INFLAMMATORY DISEASES in the CNS

27. March 2013
Tunde Csepany
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
- **Subacute, fluctuating** (tbc, leptospira, syphilis, brucella, fungus, protozoon)
- **Chronic meningitides** (immunologic)
  - Intermittent, progressive
- **Recurrent** (EB, Behcet, immunocompromise)

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, the routes of infection:
1. hematogen (abscess)
2. paranasal sinuses (meningitis)
3. respiratory tract (nose, lung) (meningoencephalitis)
4. head, spinal injury; skull fracture (epidural abscess, epidural empyema, meningitis)
5. 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

Distinguish 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

- Before culture:
  - I.v. third-generation cephalosporin - ceftriaxone, cefotaximum
  - I.v. penicillin G, or ampicillin or gentamycin
  - In severe case + Dexamethason (Streptokinase)
    - Intrathecally:
      - 10 000 units (6 mg) of benzylpenicillin in 10 ml saline (turbid fluid is found on the lumbar puncture)
      - 5-10 mg Streptomycin, 10-20 mg ampicillin
"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 LYMPHOCYCTIC (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:

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

(Lyme IgG/IgM serology)

- **ELISA**: screening test (recommended at least 4 weeks postexposure)
  - IgM for acute cases (2-6 wks after exposure) – stage 1.
  - IgG for chronic cases – stage 3.
    - *Presence of antibody indicates exposure, not active disease*
- Positive tests must be confirmed by Western immunoblot (WB) test
Treatment of Lyme disease

- 2 g/day Ceftriaxone (Rocephin) for 14 days
  - 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

Headache
Focal neurologic deficits
Fever
Papilledema (with increased ICP)
Nausea, vomiting (with increased ICP)
Focal neurologic deficit or seizure
Therapy: antibiotics, surgical
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., potvaccination, acut haemorrhagic, PML
Acute Herpes encephalitis

Herpes encephalitis

Primary (subclinical) infection of HSV1, endogenous reactivation

- Flu-like
- temporal lobe impairment
- psychoroganic 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/mm³, 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 viremic 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.
Leukoencephalitis

- Pathology: immune demyelination
- Clinical picture: acute/subacute, monophasic disease
- Parainfection - encephalomyelitis (measles, rubella, smallpox, mumps, infectious mononucleosis)
- Postvaccination - encephalomyelitis (vaccination against smallpox, measles, rabies, tetanus)
ADEM

- transient autoimmune response
- preceded by a viral illness
- children younger than 10 years
- Onset: rapid
- meningeal signs, headache, seizures, altered mental status (delirium)
- neurologic deficits vary: ataxia, optic neuritis, hemiplegia, paraplegia, sensory loss, transverse myelitis
- CSF protein level: modestly elevated (0.5-1.5 g/L), lymphocytic pleocytosis
- corticosteroids, plasmapheresis, intravenous immunoglobulin
Progressive multifocal leukoencephalopathy

- Immunosuppression (HIV, cytostatics, leukemia, malignancies)
- JC papova virus - oligodendroglia degeneration
- Clinical picture: subacute 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