

BACTERIAL MENINGITIS Changing Spectrum of Disease

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CASE PRESENTATION

- 18 month old AAM brought by parents due to:
 - Fever of 4 days duration
 - Irritability of 2 days duration, worsening
 - Associated with:
 - Anorexia
 - Nausea
 - Vomiting
 - Diarrhea

PHYSICAL EXAMINATION

- Male child, lying quietly on the cart, appears lethargic
- Cries when disturbed, even when picked up by the mother
- Temperature 39°C
- Pulse rate: 130/min
- Pulse oximetry: 98%

PHYSICAL EXAMINATION

- Skin: hot, dry, no rash
- HEENT: atraumatic, slightly dry mucous membranes
- Neck:
 - Supple
 - Kernig's sign: negative
 - Brudzinski's sign: questionably positive

PHYSICAL EXAMINATION

- Kernig's sign:
 - pain on leg extension following flexion of the hip to 90°
 - 43% of patients with bacterial meningitis
- Brudzinski's sign:
 - involuntary flexion of the hips and knees, following passive flexion of the neck
 - 66% of patients with bacterial meningitis

PHYSICAL EXAMINATION

- C/V: Rapid, Regular Rhythm without Murmur or Extra Sounds
- Lungs: Clear to Auscultation
- Abdomen: Soft, Non-Tender
- Neuro:
 - lethargic/irritable
 - moving all extremities normally when stimulated
 - reflexes symmetric
 - cranial nerves intact

What is the best approach in the ED?

- Stat labs to include CBC, Clinical Chemistry, and Blood Cultures. Monitor the child while awaiting results.
- Stat labs and Stat CT scan of the brain, followed by LP.
- Stat LP, followed by administration of intravenous antibiotics.
- Obtain blood specimens and administer intravenous antibiotics immediately

EPIDEMIOLOGY Neonatal

- 0.6 – 1.3 cases/1000 live births
- Etiology
 - Group B *Streptococcus*
 - Gram-Negative Enteric Bacilli
 - *Escherichia coli*, *Klebsiella* spp, *Enterobacter* spp, *Salmonella* spp
 - *Listeria monocytogenes*
- Incidence essentially unchanged in the past 20 years

EPIDEMIOLOGY Infant and Childhood

- 1990: children between 2 months and 5 years of age accounted for $\frac{3}{4}$ of all cases
 - 67% due to *Haemophilus influenzae* type b
 - 25% due to *Streptococcus pneumoniae*
 - 10% due to *Neisseria meningitidis*
- 2002: children 2 mos – 5 yrs are $< \frac{1}{2}$ of cases
 - *Streptococcus pneumoniae* is the most common cause between 2 mos and 2 years of age
 - Decreasing after introduction of heptavalent vaccine
 - *Neisseria meningitidis* is the most common offender in the 2 – 18 year age group

Bacteriology Immunocompromised Host

- *Staphylococcus* spp
- Gram-Negative Enteric Bacilli
- *Pseudomonas aeruginosa*

EPIDEMIOLOGY

- Now predominantly a disease of adolescents and young adults
 - College students living in dormitories
 - Military recruits

EPIDEMIOLOGY

- Conjugate polysaccharide *Haemophilus influenzae* type b vaccine introduced in 1991
- Heptavalent pneumococcal conjugate vaccine introduced in 2000
 - Covers 80% of invasive serotypes
 - Projected to prevent 12,000 cases/year

MENINGOCOCCAL VACCINES

- 5 Major Serogroups Cause Disease
 - A, B, C, Y, W-135
- Polysaccharide vaccines effective for groups A, C, Y, W-135 in older children & adults
- Poor response in young children
- No vaccines of serogroup B

MENINGOCOCCAL VACCINES

- Conjugation of polysaccharide vaccine to a protein carrier increases efficacy in infants and young children
- Conjugate serogroup C vaccine in use in UK since 1999: very effective in young children
- Conjugate vaccine for A, C, Y & W-135 under development

MENINGOCOCCAL VACCINES

- Use for 1st Year College Students Controversial in the Past
 - No cost savings
 - Low # of cases
 - High cost of vaccination
 - From individual perspective, may be worthwhile

MENINGOCOCCAL VACCINES 2005 AAP Recommendations

- Administer MCV4 to
 - 11-12 year olds, especially if at increased risk
 - Students entering high school or at age 15
 - College freshmen who will be living in dormitories

PATHOPHYSIOLOGY

- Hematogenous spread
 - blood to subarachnoid space
- Mechanical disruption
 - Fracture of the base of the skull
 - Direct extension from ear, mastoid air cells, sinuses, orbit or other adjacent structure

PATHOPHYSIOLOGY

- Pathologic changes of meningitis
 - Directly due to infection
 - Indirectly due to infection via the response of the immune system to infection

PRESENTATION

- Classic Signs
 - Headache
 - Photophobia
 - Stiff neck
 - Change in mental status
 - Bulging fontanelle
 - Nausea
 - Vomiting

PRESENTATION

- Signs of Meningeal Irritation
 - Brudzinski Sign: when the inflamed meninges are stretched with neck flexion, the hips and knees involuntarily flex.
 - Kernig Sign: when the hip is flexed to 90°, examiner is unable to passively extend the leg fully.
 - Children with meningeal irritation often resist walking or being carried
 - Absence does not rule out intracranial infection
 - Not useful in neonates and young infants

Symptoms of Bacterial Meningitis Rothrock

Clinical Feature	Untreated (175)	Pretreated (83)
Mean Duration of Symptoms	4.6 days	2.9 days
Fever	99%	95%
Lethargy or Irritability	87%	95%
Vomiting	71%	54%
URI symptoms	55%	46%
Seizure	22%	23%

Signs of Bacterial Meningitis

Fever	82-96%
Lethargy	17-95%
Irritability	18-40%
Vomiting	20-100%
Bulging Fontanelle	18-40%

Signs of Bacterial Meningitis

Altered Mental Status	53-78%
Seizure	4-23%
Focal Neuro	5-6%

Signs of Bacterial Meningitis

Nuchal Rigidity	27-95%
Kernig's Sign	0-36%
Brudzinski's	10-83%
≥ 1 Meningeal	26-93%

All signs less common in neonates except fontanelle

PRESENTATION

Neonates and Young Infants

- Less obvious signs and symptoms
- Poor Feeding
- Irritability
- Inconsolability
- Listlessness

PRESENTATION

Course of Disease

- Insidious (90%)
 - High likelihood of early presentation with non-specific illness
 - Typical of pneumococcal illness
- Fulminant (10%)
 - Typical of meningococcal illness
 - May progress rapidly to petechiae, purpura fulminans, cardiovascular collapse

DIFFERENTIAL DIAGNOSIS

Early Stage of Disease

- Gastroenteritis
- Upper respiratory infection
- Pneumonia
- Otitis media
- Viral syndrome

DIFFERENTIAL DIAGNOSIS

Later Stage of Disease

- Encephalitis
- Subarachnoid/Subdural Hemorrhage
 - Traumatic (Abuse or Unintentional)
 - Spontaneous
- Cerebral Abscess
- Reye's Syndrome
- Toxic Ingestions
- Seizure Disorders
- DKA or other altered metabolic states
- Hypothyroidism
- Intussusception

MANAGEMENT

Unstable Patients

- Always assure stability of vital functions before attempting diagnostic procedures
- Withhold lumbar puncture until after stabilization and antibiotic administration
- Shock: rapid intravenous or intraosseous infusion of crystalloid solution in 20 mL/kg aliquots until stable
- Limit fluids to maintenance rate after stabilized
 - Fluid overload can lead to worsening of cerebral edema

MANAGEMENT

Increased Intracranial Pressure

- Recognition: worsening mental status, papilledema, bulging fontanelle, widening of sutures
- Treatment
 - Elevate head of bed to 30°
 - Controlled ventilation to keep PCO₂ between 30 and 35 mmHg
 - Mannitol, 0.25 – 1 g/kg
 - Furosemide, 1 mg/kg

MANAGEMENT Stable Patients

- Phlebotomy for diagnostic studies
 - Complete Blood Count
 - Serum Electrolytes
 - Blood Glucose
 - Renal Functions
 - Blood Culture
- Lumbar Puncture for Cerebrospinal Fluid Analysis

CSF ANALYSIS Normal Values for an Infant/Child

- Cell count: 0-7 wbc/mm³ (0% PMNs)
- Glucose: 40-80 mg/dL (\geq 50% of Blood Sugar)
- Protein: 5-40 mg/dL

CSF ANALYSIS Interpretation

- Viral Etiology
 - Low wbc count
 - Predominantly mononuclear cell type
 - Normal glucose
 - Normal protein
- Bacterial Etiology
 - Elevated wbc count
 - Predominantly polymorphonuclear leukocytes
 - Low glucose
 - High protein

INITIAL ANTIBIOTIC TREATMENT Neonates

- Ampicillin, 100 mg/kg
AND
- Aminoglycoside
 - Gentamicin, 2.5 mg/kg
- Cephalosporin active against gram negative bacilli may be used instead of an aminoglycoside
 - Cefotaxime, 50 mg/kg

INITIAL ANTIBIOTIC TREATMENT Infants and Children

- Cephalosporin
 - Ceftriaxone, 100 mg/kg
OR
 - Cefotaxime, 50 mg/kg
- If unavailable:
 - Amoxicillin, 100 mg/kg
AND
 - Chloramphenicol, 25 mg/kg

INITIAL ANTIBIOTIC TREATMENT ADULTS

- Cephalosporin
 - Ceftriaxone, 2 grams IV
OR
 - Cefotaxime, 2 grams IV

INITIAL ANTIBIOTIC TREATMENT Known or Suspected Pneumococcal Infection

- Penicillin and cephalosporin resistance is possible
- Vancomycin is the only antibiotic to which all strains of pneumococci are susceptible
 - Add Vancomycin, 15 mg/kg

CORTICOSTEROID TREATMENT

- Dexamethasone, 0.15 mg/kg IV administered prior to or along with the initial antibiotics has been shown to decrease ICP, cerebral edema & CSF lactate.
- Significantly decreases neurologic sequelae, including deafness

SEQUELAE

- Mortality: 20-40%
- Long-Term Sequelae: 20%

SUMMARY

- Vaccinations for *H flu* & Pneumococcus are highly effective
- Bacterial meningitis is now predominantly a disease of adolescents and young adults
- Development of an effective meningococcal vaccine has proved more challenging

SUMMARY

- Classic signs & symptoms are often missing, even in older children
- Paradoxical irritation may be seen
- Initiate antibiotics before diagnostic work-up in toxic-appearing patients
- CT scan before LP needed only if you suspect a mass lesion

SUMMARY

- Empiric Antibiotics for Neonates
 - Ampicillin & Aminoglycoside
 - OR
 - Ampicillin & Cefotaxime
- Empiric Antibiotics for Infants/Children/Adults
 - Ceftriaxone & Vancomycin
- Corticosteroid Treatment
 - Dexamethasone prior to or along with the initial antibiotics