Neuroinfections

- Diseases of the NS cause by viruses, bacteria, candides, parasites, sometimes fulminant course of disease and fatal complications

Neuroinfections

- 1. Bacterial
- 2. Viral
- 3. Fungal
- 4. Specific

Etiopatogenesis

- Spread of viruses to the CNS
- by the Hematogeneous or neural route.
- Hematogeneous - the viruses gain the CNS through perivascular spaces, entrance in the CSF is through the epithelial cells of the choroid plexus.
- Neural - (Herpes simplex virus - HSV, Varicella zoster virus - VZV).
- Direct spreading from – ear, nose, injury

Meningitis

- The germs that cause bacterial meningitis are very common and live naturally in the back of the nose and throat.
- People of any age can carry these germs without becoming ill.
- They spread between people by coughing, sneezing and kissing, they cannot live outside the body for long.
Meningitis

• Etiological agents
  • Streptococcus pneumoniae
  • Neisseria meningitidis

Meningitis

• Etiological agents (G-)
  • E. coli
  • Klebsiella pneumoniae
  • H. influenzae
  • Pseudomonas
  • Enterobacter species
  • Listeria monocytogenes

Meningitis

• Enteroviral inf. – Echovirus, Coxackie /Aug, Sept/
• Mumps (late winter and spring)
• Herpes simplex, typ 2, Epstein-Barr
• Lymphocytic choriomeningitis (winter)
• Adenovirus infections
• HIV

Patogenesis

• Bacteria from the place of primary infection → to blood, from blood → to CSF through choroid plexus of the lateral ventricles, or other areas of altered HEB permeability

• Germs multiply rapidly in the subarachnoid space. Recruitment of inflammatory cytokines (IL-1, TNF), recruitment of polymorphonuclear leukocytes

Patogenesis

• Result – purulent exudate in subarachnoid space, which is the basis of the neurological complications
• Obstruction of flow of CSF
• Adherence of leukocytes to the cerebral capillary endothelial surface increase the permeability of cerebral vessels → allowing for leakage of plasma proteins through open intercellular junctions → vasogenic brain edema
Patogenesis

• The leukocytes → cytotoxic edema
• The purulent exudate → decrease resorption through the arachnoid granulations → transependymal movement of the fluid into the brain parenchyma → interstitial edema
• Cerebral perfusion pressure is affected
• cerebral blood flow begins to decrease (also loss of cerebral autoregulation)

Clinical features

• Headache
• Fever ↑ (↓ - sepsis)
• Neck stiffness (not present in sepsis !)
• Photophobia
• Vomitus
• Intracranial hypertension
• Altered level of consciousness
• Seizures

Meningitis

Pneumococcal meningitis

What is bacterial meningitis?

Meningitis is an inflammation of the meninges associated with the invasion of bacteria into the subarachnoid space. The inflammatory process also affects the brain parenchyma and the ventricles.

Meningeal syndrome

Kernig – flexion of passive extended LE

MEDICAL EMERGENCY!
Petechial rash in meningococcemia (Neisseria meningitidis) – develops in few hours
(trunk, LE, mucous membranes, conjuctiva, palms, soles)

Meningococcal meningitis

Clinical feature

Clinical features – neonates!
• Fever or hypothermia
• Lethargy
• Seizures
• Irritability
• Bulging fontanel
• Poor feeding
• Vomitus
• Respiratory distress
• Absence of meningeal syndrom – can be

CSF
• Increased pressure
• Viral meningitis
• Pleocytosis – ↑ lymphocytes, proteins +-, sugar is normal – viral
• Bacterial meningitis
• Pleocytosis – polymorfonuclear leukocytes
• ↑ proteins, ↓ sugar
• Blood ↓ Leu, FW, CRP

Brain CT
Therapy

- The 3rd.-generation Cephalosporins
- Ampicillin
- Dexamethason – inhibits the synthesis of inflammatory cytokines – IL-1, TNF
- Antiedematous treatment – Mannitol
- Symptomatic therapy

TBC

- TBC – frequent in 20th century
- Chopin, Keats, Paganini, Modigliani, Thomas Wolf – died because of TBC
- 90-ties of 20th century – again increased number of TBC

TBC meningitis

- Etiology - Mycobacterium tuberculosis
- During dissemination from caverna - exudate, which is located predominantly in basilar cisterns, surrounds the cranial nerves and major blood vessels at the base of the brain

TBC meningitis

- Headache
- Meningeal syndrome
- Cranial nerves lesions - VI, III, IV, VII
- Changes in behaviour, desorientation
- Hydrocephalus
- Brain edema

CSF

- Increased pressure
- Pleocytosis – Ly
- ↓↓ sugar, ↑ proteins
- Positive cultivation
- PCR

- Contrast-enhanced T1-weighted axial MRI
- diffuse, thick, and sometimes nodular enhancement of the basal meninges (arrows), presumably due to inflammation.
**Therapy**

- INH, Rifampicin, Pyrazinamid
- Corticosteroid
- Manitol
- Symptomatic therapy

**Encephalitis**

- Frequently with meningitis
- Impairment of consciousness – confusion, stupor, coma
- Seizures
- Aphasia, hemiparesis, involuntary movements, cerebellar ataxia, polymyoclonus, cranial nerves
- Except herpetic - seasonal, epidemic form

**Encephalitis**

- Herpetic encephalitis
- Epstein-Barr virus encephalitis
- Tick-borne encephalitis
- CMV encephalitis
- Varicella zoster encephalitis

**Herpes simplex encephalitis**

- Herpes simplex virus 1
- Incidence – 4/1 million people/year
- Most severe, most frequent
- Without therapy – mortality 70%

**Herpes simplex encephalitis**

- After primary infection – most often oropharyngeal – virus is transported to ganglion Gasser, virus survives latent for all life
- In the case of reactivation - there is retrograde transport of the virus by route of n.V.
Herpes simplex encephalitis

• Clinical feature
• High fever
• Headache, vomiting
• Disorientation, confusion, memory problems
• Focal neurological symptoms
• Seizures

Herpes simplex encephalitis

• Brain edema – can be temporal herniation
• Signs from temporal lobe – changes in personality and behaviour, aphasia, seizures
• Inflammation, bleeding and necrosis of nearly all tissue elements

Herpetic encephalitis

cyrosis of temporal lobe

Herpetická encefalitis
Herpes simplex encephalitis - diagnosis

- CSF – ↑ Ly, proteins
- CT, MRI
- EEG – high, periodical waves in temporal regione, and complex of slow waves in interval 2-3 sec.
- ½ of patients – do not survive
- Th: Acyclovir 30 mg/kg/D 14 days – the better prognosis after soon beginning

Herpetic encephalitis

Herpetic encephalitis

Therapy

- Th: Acyclovir 30 mg/kg/day 14 days
- Antiedematous therapy
- Symptomatic

Tick-born encephalitis

Tick-born encephalitis

• TBE is caused by tick-borne encephalitis virus (TBEV), a member of the family Flaviviridae.
• Transmitted by Ixodes ricinus
• Initially isolated in 1937
• Clinical course – non-specific with symptoms that may include fever, malaise, anorexia, muscle aches, headache, nausea, and/or vomiting
Tick-born encephalitis

- The central nervous system - symptoms of meningitis (e.g., fever, headache, and a stiff neck) or encephalitis (e.g., drowsiness, confusion, sensory disturbances, and/or motor abnormalities such as paralysis) or meningoencephalitis
- Meningoencephalitis, myelitis
- Consequences – 10% patients

Tick-born encephalitis

- CSF - an increase in the number of white blood cells in the cerebrospinal fluid
- Low white blood cell count (leukopenia) and a low platelet count (thrombocytopenia)
- There is no specific drug therapy for TBE.
- Anti-inflammatory drugs, such as corticosteroids, may be considered

Spirochete infections

- *Boreliosis (Lyme disease)*
  - *Borrelia burgdorferi*
- *Syphilis (Lues)*
  - *Treponema pallidum*

Encephalitis

- *Varicella zoster encephalitis* (VZV)
  - through n.V.
- *Epstein-Barr virus* (EBV)
  - EBV in 90% people
  - Manifestation – mononucleosis, with meningitis, encephalitis
- *CMV encephalitis*
  - Immunodeficient people - AIDS

Borrelia burgdorferi

![Image of Borrelia burgdorferi](image)

Lyme disease

- After tick bite
- Skin lesion
Lyme disease - patogenesis

- Spreading – by spirochetemia, spreading in all the body
- CNS – clinical feature
- Early syndromes
  - meningitis, facial nerve palsy (less other cranial nerves), radiculoneuritis
- Late syndromes
  - encephalopathy
  - sensorimotor polyradiculoneuropathy

Lyme disease - meningitis

- Within 12 weeks of infection
- Headache, fatigue, myalgia, artralgia
- CSF: pleocytosis – Ly, ↑ proteins
  - sugar – normal
  - intrathecal production of BB antibodies (IgG, IgA)
- PCR

Lyme disease – facial palsy

- In 4 weeks from erythema migrans
- Unilateral or bilateral facial palsy
- Other cranial nerves - rarely
- ELISA
- CSF: pleocytosis – Ly, intrathecal production of antibodies (about 10%)
- Th: Doxycycline (2x100 mg/D, 2W) CSF negat.
  - i.v. ceftriaxone – CSF pozit.
A 50-year-old woman with a history of tick bite and erythema migrans rash treated with doxycycline, who had recurrent erythema migrans rash with headache, fever, nausea, and neck rigidity.

Lyme disease - radikuloneuritis

- Severe, sharp, jabbing or deep and boring pain, in a radicular nerve distribution
- Within days, weeks: sensory loss, weakness, hyporeflexia, if there is myelitis – sphincter dysfunction, + Babinski
- CSF: Ly, ↑ proteins, intrathecal production of antibodies
- EMG: axonal lesion

Lyme disease - encephalopathy

- In patients with systemic manifestation and arthritis
- Confusional state, memory and cognitive slowing
- CSF – only in 5 % pozit. Ly less than in 50 % pozit. antibodies

A 56-year-old woman with neck, bilateral shoulder, and bilateral arm pain.

A 74-year-old man with 2-year cognitive decline and memory loss.

Lyme disease– senzorimotoric polyradiculoneuropathy

- Chronic radiculoneuropathy – sensory symptoms, particularly distal paresthesias in a stocking and glove distribution, less severe than in acute polyradiculoneuritis G.-B.
- EMG – axonal lesion
- Likvor – frequently negat.
Syphilis (Lues)

- 1/3 nontreated patients – neurovascular complications of syphilis

Neurosyphilis

- Patogenesis
  - Perivascular infiltration of the meninges, focal meningeal inflammation – formation of hypertrophic meninges, or gumma,
  - Inflammatory cells invade blood vascular wall – arteritis (luminal occlusion)
  - Parenchymal involvement – glosis in late stages
  - Ly infiltration of preganglionic portion of dorsal roots and posterior columns atrophy of posterior columns

Neurosyphilis – acute symptomatic meningitis

- Headache, nauzea, vomitus, neck stifness
- Abnormalities of cranial nerves II, VI, VII, VIII
- CSF: Ly, decreased sugar, ↑ proteins
- Pozit. TP-TA (Treponema pallidum particle agglutination) test

Neurosyphilis - meningovascular

- Within 5 – 7 years after initial infection
- Inflammatory obliterative endarteritis involving small and medium-sized arteries (MCA)
- Focal signs from local ischemia
- CSF: Ly, increased proteins, pozit. VDRI.
- AG: diffuse narrowing of arteries
- MRI: multiple areas of narrowing
- Spinal arteries – transversal myelitis
Neurosyphilis

- Fig. 1. A and B - T1 weighted coronal MRI (after contrast) and T2 weighted coronal MRI (without contrast) showing a left fronto-parasaggital lesion surrounded by an oedematous interhemispheric area. The left temporal and subcortical areas, amygdala (A), and lateral ventricular walls (B) are involved by a hypointense lesion. The absence of bleeding is evidenced. After contrast, contrast enhancement is evidenced, extending along the frontal and interhemispheric areas.

- C and D - MRA and MRA-3D Reconstruction showing 2 aneurysms of distal A2 segment of both ACAs. The right-sided aneurysm is about 5 mm in diameter, while the left-sided aneurysm is approximately 3 mm in diameter, and is located in the terminal part of A2 hypoplastic ipsilateral segment.

- E - T1 weighted coronal MRI (after contrast) performed after biopsy, showing signs of previous surgery, with left frontal craniotomy and an underlying cavity. In respect to the previous neuroimaging investigations, the absence of frontal cortical swelling is evidenced. After contrast, the leptomeningeal enhancement persists, extending along the frontal and interhemispheric areas.

MRI

Neurosyphilis

- Treatment
  - PNC, ceftriaxone – 2 weeks
  - Meningovascular – also antithrombotic therapy

Acquired immunodeficiency syndrome (AIDS)
Human immunodeficiency virus (HIV)

- Neurological complications
- Aseptic meningitis
- Cognitive disturbances – adults
- Progressive encephalopathy – children
- Myelopathy
- Neuropathy (inflammatory demyelinating polyneuropathy, brachial plexopathy, mononeuritis)
- Myopathies – myopathy, myositis

AIDS

- tumors
  - Primary lymphoma of CNS (PCNSL) most frequent, children, adult – 5% clinical feature – headache, confusion, impaired memory, seizures, cran. nn. )
  - MTS non-Hodgkin lymphoma into CNS
  - Kaposi sarcoma
AIDS

- Oportune infections
- Bacterial — (Mycobacterium tuberculosis, Treponema pallidum, Nocardia, ...)
- Viral — (Cytomegalovirus, Herpes simplex, Varicella zoster, JC, ...)
- Fungal — (Cryptococcus neoformans, candida, ...)
- Protozoa — (Toxoplasma gondii, ...)

AIDS dementia complex (ADC)

- Brain atrophy, wide ventricles and subarachnoid space

AIDS dementia complex (ADC)

- T2- MRI:
  - Enlargement of ventricles,
  - hyperintensity in subcortical white matter of both frontal lobes

Brain abscess

- A rare complication in immunocompetent individuals
- AIDS
- Chronic corticosteroid therapy
- Immunosupression after bone marrow transplantation

Clinical feature

- Headache
- Fever
- Vomitus
- Focal neurological deficit
- Focal or generalized seizures
- ICH – letargy, confusion, coma,
- Papilledema
- Palsy of cranial nerves III, VI, or both
Brain abscess - CT
Brain abscess in 2 years old child
Ptosis, fever, papilloedema
60 ml of pus Gram + and Gram – bacteria

Diagnosis and therapy
- CT
- CSF – lumbar puncture – contraindicated in brain abscess
- Therapy:
  - Aspiration or extirpation abscess + antibiotics

Herpes zoster (shingles)
- Varicella zoster virus
- Incidence 3-5 /1000/ year – old people, with malignancies, mainly lymphoma and M. Hodgkin
- Reactivation of varicella virus – latent in senzoric ganglia after the primary infection with chicken pox
Herpes zoster

- Radicular pain – sometimes before eruption
- Vesicular cutaneous eruptions spread over two or three dermatomes on one side
- Most often - thoracic part
- Cranial ganglia – oftalmic paresis
  Ramsay Hunt - n. VII. palsy, vertigo, deafness

Herpes zoster

- CSF –↑elements and proteins
- Pain 1 – 4 weeks
- Later – postherpetic neuralgia
- Treatment – Acyclovir 800 mg 5x/day, 7 days
  reality – 5 x 200 mg

Herpes zoster

- Postherpetic neuralgia
- Paint in territory of herpes zoster, lasting minimally 3 month after eruptions

- 10 -15% patients
- Treatment – Gabapentin 3 x 300 – 3 x 1200 mg, pregabalin
  Common analgetics are not effective!