

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 / mm³)
- 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 / mm³, 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 encephalomeningitis
- 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
normal	<5	limphocytes	<45mg%	>40mg%
purulent	>200	granulocytes	above normal	<normal
purulent	<200	limphocytes	normal or > normal	normal
tuberculosis	<200	limphocytes	>normal	<normal
tuberculosis				

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 Perinatal infections	E.coli, Streptococcus agalactiae, Listeria monocytogenes, Klebsiella sp, and others, Gram minus intestinal bacilli	Ampicilin and Cefotaksym or 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