can be transmitted from one host (person or animal) to another directly or indirectly.
- Also known as Communicable Disease.
- Transmission means that an infectious agent is moved through the environment from an infected host or reservoir to a susceptible host.
Meningitis

- refers to an inflammatory process of the leptomeninges and CSF within the subarachnoid space.
- usually caused by an infection
- but chemical meningitis may also occur in response to a nonbacterial irritant introduced into the subarachnoid space.
Infectious meningitis

Can be divided into three types:

- Acute purulent meningitis (usually caused by bacteria)
- Acute lymphocytic meningitis (usually caused by viruses)
- Chronic meningitis (may be caused by a number of different infectious agents)
Acute purulent meningitis Etiology

The microorganisms (the most common cause) vary with the age of the patient:

- **In neonates**: *Escherichia coli*
- **group B streptococci**

- **Among children older than 6m of age**:
  - **formerly**: *Haemophilus influenzae* (declined recently because of effective vaccine)
  - **currently**: *Streptococcus pneumoniae*

- **In older children, adolescents, and young adults**:
  - **meningococcus** (*Neisseria meningitidis*).
Epidemic Cerebrospinal Meningitis (Meningococcal Meningitis)

Definition:

Acute purulent inflammation of leptomeninges, subarachnoid space and the spinal meninges caused by meningococci (Neisseria meningitidis).

High fever, headache, vomiting, Skin eruption (petechia and ecchymosis) and meningeal irritation, even shock and death.
Epidemic features

**Source of infection:**
Patient in disease
Pathogen carrier without symptoms

**Route of transmission:**
Air transmission, e.g. by cough, sneezing
Intimate touch, e.g. kiss, breast-feeding

**Susceptible population:**
6 months old – 2 years old in peak Susceptible population.

**Epidemic season:**
Predominantly seasonal rhythm, most in spring and winter
Pathogenesis
systemic defense function ↑

upper respiratory inflamed stage

meningococcus → upper respiratory passage → asymptomatic stage

systemic defense function ↓

infection of upper respiratory passage

septicemia stage

septicemia

Meningitis stage

A. Ordinary type
   purulent meningitis

B. fulminant type
   (Waterhouse Friderichsen’s syndrome)
Pathological features of purulent meningitis

- The purulent exudates is most abundant over the surface of the brain, and extension commonly occurs to the spinal meninges.

- The infection usually spreads to the choroids plexus and the interior of the ventricles.
Morphology

Grossly:

- Leptomeningeal purulent exudates
- Edema
- Leptomeningeal Congestion
- Subarachnoid exudates
The normally clear CSF is cloudy and sometimes frankly purulent.

The meningeal vessels are engorged and stand out prominently.

From the areas of greatest accumulation, tracts of pus can be followed along blood vessels on the surface of the brain.
The purulent exudate is most abundant over the surface of the brain, which fill up leptomeninges and subarachnoid space with congestion of blood vessels on the surface.
A thick layer of suppurative exudate covers the brain stem and cerebellum and thickens the leptomeninges.
Microscopically:

Hyperemia, fibrin formation, and inflammatory cells.

- The subarachnoid space contains purulent exudate with varying amounts of fibrin.
- In most severe cases, the entire subarachnoid space is filled with purulent exudate.
- Brain substance unaffected, at least in early stages.
The subarachnoid space contains a large mount of purulent exudates.
Microscopically, the subarachnoid space contains a neutrophilic exudation that has varying amount of fibrin.
Microscopically, the subarachnoid space enlarges with full of the purulent exudates.
Suppurative meningitis
Clinicopathologic association

1) Signs of meningeal irritation
2) Increased intracranial pressure
3) Changes of cerebrospinal fluid (CSF)
Clinicopathologic association

Signs of meningeal irritation

Heavy headache
Photophobia
Kernig’s sign (+)
Stiff neck
Clouding of consciousness

Kernig’s sign (+): inability to straighten the raised leg because of pain.
Nerve root irritation signs

Stiff neck and episthiontonus
Clinicopathologic association

Increased intracranial pressure

- Some degree of acute internal hydrocephalus results from an increased permeability of the choroids plexus, an outpouring of exudates into the ventricular.

- This condition, along with edema, congestion of blood vessels, and subarachnoid exudates, increases the intracranial pressure, which causes tri-signs in intracranial pressure: heavy headache and dizziness, jetting-vomiting and hernia formation.
The brain is enclosed in a rigid skull while it affords protection against injury, of necessity it also restricts expansion of the intracranial contents.

Small expansions can be accommodated by shifts of cerebrospinal fluid (CSF) and reduction in venous volume, but any further increase in intracranial volume will cause a rise in intracranial pressure. The principal detrimental effect of this rise in pressure is a reduction of cerebral arterial perfusion pressure and, therefore, cerebral blood flow.
Small rises in intracranial pressure are compensated for by rises in the arterial blood pressure, but at higher levels of intracranial pressure (persistent elevation above 20 mmHg) there is a progressive fall in cerebral perfusion pressure and blood flow and an increasing cerebral ischemia.
Clinically,

The first symptom of raised intracranial pressure is usually headache.

If intracranial pressure is raised for more than a week or two, papilledema of the head of the optic nerve and retinal hemorrhages may develop secondary to compression of the venous drainage, with consequent congestion of the retinal vasculature.

With increasing severity, there may be dizziness and vomiting progressing to coma.
Cerebral herniation is one of the most ominous developments in patients with focal space-occupying lesions or diffuse brain swelling.

Conception: The skull cavity is partly divided into compartment by dural folds. Focal enlargement of any one compartment will tend to displace brain into adjacent compartments. This is called herniation.
heavy edema bringing about hernia formation

Tonsillar herniation is displacement of the cerebral tonsils through the foramen magnum. This compresses the medulla and its respiratory center will cause respiratory irregularities and eventually apnea and death.
Clinicopathologic association

Changes of CSF:

lumbar puncture is the key investigation.

Cloudy or frankly purulent, raised protein level and neutrophils, reduced glucose levels, under increased pressure in a spinal tap.
Figure 4.89. Pleural effusions: a, Serous (transudate). b, Serofibrinous (exudate). c, Hemorrhagic.
Type B Epidemic Encephalitis

Definition:
Acute inflammation of cerebrospinal parenchyma.

Acute viral infections of the brain have a wide spectrum of manifestations, ranging from a catastrophic acute necrotizing panencephalitis (e.g., neonatal herpes simplex encephalitis) to an infection that affects only specific subpopulations of neurons. (e.g., polio myelitis).
Etiology

- A great many viruses may cause epidemic encephalitis.
- In China, India, Southeast Asia and Korea, as well as Japan, epidemic encephalitis is caused by a flavivirus, Japanese encephalitis virus.
Epidemics

Sources of infection:  *Pigs, cows, sheep, dogs, chicken, duck and goose infected*

Route of transmission:  Vector: *mosquito*

Susceptible population:

Epidemic features:
*It has a seasonal incidence and mosquito vector, mainly occurring in summer and often affecting the children (most of 2-7 years of age).*
Clinical pictures:
high fever
somnolence
headache
vomitting,
convulsion
coma
some sequela etc
Pathogenesis

- Pigs → Mosquitoes → Pigs
- Mosquitoes
- Human
  - Propagation in Mononuclear-macrophages
  - Viremia → Covert infection
  - Leak of Blood-CSF Barrier
  - Attack to Central nervous system
  - Alterations of cerebral parenchyma
Morphology

Mainly involves cerebrospinal parenchyma

Gross appearance:

*not characteristic*

leptomeningeal congestion and cerebral edema

pinpoint-like focus (softening foci) in cerebral parenchyma, especially in cortical.
Microscopically:

1. Degeneration and necrosis of neurons.
2. Softening foci formation.
3. Perivascular inflammatory cell infiltration.
4. Proliferation of microgliacyte.
Microscopically:

1. Degeneration and necrosis of neurons:
   - cellular swelling, disappearance of Negri body, or pyknosis, karyolysis in severe cases.

   - **Neuronophagia phenomenon**: individual neuron necrosis and phagocytosis by micro-glial cells.

   - **Satellitosis**: A condition marked by an accumulation of neuroglia cells around the neurons, often as a prelude to neuronophagia.
Necrosis of neurons
Neuronophagia phenomenon
2. Softening foci formation:

Focal neuronal necrosis
Well-circumscribed and loose, pale stained incompletely necrotic area (sieve structure).
Softening foci
3. Perivascular inflammatory cell infiltration

The most characteristic histologic change in acute viral disease is a mononuclear cell infiltrate (lymphocytes, plasma cells, and macrophages), generally located around blood vessels (perivascular cuffing).
perivascular cuffing
4. Proliferation of microgliacyte:

microglial nodules

The presence of glial nodules and neuronophagia (individual neuron necrosis and phagocytosis) also suggests viral disease.
Epidemic encephalitis B
Epidemic encephalitis B
Clinicopathologic Association

- In acute phase:
  Most infected people develop only mild symptoms or no symptoms at all.

- In more severe cases:
  viremia
  High fever, chills, headache, nausea, vomiting

- Symptoms of nerve cell injury:
  Tri-signs: High fever-convulsion-respiratory failure.
  Clouding of consciousness, somnolence
Sequela

- Case-fatality range from 0.3% to 60%, and about 30% cases present serious neurologic sequela.

- paresthesias(感觉异常), mental retardation, limb paralysis, facial paralysis
Infection of the brain is almost invariably accompanied by some reaction in the meninges, so that there will be inflammatory cells, usually lymphocytes, in the CSF.

CSF examination shows a raised lymphocyte count, with slightly raised protein and normal glucose, but may be entirely normal.
Summary briefly:

- The most characteristic histologic change in acute viral disease is a mononuclear cell infiltrate (lymphocytes, plasma cells, and macrophages), generally located around blood vessels (perivascular cuffing).

- The presence of microglial nodules and neuronophagia (individual neuron necrosis and phagocytosis) also suggests viral disease.

- A more direct expression of viral involvement is the presence of intranuclear inclusion bodies in some forms of viral infection. A well-known diagnostic inclusion is the intracytoplasmic Negri body of rabies.
Epidemic encephalitis is a meningoencephalitis characterized by perivascular inflammatory cells, many focal areas of necrosis (softening areas), and selective neuronal necrosis with neuronophagia.

In all cases there is proliferation of microglial cells, which maybe diffuse in pattern or local with glial node formation.

Alterative inflammation commonly in Summer and autumn.

In severe cases there may be a vasculitis, and vascular necrosis.
Tumor

• **Type:** primary tumor and metastatic tumor

• **Primary tumor:** glioma (40%), meningioma (15%), acoustic nerve tumor (8%)

• **metastatic tumor:** metastatic pulmonary carcinoma

• **Children:** glioma, medulloblastoma

• **Common characteristic:** local neurosis, intracranial hypertension
Glioma

Characteristic:
① local infiltration
② intracranial metastasis
Astrocytoma  （星形胶质细胞瘤）

Fibrillary astrocytoma
（纤维型星形细胞瘤）

Protoplasmic astrocytoma
（原浆型星形胶质细胞瘤）

Gemistocytic astrocytoma
（肥胖型星形胶质细胞瘤）

Anaplastic astrocytoma
（间变性星形细胞瘤）malignant tumor
Fibrillary astrocytoma

星形胶质细胞瘤
瘤细胞胞浆少，有细长的突起，胞核大小不一
原浆型星形胶质细胞瘤（2级）
瘤细胞核呈圆形，胞浆突起不明显。瘤细胞之间排列稀疏，形成微小囊腔，这是该瘤特征之一。
肥胖型星形胶质细胞瘤
瘤细胞胞浆嗜伊红染色，胞体肥大（↓所示）。
Astrocytoma
Glioblastoma multiforme, GBM
(胶质母细胞瘤)

Pilocytic astrocytoma
(毛发细胞型星形胶质细胞瘤)

children, teenagers
Glioblastoma multiforme
多形性胶质母细胞瘤
瘤细胞密集，形态多种多样，瘤细胞围绕在坏死灶周围，排列成假栅栏状（如图所示）
毛发细胞型星形胶质细胞瘤
Oligodendrogloma (少突胶质细胞瘤)

30-50-year-old, superficial layer of cortex
G: gray-red, infiltrative growth, bleeding, cystic degeneration, calcification
M: single, round, Perinuclear halo (核周晕),
少突胶质细胞瘤
瘤细胞大小一致，形态单一，圆形，核圆形居中，有核周晕
Meningioma (脑膜瘤)
1) Endothelial type
2) fibroblast type
3) vascular type
4) Pebbles type (砂粒型)
5) mixed type
6) malignant meningioma
Meningioma

Fig14-09a Meningioma

Fig14-09b Meningioma
Meningioma
脑膜瘤
瘤细胞长梭形，排列成交织束状，其间有网状及胶原纤维，可见少数脑膜细胞呈小岛状
Medulloblastoma  （髓母细胞瘤）
髄母細胞瘤
Ependymoma (室管膜瘤)
Ependynoma
室管膜瘤
瘤细胞大小形态一致，细胞围绕空腔呈腺管状排列形成菊形团（如↓所示）
Tumor of peripheral nerve

Neurilemmoma (Schwannoma, 神经鞘瘤)
Neurilemmoma

图14-11a 神经鞘瘤
Fig14-11a Neurilemmoma

图14-11b 神经鞘瘤
Fig14-11b Neurilemmoma
Neurilemmoma
神经鞘瘤
胞核梭形，互相紧密平行排列成栅栏状（↑），称为Verocay小体。
Neurofibroma（神经纤维瘤）
神经纤维瘤
由增生的神经鞘膜细胞和纤维母细胞构成，以纤维母细胞为主。细胞长梭形，紧密排列成束状，之间有淡染的粘液基质及纤维。
Metastatic tumor: 1/5

lung cancer, breast cancer, melanoma and so on

Hemorrhage, necrosis, cystis degeneration
THANKS!