CNS Infections
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- Meningitis
- Meningoencephalitis
- Brain abscess
- Subdural empyema
- Epidural abscess
- Septic venous sinus thrombophlebitis
Epidemiology

- Influence of vaccines (Hib and conjugated pneumococcal)
- ↑ing incidence of *S. pneumoniae* (50+% of cases in US)
- Shift from pediatric disease to adult disease
- ↑ing incidence of ATB-resistant organisms, esp. *S. pneumoniae*
  - PCN resistance ~35% (15-20% high level)
  - Ceph resistance 15-20% (5-10% high level)

Epidemiology

- 1805-1900’s: ~100% fatal
- 1913: Flexner: intrathecal meningococcal antiserum. Prevented some deaths
- 1930’s: Antibiotics. Improved survival
- Current data:
  - Adults: 25% mortality,
  - 21-28% neurologic sequelae
Clinical Features

- 25% of adult cases “classic”
  - Rapid development of
    - Fever
    - HA
    - Stiff neck
    - Photophobia
    - Change in MS
- Nonspecific signs/symptoms in very young/old
- 25% will develop seizures

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPP</th>
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<tbody>
<tr>
<td>Nuchal rigidity</td>
<td>30%</td>
<td>68%</td>
<td>26%</td>
<td>73%</td>
</tr>
<tr>
<td>Kerning’s</td>
<td>5%</td>
<td>95%</td>
<td>27%</td>
<td>72%</td>
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<tr>
<td>Brudzinski’s</td>
<td>5%</td>
<td>95%</td>
<td>27%</td>
<td>72%</td>
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Thomas KE et al, CID 2002, 35:46-52

APPROACH TO THE PATIENT WITH SUSPECTED MENINGITIS

Decision-Making Within the First 30 Minutes

Clinical Assessment
Mode of presentation
  - Acute (< 24 hrs)
  - Subacute (< 7 days)
  - Chronic (> 4 wks)
Historical/physical exam clues
Clinical status of the patient
Integrity of host defenses
Brain CT scan: role in meningitis

- Over-employed diagnostic modality → Leads to unnecessary delays in Rx & added cost
- Rarely indicated in patients with suspected acute meningitis
- Mandatory in patients with possible focal infection
- Increased sensitivity with contrast enhancement

301 patients with suspected meningitis; 235 (78%) had CT prior to LP
- CT abnormal in 56/235 (24%); 11 patients (5%) had evidence of mass effect
- Features associated with abnormal CT were age >60, immunocompromise, H/O CNS disease, H/O seizure w/in 7d, & selected neuro abnormalities

Hasbun, NEJM 2001;345:1727

Neuro abnormalities included altered MS, inability to answer 2 consecutive questions or follow 2 consecutive commands, gaze palsy, abnormal visual fields, facial palsy, arm or leg drift, & abnormal language
- 96/235 patients (41%) who underwent CT had none of features present at baseline
- CT normal in 93 of these 96 patients (NPV 97%)

Hasbun, NEJM 2001;345:1727
CSF STUDIES

- Color/Clarity
- Cell counts/WBC diff
- Chemistries (protein, glucose)
- Stains/Smears (Gram)
- Cultures (routine)
- +/- Antigen screens
- PCR

BACTERIAL VS VIRAL MENINGITIS

- Predictors of bacterial etiology:
  - CSF glucose < 34
  - CSF: Serum glucose ratio < 0.23
  - CSF protein > 220
  - CSF WBC count > 2000
  - CSF neutrophil count > 1180

  [Presence of any ONE of the above findings predicts bacterial etiology with > 99% certainty]

Gram stain and meningitis

- Gram stains are + in 60-90% of patients with untreated bacterial meningitis
- With prior ATB Rx, positivity of Gram stains decreases to 40-60%
- REMEMBER: + Gram stains = Heavy organism burden & worse prognosis
Bacterial antigens

- Bacterial antigen screens detect *S. pneumoniae*, *N. meningitidis*, Hib, and GBS; + in 50-100% of patients (esp. useful in patients with prior ATB Rx)
- Crypto antigen screen detects *C. neoformans* + in 90-95% of patients with cryptococcal meningitis
- Should NOT be ordered routinely

Meningitis treatment

- First priority
  - Antibiotics
- Second priority in some cases
  - Anti-inflammatory
- Third priority
  - Counter the adverse effects of increased ICP & vasculopathy

THE THERAPY OF MENINGITIS
Desirable Properties

- Activity vs suspected pathogen(s) [preferably bactericidal]
- Adequate CSF diffusion
- High dose
- Acceptable risk of toxicity
- Initiate treatment within 30 minutes
CORTICOSTEROIDS AND MENINGITIS

- Role of steroids still somewhat uncertain
- Recent European study in adults suggested that Rx with dexametasone associated with ↓ in risk of unfavorable outcome (25%→15%, RR 0.59) & in mortality (15%→7%, RR for death 0.48)
- Benefit primarily ltd to pts w/S. pneumoniae
- Dose of dexametasone was 10mg IV q6h X 4d; per protocol, dexametasone given concurrent with or 15-20 minutes before 1st dose of ATBs

(Cont)

- Only patients with cloudy CSF, + CSF GmS, or CSF WBC count >1000 were enrolled
- Accompanying editorial raised concerns about use of steroids in patients with DRSP who are being Rx’ed with vancomycin b/o ↓ in CNS concentration of vancomycin with concurrent steroid use
- Practically speaking, almost all patients with presumed bacterial meningitis are candidates for at least 1 dose of dexametasone

Infection Control Issues:

- Meningococcal meningitis:
  - Droplet precautions
  - Duration: 24 post initial of appropriate therapy
  - Treatment indicated in households, day care where child attends >25 h/wk, kids are >2 years old, & 2 cases have occurred, Day care where kids not all vaccinated
  - Persons who have had "intimate contact" w/ oral secretions prior & during 1st 24 h of antibiotics
  - "Intimate contact" = kissing, eating/drink
  - utensils, mouth-to-mouth, suctioning, intubating)
- No Prophylaxis or isolation needed for pneumococcal or viral meningitis
Viral meningitis / Encephalitis

**Herpesviruses**
- Herpes simplex
- Varicella-zoster
- Epstein-Barr
- Cytomegalovirus

**Myxo/paramyxoviruses**
- Influenza/parainfluenzae
- Mumps
- Measles

**Miscellaneous**
- Adenoviruses
- LCM
- Rabies
- HIV

**Enteroviruses**
- Polioviruses
- Coxsackieviruses
- Echoviruses

**Alphaviruses and Flaviviruses**
- Eastern equine
- Western equine
- Venezuelan equine
- St. Louis
- Powasson
- California
- West Nile

Nonviral causes of encephalitis

- Rocky Mountain spotted fever
- Typhus
- Mycoplasma
- Brucellosis
- Subacute bacterial endocarditis
- Syphilis (meningovascular)
- Relapsing fever
- Lyme disease
- Leptospirosis
- Tuberculosis
- Cryptococcus
- Histoplasma
- Naegleria

- Acenathamoeba
- Toxoplasma
- Plasmodium falciparum
- Trypanosomiasis
- Whipple's disease
- Behcet's disease
- Vasculitis

Viral Encephalitis

- Supportive
- No antibiotics (antiviral may be necessary: HSV)
- Analgesia
- Fever control
- Often feel better after LP
- No isolation - Standard precautions
Brain abscess

- Brain abscess is rare but life-threatening infection.
- Accounts for ~ 1 in 10,000 hospital admissions in US (1500-2500 cases/yr)
- It was uniformly fatal before the late 1800’s
- Advances in diagnosis & management the last century, & especially over the past three decades have lead to a significantly lower mortality.
- Mortality down to 0-24% over the past three decades, with:

Brain Abscess: Pathogenesis

- Direct spread from contiguous foci (40-50%)
- Hematogenous spread (25-35%)
- Penetrating trauma/surgery (10%)
- Cryptogenic (15-20%)
Brain abscess: pathophysiology

- Begins as localized cerebritis (1-2 weeks)
- Evolves into a collection of pus surrounded by a well-vascularized capsule (3-4 weeks)

- Lesion evolution (based on animal models):
  - Days 1-3: “early cerebritis stage”
  - Days 4-9: “late cerebritis stage”
  - Days 10-14: “early capsule stage”
  - > day 14: “late capsule stage

MICROBIOLOGY OF BRAIN ABSCESS

<table>
<thead>
<tr>
<th>AGENT</th>
<th>FREQUENCY (%)</th>
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<tbody>
<tr>
<td>Streptococci (S. intermedius, including S. anginosus)</td>
<td>60–70</td>
</tr>
<tr>
<td>Bacteroides and Prevotella spp.</td>
<td>20–40</td>
</tr>
<tr>
<td>Enterobacteriaceae</td>
<td>23–33</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>10–15</td>
</tr>
<tr>
<td>Fungi†</td>
<td>10–15</td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>&lt;1</td>
</tr>
<tr>
<td>Protozoa, helminths (vary geographically)</td>
<td>&lt;1</td>
</tr>
</tbody>
</table>

† Protozoa, helminths (Entamoeba histolytica, Schistosomes, Paragonimus)  
† Fungi (Aspergillus, Candida, Cryptococci, Coccidioides, Cladosporium, Inchoideae, Pseudallescheria, boydi)

Brain abscess: clinical

- Classic triad
  - HA, fever, focal deficit
  - >1/3 of cases
  - Toxic appearance is rare
  - Seizures, vomiting, confusion, obtundation possible
  - Frontal lobe-hemiparesis
  - Temporal lobe- homonymous superior quadrant visual field deficit or aphasia
  - Cerebellum-limb incoordination or nystagmus
Brain Abscess: Pathophysiology

- Direct destruction
- Compression of parenchyma
- Elevation of intracranial pressure
- Interfering with blood &/or CSF flow

Brain Abscess: Work-up

- MRI is the procedure of choice
  - more sensitive especially for early cerebritis, satellite lesions, necrosis, ring, edema, especially for posterior fossa & brain stem abscesses
- CT scan with contrast enhancement is 95% sensitive
- Skull roentgenograms usually normal
- Biopsy or aspiration needed for definitive diagnosis
- Laboratory findings often not helpful
- Lumbar puncture contraindicated

Brain Abscess: Treatment

- Medical & surgical
- Obtain Neurosurgical Consult ASAP
- Aspiration or excision
- Antibiotics
  - Initially selected based on:
    - Likely pathogen: considering primary source, underlying condition, & geography
    - Antibiotic characteristics: MICs for usual pathogens, CNS penetration, activity in abscess cavity
- Duration of abx: usually 6-8 weeks
- After surgical excision, a shorter course may suffice
Thanks

Q & A