

# Neuroinfections

# Classification

## A. Localization

- Meningitis- inflammation of meninges
- Encephalitis-brain inflammation
- Myelitis- spinal cord onflammation

## B. Etiology

- Bacterial
- Viral
- Fungal
- Parasitic
- Prion diseases

## C. According to cerebro-spinal fluid character

- Purulent
- Non-purulent

# Bacterial

- Pneumococci - *Streptococcus pneumoniae* - Gram-positive bacteria
- Meningococci- *Neisseria meningitidis* - Gram negative bacteria
- *Haemophilus influenzae*
- *Mycobacterium tuberculosis*
- *Borrelia burgdorferi*

S. pneumoniae, H.influenza- carriers in the nasal cavity

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graph TD; A[S. pneumoniae, H.influenza- carriers in the nasal cavity] --> B[bacteriemia]; B --> C[seeding of the bacteria to different locations, this gives rise to:]; C --> D[Sepsis<br/>Purulent meningitis<br/>Disseminated pneumonia];
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bacteriemia

seeding of the bacteria to different locations, this gives rise to:

Sepsis

Purulent meningitis

Disseminated pneumonia

# Symptoms of bacterial meningitis/ encephalitis

- headache
- nausea
- vomiting
- photophobia
- high body temperature
- disorders of consciousness
- petechiae
- convulsions
- symptoms of cranial nerve damage and focal brain damage

# Brain abscess

- Etiology: staphylococci, streptococci, bacilli anaerobic bacteria
- Secondary to some purulent inflammation- nasal sinuses, middle ear, infected fractures of the skull.

# Symptoms

- headache, signs of focal brain injury depending on the location,
- diagnostic tests: computed tomography, magnetic resonance imaging of the brain
- Treatment: surgery with simultaneous antibiotic therapy

# Tuberculous meningitis (*Mycobacterium tuberculosis*)

- Source of infection: a sick man
- The route of infection: blood-derived mostly from the primary focus in the lungs, lymph nodes or organ tuberculosis
- Rare incidence
- People with immunodeficiency.

# Symptoms

Prodromal stage:

- increased body temperature
- chills
- weakness
- night sweats
- headaches
- nausea
- vomiting

Developed stage of the disease:

- symptoms of meningitis
- damage to the cranial nerves
- focal symptoms
- rarely seizures

# Lyme disease

- Neuroborreliosis – bacteria-Borrelia spirochete, the symptoms of nervous system involvement may occur at any stage of the disease (early / late)
- Radiculopathy, mononeuropathies
- Meningitis
- Encephalitis
- Cranial nerve palsies

## Symptoms:

- asymptomatic infection
- mild aseptic meningitis
- headache, photophobia, neck stiffness, fever

# Viral

- Enteroviruses - polio, echo, coxsackie
- Paramyxoviruses - mumps virus, measles
- Herpes Viruses - HSV type 1 and 2, CMV, Epstein-Barr virus
- Tick-borne encephalitis (TBE) virus
- Rabies virus

# Epidemiology- TBE

- Subtypes of tick-borne encephalitis (TBE):
  - European
  - Siberian
  - Far- east
- Mortality infection subtype of the Far East - 15-20%, the remaining 1-4%
- 10-12000 new cases of TBE in the world each year
- According to the National Institute of Hygiene in Poland, the average annual incidence of approx. 0.7-0.9 /100 000 - approx. 260 cases

# TBE virus

- TBE is typically characterized by a biphasic course:
  - Phase I: non-specific flu-like symptoms and the latency period
  - Phase II: meningitis, meningoencephalitis, or inflammation of meninges, brain and spinal cord
- Patients with TBE viral infection:
  - 30% do not develop clinical signs and symptoms
  - 30% -50% experience only 1 phase of the disease
  - 30% of patients develop 2 phase- CNS activity.
- M>F
- all age groups
- More severe in the elderly
- Even 46% of patients in the Phase 2 TBE developing late complications

- The diagnosis of TBE is only on the basis of signs and symptoms which may be easily overlooked.
- In children with neurological symptoms, residing in areas endemic for TBE virus-> serological tests for the presence of anti-TBE.

# 2 phase of TBE viral infection- symptoms

- Fever, whose value often exceeds 40°C.
- Meningitis accompanied mainly headache, nausea, vomiting, dizziness and neck stiffness.
- Encephalomenigitis is accompanied mainly cerebellar signs and symptoms, which usually belongs ataxia.
- Other neurological symptoms-meningeal signs, confusion, convulsions, slurred speech, tremors.
- Paralysis of the spinal nerves was observed in 11-15% of patients.
- Occurrence paresis of limbs in patients with inflammation of the meninges, the brain and spinal cord, upper limbs are more affected than lower
- Seizures are rare

# Laboratory tests

## Signs of infection in blood serum

- Leukocytosis, which is much higher than other forms of viral meningitis (6600-14600 / mm<sup>3</sup>)
- Elevated ESR (up to 100 mm / hr.)
- Elevated CRP

## Cerebrospinal fluid (CSF)

- Rarely the virus can only be detected in a sample of CSF, not in blood
- Pleocytosis (predominance of lymphocytes) to 5000 / mm<sup>3</sup>, higher number of rod-shaped granulocytes (60% -70%) than lymphocytes (30% -40%)
- Protein 50-200 mg/dl
- Increased ratio of albumin in the CSF to albumin serum - impairment of the blood-CSF transfer

- The diagnosis of TBE - detection of specific antibodies
- Typically, IgM and IgG antibodies are present in the first serum samples when the symptoms from the CNS appear
- It is rare to detect only IgM antibodies in the first serum sample. In this case - repeat the test. The presence of IgM antibodies is not enough to establish the diagnosis.
- A few days later, IgM and IgG antibodies are detected in the CSF.
- IgM antibodies can be detected in serum for several months.
- IgG antibodies persist for the lifetime of the patient.

# TBE in children

TBE in children has less severe course than in older patients, but

- about 20% -30% of the affected children develop encephalomeningits
- about 25% develop long-term disturbance in attention and concentration deficits
- about 2% suffer from permanent consequences of neurological disease

Long - term consequences of TBE infection in children are unknown, which underlines the importance of an accurate diagnosis.

# Long- term symptoms of TBE

- Ataxia, confusion, double vision, urinary retention and mild limb paresis
- Quadriplegia, coexisting paralysis of the respiratory muscles, dysphagia, dysarthria



# TBE treatment

- The results of the laboratory tests did not affect the treatment - are used to distinguish between the TBE and the other infections
- TBE infection - no antiviral treatment.
- treatment- only symptomatic:
  - maintaining fluid and electrolyte balance
  - ensure adequate supply of calories
  - analgesics and antipyretics
  - administration of anticonvulsant drugs- if necessary
  - use of physiotherapy infected limbs in order to prevent muscle atrophy
  - use IGV- good results
- The most effective prevention of TBE vaccination

# TBE virus vaccination

The two vaccines:

- Encepur
- FSME Immun Inject

Standard scheme:

- I dose of 0.5 ml
- II dose - 0.5 ml, after 1-3 months
- III dose - 0.5 ml , 9-12 months after the second dose

Shorten scheme:

- I dose of 0.5 ml
- The second dose on day 7 0.5ml
- III dose of 0.5 ml in 21 days
- Revaccination every 3-5 years

# CSF examination

|                     | Cell number | Cell type    | protein            | glucose |
|---------------------|-------------|--------------|--------------------|---------|
| <b>normal</b>       | <5          | limphocytes  | <45mg%             | >40mg%  |
| <b>purulent</b>     | >200        | granulocytes | above normal       | <normal |
| <b>purulent</b>     | <200        | limphocytes  | normal or > normal | normal  |
| <b>tuberculosis</b> | <200        | limphocytes  | >normal            | <normal |
| <b>tuberculosis</b> |             |              |                    |         |

# Symptoms of purulent meningitis in adults

- headache, nausea, vomiting
- photophobia, hypersensitivity to sounds
- anxiety then progressive loss of consciousness, confusion, coma
- abnormal rhythm of sleep and wakefulness
- the physical examination: neck stiffness and positive signs of meningeal syndrome (Brudzinski, Kernig)

# Meningeal signs

Brudzinski sign :

Neck : the patient lying on his back -> neck flexion -> limbs flexion in the knee and hip joints

Symphyseal : pressure on the pubic symphysis elicits a reflex flexion of the hip and knee, and abduction of the leg

Kernig sign:

positive when the thigh is flexed at the hip and knee at 90 degree angles, and subsequent extension in the knee is painful (leading to resistance)

# Meningeal signs

Nuchal rigidity is the inability to flex the neck forward due to rigidity of the neck muscles

Amoss sign:

indication of painful flexion of the spine in which it is necessary to support a sitting position by extending the arms behind the torso and placing its weight on the hands.

# Symptoms of purulent meningitis in infants

- meningeal symptoms usually are absent
- tense and arched front fontanelle
- hyperacusis skin
- anxiety
- groans
- convulsions

# Viral meningitis encephalitis

- the summer months and early fall
- relate to young people up to 40 years of age
- very rare in infants
- usually mild, without permanent sequelae
- sometimes accompanied by inflammation of the brain (encephalomeningitis, meningoencephalitis)

# Viral encephalitis- etiology

- Viruses originally neurotrophic: rabies virus, arboviruses (exotic encephalitis virus)
- Infectious diseases complicated by encephalitis: measles, mumps, rubella, chicken pox, shingles, flu
- Other adenoviruses, rotaviruses, enteroviruses
- Encephalitis caused by the herpes simplex viruses:
  - Herpetic encephalitis
  - Herpes simplex encephalitis (HSE)

# CSF fluid in viral encephalitis

- changes as in lymphocytic meningitis
- in untreated HSE mortality rate of 60-80%, recovery without residual 2.5% of patients
- drug of choice: acyclovir (Zovirax) 10 mg / kg. every 8 hours

# Bacterial meningitis

- Life- threatening condition- should be treated as soon as possible
- Before treatment:
  1. Lumbar puncture - if there is no contraindications – cytological and biochemical tests, latex tests, direct preparation, culture, PCR
  - 2. Blood test - to 2 tubes with 2 different sites for culture
- latex tests, PCR.

# Actual diagnostic guidelines

From the first contact with the doctor to give empirical therapy is time <3 hours

in the case of meningococcal etiology for 30 minutes.

Antibiotics - given i.v. ,maximum doses (limited penetration into the CNS).

For the empirical therapy at least two antibiotics

# Recommended treatment

| Age                             | Etiology   | Antibiotics   |
|---------------------------------|--|---|
| Infants<br>Perinatal infections | E.coli, Streptococcus agalactiae, Listeria monocytogenes, Klebsiella sp, and others, Gram minus intestinal bacilli       | Ampicilin and Cefotaksym<br>or<br>Ampicilin and aminoglikozyd |
| Infants- nosocomial infections  | Streptococci, Gram minus intestinal bacilli , Pseudomonas aeruginosa   | Ceftazidim and vancomicin                                     |
| Infants 1-3 mo                  | Neisseria meningitidis, Haemophilus influenzae, Streptococcus pneumoniae and some pathogens from infants group           | Cefotaxim or ceftriaxon and vanconicin, sometimes ampicilin   |
| 3 mo- 5mo                       | Neisseria meningitidis, Haemophilus influenzae, Streptococcus pneumoniae   | Cefotaxim or ceftriaxon and vanconicin                        |
| 5-50 yr                         | Neisseria meningitidis, Streptococcus pneumoniae   | Cefotaxim or ceftriaxon and vanconicin                        |
| >50yr                           | Neisseria meningitidis, Streptococcus pneumoniae Streptococcus agalactiae, Listeria monocytogenes Haemophilus influenzae | Cefotaxim or ceftriaxon and vanconicin and ampicilin          |

# Time of standard treatment

| Bacteria  | Duration   |
|---|------------|
| <i>Neisseria meningitidis</i>   | 7 days     |
| <i>Haemophilus influenzae</i> typ b   | 7-10 days  |
| <i>Streptococcus pneumoniae</i>   | 10-14 days |
| <i>Streptococcus agalactiae</i>   | 14-21 days |
| <i>Staphylococcus aureus</i>  | 14 days    |
| <i>Listeria monocytogenes</i> , <i>Pseudomonas aeruginosa</i> , Gram minus intestinal bacilli | >21 days   |
| Unknown etiology  | 10-14days  |

# Viral encephalomeningitis

- Treatment - infections caused by viruses of herpes: acyclovir (Zovirax) 10 mg / kg / dose every 8 hours
- In infections CMV ganciclovir (Cymevene) 5 mg / kg / dose every 12 hours
- Drugs antioedematous:
- 20% Mannitol 200 ml (children 10 ml / kg / day) every 8-12 hours, Dexamethasone 8 mg (children 0.6-1 mg / kg / day) every 6-8 hours
- Anticonvulsants (Luminal, Relanium)
- Anti-inflammatory, antipyretic

# Supervision of diagnosis and treatment neuroinfections

- KORUN - National Reference Centre for Bacterial Infections of the Central Nervous System
- KORLD- National Reference Centre for Antimicrobial Susceptibility Testing