Infectious diseases of CNS

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Headache

- Most common complaint - in general neurological practice.
- The large majority of headaches are not life-threatening
  - migraine, tension, or chronic daily headaches.
- serious underlying causes:
  - space-occupying intracranial lesions such as neoplasm or abscess, subarachnoid hemorrhage, hydrocephalus, meningitis, or encephalitis.

Signs and symptoms of increased intracranial pressure:

- Bulging fontanelle (infants)
- Large head (infants)
- Nausea
- Projectile vomiting
- Headache
- Reduced retinal venous pulsations
- Papilledema
- Cranial nerve VI palsy
- Bradycardia (severe cases)

Terminology of CNS infection

- Affect CNSs coverings: meningitis.
- brain parenchyma: encephalitis
- spinal cord: myelitis.
- all are affected: "meningoencephalomyelitis„
- Localized:
  - within the brain or spinal cord: abscess, sinus thrombophlebitis
  - outside: epidural abscess or subdural empyema.

MENINGITIDES

Dynamics

- Acute: monophasic, biphasic
  - purulent (bacterial) meningitis
  - „aseptic" lymphocytic meningitis
- Subacut, fluctuating (tbc, leptospira, syphilis, brucella, fungus, protozoon)
- Chronic meningitides (immunologic)
  - Intermittent, progressive
- Recurrent (EB, Behcet, immuncompromise)

Bacterial meningitis: 3-10/100,000 per year

Acute pyogenic meningitis

Pathology:

- 1. meningeal infiltration
- 2. blood-brain barrier damage

- 3. diffuse degeneration, **necrosis with glial proliferation** in the cortex or the spinal cord
  - **infiltration**
  - thrombosis of the venous sinuses
  - **hydrocephalus**
  - **endarteritis** giving cerebral ischaemia and infarction

- 4. Damage of the nervous tissue (neuron, axon, myelin sheets)

ACUTE MENINGITIS

Aetiology, source of infection:

1. hematogenous

- respiratory tract: pneumonia, abscess
- middle ear - otitis!
- skin

2. direct

- paranasal sinuses
- mastoid cells
- head, spinal injury; skull fracture

3. peripheral nerves

- rabies, HSV,VZV

Clinical picture

- General: fever, weakness
- **Meningeal irritation:**
  - hyperirritability
  - headache increasing in severity
  - vomiting
  - convulsions (in children)
- **Signs of meningeal irritation:**
  - nuchal rigidity (spasm of the extensor muscle)
  - head retraction
  - Kernig's and Brudzinski's signs

Diagnosis=Cerebrospinal fluid

- CSF: green-like
- is under increased pressure
- the **cells** numbers:
  - 1000 to several 10 000 cells/µl (polymorphonuclear leucocytes)
- the **protein** is increased (5.0 g/l)
- **glucose** is reduced
- lactate rises

Therapy: based on the culture

Diagnosis of meningitis

Distinguishe from:

- 1. acute general infections
- 2. meningism (the CSF is normal)
- 3. meningoencephalomyelitis, intracranial abscess
- 4. subarachnoid haemorrhage
- 5. other forms of meningitis (virus, sarcoidosis, carcinomatosis)

Treatment

- Based on culture!

- Before culture:
- I.v. third-generation cephalosporin – ceftriaxone (2x2 g), cefotaximum (6x2 mg)
- PLUS
- I.v. vancomycin (2x1 g)
- In case S. pneumoniae, H. influenzae +Dexamethason

"ASEPTIC" or LYMPHOCYTIC (serosus) MENINGITIS

- **Signs and symptoms**
  - Headache
  - Fever
  - Viral syndrome
  - Meningismus
- Clinical picture
  - Incubation: 7-10 days, „dromedary" course

"ASEPTIC" or LYMPHOCYTIC (serosus) MENINGITIS

Pathogens:

- Virus
  - HSV, HZV, EBV, CMV
  - Entero (Echo, Coxackie, Polio etc.)
  - Arbo (tick-bite encephalitis virus)
  - Adeno, LCMV, HIV etc.
- Spirochete (Leptospira, Borrelia, Treponema)

"ASEPTIC" or LYMPHOCYTIC (serosus) MENINGITIS

Diagnosis: **CSF**

- **cell** count: < 100-1000 cells/μl
  - mononuclear and lymphocytic cells
- **protein**: slightly elevated (0.4-1 g/l)
- glucose level: **normal in viral forms, ~ reduced in tuberculosis or fungus**
- Microbiol. culture: negative
- Dg: serology (repeated)
- Therapy: supportive

Stages of Lyme disease:			
Stages:	**1.** Localized early (acute) stage: From 7-10 to 30 days	**2.** Early disseminated stage In weeks	**3. Late stage** Several years after the onset
Skin	Erythema migrans (localized)	Erythema migrans (multiplex) Lymphadenosis benigna cutis	Acrodermatitis chronica atrophicans
Neurological	No or meningismus	Lymphocytic meningitis Meningoradiculitis (Bannwarth syndroma)	Chronic polyneuropathy Chronic progressive encephalomyelitis
Other	Lymphadenopathy Flu like symptoms	Carditis Arthralgia, arthritis	Chronic arthritis

The diagnosis of Lyme disease

European Journal of Neurology 2010, 17: 8–16 doi:10.1111/j.1468-1331.2009.02862.
EFNS GUIDELINES/CME ARTICLE

EFNS guidelines on the diagnosis and management of European Lyme neuroborreliosis

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Criteria

(i) neurological symptoms

(ii) cerebrospinal fluid (CSF) pleocytosis

(iii) Bb-specific antibodies produced intrathecally

- IgM for acut cases (2-6 wks after exposure) – stage 1. and 2.
- IgG for chronic cases – stage 3.

- three criteria should be fulfilled for definite LNB, and two of them for possible LNB

Treatment of Lyme disease

- 2 g/day Ceftriaxone (Rocephin) for 14 day
  - For 21 days in late stage
- long term tetracycline (Doxycyclin) – 200 mg/day doxycycline for 21-28 days

Subacute/CHRONIC MENINGITIS

- Pathogens
- Infective
  - Mycobacterium tuberculosis, mycoplasma, Brucellosis
  - Fungus
  - Virus (LCMV)
  - Toxoplasma gondii
- Non-infective
  - (leukemia, Mollaret's meningitis, CNS vasculitis, SLE, Behcet sy., neurosarcoidosis, neoplasm –esp. lung, breast)
- Clinical pictures (weeks-to months)
  - headache
  - Intermittent febrile status
  - Slowly progressive mental changes
  - mild (or absent) meningeal signs,
  - progressive cranial nerves palsies

TBC

Fever +/-, headache, meningismus, mental status changes

increased intracranial pressure

Cranial nerve palsies

CSF : lymphocytic pleocytosis, elevated protein, reduced glucose.

Direct Ziehl-Neelsen staining of acid-fast bacilli!

Therapy: prolonged--isoniazid, rifampin and pyrazinamide - for two months

Abscess in brain

Headache

Focal neurologic deficits

Fever

Papilledema (with increased ICP)

Nausea, vomiting (with increased ICP)

Focal neurologic deficit or seizure

Dg: CT

Therapy: antibiotics, surgical

Myelitis and spinal epidural abscess

- Symptoms
  - Fever
  - Back pain
  - Limb weakness or sensory changes
  - Bowel or bladder dysfunction
- Dg:
  - Characteristic signs and symptoms
  - MRI of the spine at the level suggested by the clinical exam.
  - Lumbar puncture for suspected myelitis, but not for spinal epidural abscess
- Therapy:
  - mainly supportive, but high dose steroids is worth considering
  - Spinal epidural abscess is a medical emergency
  - antibiotic therapy is essential

ENCEPHALITIS

- Meningoencephalitis
  - *generally purulent*
- Panencephalitis
  - *generally viral*
  - *white matter+gray matter*
  - *SSPE, herpes, rubella, B encephalitis*
- Polioencephalitis
  - *generally viral*
  - *gray matter*
  - *poliomyelitis, lyssa, tick*
- Leukoencephalitis
  - *generally viral*
  - *white matter*
  - *acut disseminated enceph., postvaccination, acut haemorrhagic, PML*

Herpes encephalitis

Primary (subclinical) infection of HSV1, endogenous reactivation

- Flu-like
- temporal lobe impairment (memory loss, seizures, behavioural changes, aphasia)
- psychoorganic syndrome

- EEG: first 5-7 days of illness: nonspecific slow-wave activity
- CT (MRI): localized oedema, low density lesions, haemorrhage
- CSF: nonspecific, lymphocytic pleocytosis, 5-500 cells/mm^3 , protein level almost normal (< 0.5 g/l) or increased (up to > 2 g/l)
- Diagnosis: HSV DNA detection in CSF by PCR
- Therapy: acyclovir

Arthropod-borne **encephalitis**

West Nile Virus (WNV)

- New York in 1999
- transmitted from birds to humans (by Culex mosquitoes)
- Incubation: 2-15 days
- age (80 y)
- Symptoms: flaccid weakness due to involvement of anterior horn cells, or less commonly parkinsonism, ataxia, polyradiculopathy, seizures, and cranial neuropathy
- Mortality: about 10%
- Diagnosis: clinical history, serology (IgM), CSF findings

Progressive multifocal leukoencephalopathy

- Immunosuppression (HIV, cytostatics, leukemia, malignancies)
- JC papova virus - oligodendroglia degeneration
- Clinical picture: subacut onset, personality changes, pyramidal signs, ataxia, dementia, death within a few months
- CSF: unremarkable
- MRI: demyelination, confluent, no enhancement
- Dg: CSF, biopsy
- Th: stop immunosuppression, symptomatic