Dilemmas in the Management of Meningitis & Encephalitis

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HEADACHE AND FEVER

What is the best initial approach for fever, headache, meningisums?

32 yo man presents to the ED with temp of 102, severe headache x 18 hrs, stiff neck, no focal neurologic signs.

What is the next best step?

A. Head CT
B. MRI of brain
C. Start empiric ceftriaxone
D. Lumbar puncture with cell count, gram stain, protein/glucose
DIFFERENTIAL DIAGNOSIS

• Infectious
  – Acute bacterial meningitis

ACUTE BACTERIAL MENINGITIS

• Clinical findings
  – Acute onset
  – Triad: fever, headache, nuchal rigidity
  – Meningeal signs: Kernig, Brudzinski
  – Alteration in mental status (75%)
    • Lethargy to coma
  – Seizures (40%)
  – Rash

Presenting Signs and Symptoms

<table>
<thead>
<tr>
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<th>Frequency (%)</th>
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<tbody>
<tr>
<td>Headache</td>
<td>&gt;85</td>
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<tr>
<td>Fever</td>
<td>&gt;80</td>
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<tr>
<td>Meningismus</td>
<td>&gt;80</td>
</tr>
<tr>
<td>Altered sensorium</td>
<td>&gt;75</td>
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<tr>
<td>Vomiting</td>
<td>~35</td>
</tr>
<tr>
<td>Seizures</td>
<td>~30</td>
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<tr>
<td>Focal neurologic findings</td>
<td>10-35</td>
</tr>
<tr>
<td>Papilledema</td>
<td>&lt;5</td>
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CLINICAL FINDINGS
• Classical triad of fever, nuchal rigidity and altered sensorium, but
  – In 1993 review, only 66% all three
    • all had at least one
  – In 2004 review, triad present in 44%
    • But 95% had 2 of 4 (including headache)

DIFFERENTIAL DIAGNOSIS
• Infectious
  – Acute bacterial meningitis
  – Aseptic meningitis syndrome

ASEPTIC MENINGITIS SYNDROME
• Meningitis where no bacterial pathogen isolated by standard culture
• Clinical
  – Fever, headache, nuchal rigidity
  – Develops over days
  – Meningeal signs
ASEPTIC MENINGITIS SYNDROME

- CSF findings
  - OP: <250
  - WBC 50-1000; mostly lymphocytes
  - ↑ Protein
  - normal glucose

DIFFERENTIAL DIAGNOSIS

- Infectious
  - Acute bacterial meningitis
  - Aseptic meningitis syndrome
  - Encephalitis

ENCEPHALITIS

- Clinical findings:
  - Acute febrile illness
  - Nuchal rigidity may be present
  - Alteration in mentation (hallucinations, personality changes) or level of consciousness
  - Focal seizures (>50%)
DIFFERENTIAL DIAGNOSIS

• Infectious
  – Acute bacterial meningitis
  – Aseptic meningitis syndrome
  – Encephalitis
• Intercranial hemorrhage
• Tumor

ACUTE BACTERIAL MENINGITIS

• Diagnosis
  – Emergency lumbar puncture
    • if no focal neurologic signs
  – CSF
    • OP: 200-500 mm H₂O
    • WBC 1000-5000; neutrophils
    • ↓ Glucose (<40)
    • ↑ Protein (100-500)
    • Gram stain shows organism 70-85%
  – Blood culture

What is the next best step?

32 yo man presents to the ED with temp of 102, severe headache x 18 hrs, stiff neck, no focal neurologic signs.

A. Head CT
B. MRI of brain
C. Start empiric ceftriaxone
D. Lumbar puncture with cell count, gram stain, protein/glucose
HEADACHE AND FEVER

What empiric therapy should be given for fever, headache, meningismus?

What is the next best step?

32 yo woman presents to the ED with temp of 102, severe headache x 18 hrs, stiff neck, rash, no focal neurologic signs.

A. Ceftriaxone
B. Ciprofloxacin
C. Ceftriaxone plus vancomycin
D. Ceftriaxone plus vancomycin plus corticosteroid
E. Ceftriaxone plus vancomycin plus ampicillin

To choose an empiric antimicrobial regimen, you must first construct a list of the most likely causative organisms.
EPIDEMIOLOGY

• Acute bacterial meningitis
  – 3.0 cases per 100,000 adults per year
    • Surveillance study 1978-81
  – Because of Hib vaccine, rates have decreased in the US and median age has risen
    • Median age 15 mo in 1980s
    • Median age 25 yrs in 1995
    • Median age 39 yrs in 1998-2003

ETIOLOGY IN US

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<td>H. flu</td>
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<tr>
<td>N. mening</td>
<td>20</td>
<td>14</td>
<td>25</td>
<td>16</td>
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<td>S. pneumo</td>
<td>13</td>
<td>18</td>
<td>47</td>
<td>61</td>
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<td>Gp B strep</td>
<td>3</td>
<td>6</td>
<td>12</td>
<td>14</td>
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<td>Listeria</td>
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<td>3</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Other</td>
<td>8</td>
<td>14</td>
<td>---</td>
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ACUTE BACTERIAL MENINGITIS

- Therapy
  - Immediate administration of antibiotics
    - 3rd generation cephalosporin + vancomycin + ampicillin
  - Corticosteroids
    - Recently called into question by 2 studies showing no benefit
- Droplet precautions for 24 hours
## PROGNOSIS

- *Strep pneumoniae*
  - Mortality 19-37%
  - Neurologic sequelae 30%
    - Hearing loss, focal defects
- *N. meningitidis*
  - Mortality 3-13%
  - Neurologic sequelae 3-7%

## Neisseria meningitidis PROPHYLAXIS

- Pre-exposure prophylaxis: Vaccine
  - Serogroups A, C, Y, W135
  - No effective vaccine against Type B
- Post-exposure Prophylaxis
  - Household contacts (droplet spread)
  - Rifampin for 2 days
  - Alternates: ciprofloxacin (1 dose), minocycline

### What is the next best step?

32 yo woman presents to the ED with temp of 102, severe headache x 18 hrs, stiff neck, rash, no focal neurologic signs.

- A. Ceftriaxone
- B. Ciprofloxacin
- C. Ceftriaxone plus vancomycin
- D. Ceftriaxone plus vancomycin plus corticosteroid
- E. Ceftriaxone plus vancomycin plus ampicillin
HEADACHE AND FEVER

What is the best approach for fever and headache for 1 week?

What is the next best step?

22 yo man presents to the ED with temp of 102, severe headache x 5 days, stiff neck, myalgias, no focal neurologic signs.

A. MRI of brain
B. Start ceftriaxone and vancomycin
C. Start antibiotics and steroids
D. Lumbar puncture with cell count, gram stain, protein/glucose

ASEPTIC MENINGITIS

• Viral
  – Enteroviruses (Picornaviridae)
  • 75-90% of cases of aseptic meningitis
  • Coxsackievirus, echovirus, polio virus, human enterovirus 68-71
  • Summer and early fall months
  • Diagnosis: CSF viral RNA amplification, culture with poor yield
ASEPTIC MENINGITIS

- Viral
  - Enteroviruses (Picornaviridae)
  - Arboviruses
    - Summer months
    - Cause either encephalitis or meningitis
    - WEE, EEE, St. Louis encephalitis, California encephalitis (not in California), West Nile
  - Other
    - HSV-2, VZV, EBV, mumps, LCM virus, HIV

ASEPTIC MENINGITIS

- Viral
- Mycobacterium tuberculosis
- Fungal meningitis
  - Coccidioides immitis
- Syphilis
- Lyme disease
- Partially treated bacterial meningitis
- Drugs
ASEPTIC MENINGITIS SYNDROME

- CSF findings
  - OP: <250
  - WBC 50-1000; mostly lymphocytes
  - ↑ Protein
  - normal glucose

DIAGNOSTIC TESTING

- Depends on the clinical presentation
  - Nothing further for most patients (probable enterovirus)
  - Serum testing for syphilis, HIV
  - Regional: testing for Lyme or Coccidioides

What is the next best step?

22 yo man presents to the ED with temp of 102, severe headache x 5 days, stiff neck, myalgias, no focal neurologic signs.

A. MRI of brain
B. Start ceftriaxone and vancomycin
C. Start antibiotics and steroids
D. Lumbar puncture with cell count, gram stain, protein/glucose
HEADACHE AND FEVER

What is the best initial approach for fever, headache, confusion?

What is the next best step?

48 yo woman presents to the ED with temp of 102, severe headache x 3 days, confusion and bizarre behavior, seizure this morning.

A. MRI of brain
B. Start empiric ceftriaxone and vancomycin
C. Start empiric antibiotics and steroids
D. Lumbar puncture with cell count, gram stain, protein/glucose

ENCEPHALITIS

- Infection and inflammation of the brain parenchyma
- Often with meningeal involvement
- >20,000 cases/yr in US
ENCEPHALITIS

• Clinical findings:
  – Acute febrile illness
  – Nuchal rigidity may be present
  – Alteration in mentation (hallucinations, personality changes) or level of consciousness
  – Focal seizures (>50%)

ENCEPHALITIS

• Viruses
  – HSV-1 and 2
  – Arboviruses (including WNV)
  – Enteroviruses
  – HIV
  – CMV, EBV, VZV, measles
  – Rabies
  – Mumps

HSV ENCEPHALITIS

• Responsible for 10% of encephalitis
  – most common cause of non-epidemic encephalitis
  – Frequency: between 1:250,000 and 1:500,000 persons per year
• 30% from initial infection with HSV
  – 70% caused by reactivation of an earlier infection
• >½ of untreated cases are fatal
HSV ENCEPHALITIS: DIAGNOSIS

• Clinical presentation does not distinguish HSE from encephalitis caused by other viruses
• Culture of HSV from CSF of adults has sensitivity <10%
• PCR testing
  – Sensitivity: 96%–98%
  – Specificity: 95–99%

HSV ENCEPHALITIS: THERAPY

• Acyclovir: 10 mg/kg intravenously every 8 h for 14–21 days
  – in patients with normal renal function
• Morbidity and mortality remain high
  – 28% mortality at 18 months

What is the next best step?

48 yo woman presents to the ED with temp of 102, severe headache x 3 days, confusion and bizarre behavior, seizure this morning.

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B. Start empiric ceftriaxone and vancomycin
C. Start empiric antibiotics and steroids
D. Lumbar puncture with cell count, gram stain, protein/glucose
HEADACHE AND FEVER

What is the best initial therapy for fever, headache, confusion; LP with 250 WBCs?

What is the next best step?

30 yo man presents to the ED with temp of 102, severe headache x 3 days, confusion and bizarre behavior, seizure this morning.

A. Ceftriaxone plus vancomycin
B. Antibiotics plus corticosteroids
C. Acyclovir
D. Acyclovir plus steroids

West Nile Virus Transmission Cycle
West Nile Virus in the US

How did WNV get here?

- Infected human host
- Human-transported vertebrate host
  - Legal
  - Illegal
- Human-transported vector(s)
- Storm-transported vertebrate host (bird)
- Intentional introduction (terrorist event)
**WNV Neuroinvasive Disease 2011**

**WNV CLINICAL FINDINGS**

- 80% with asymptomatic illness
- 20% with WNV Fever (febrile illness)
- < 1% West Nile neuroinvasive disease
  - Aseptic meningitis
  - Encephalitis
  - Acute flaccid paralysis
- < 1% mortality rate

**WNV ENCEPHALITIS**

- Fever, HA, AMS: 100%
- Variable frequency:
  - Tremors
  - Weakness
  - Cerebellar signs/symptoms
  - Brainstem/CN findings (> 50%):
    nystagmus, dysphagia, ↓ gag
  - “locked-in” syndrome
WNV FLACCID PARALYSIS

- Acute flaccid paralysis syndrome
- Clinical description
  - Acute onset of asymmetric weakness without pain or sensory loss
  - CSF: pleocytosis, elevated TP
  - EMG: motor involvement and not demyelinating process

WEST NILE VIRUS: DIAGNOSIS

- Serological diagnosis primary method
- IgM/IgG Capture ELISA preferred test
- PRNT (Plaque Reduction Neutralization Test)
- Nucleic Acid Amplification to detect the presence of virus
  - Used in screening of blood products
  - Maybe useful in diagnosing patients who are immunocompromised and may not be able to mount an immune response

WNV TREATMENT

- SUPPORTIVE CARE
- Experimental
  - Interferon: trials ongoing
  - Israeli IVIG product (Omrix)
    - Trial at LAC; Dr. Robert Larsen PI
  - Interferon alpha-2b
  - Ribavirin
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