MENINGITIS

Overview

Meningitis is a clinical syndrome characterized by inflammation of the meninges, 3 layers of membranes that enclose the brain and spinal cord. It is a medical emergency and one that needs to be recognized promptly so that the patient (pt) can begin to receive antibiotics as quickly as possible. Without treatment the mortality of meningitis approaches 100%. In Canada between 1994 and 2007 there were 7,227 reported cases of meningitis hospitalizations in Canada. The annual occurrence rates were between 1,072 and 940 per year giving a ratio of 3.66 to 3.37 per 100,000. Of these there was an 11.3% case fatality ratio with 25% of the deaths occurring within 48 hrs of hospital admission.

Diagnostic Considerations

History/Physical

The presentation of meningitis is variable. Neonates and children may present with fever, nausea, vomiting, lethargy, irritability, a bulging fontanel, or poor feeding. Older children and adults may present with fever, headache, neck stiffness, confusion, nausea, vomiting, lethargy, meningeal irritation, altered level of consciousness, seizures, petechial rash and/or focal neurological signs. These symptoms may often be preceded by symptoms of an upper respiratory tract infection.

Meningeal irritation or meningismus is detected by several physical exam findings:
- **Brudzinski Sign:** passive flexion of the pt's neck causes an involuntary flexion of their hips and knees
- **Kernig's Sign:** with the pt supine and the patient's hip flexed to 90° the patient experiences pain with extension of their knee
- **Opisthotonas:** the pt's body will be in a spasm with their head and heels bending backwards and their torso bowing forwards

Differential Diagnosis

All of the below diagnoses may present with signs and symptoms similar to those of meningitis.
- Encephalitis
- Subarachnoid hemorrhage
- Brain abscess
- Cerebral toxoplasmosis
- Stroke
- CNS vasculitis
- Noninfectious meningitis, including medication-induced meningeal inflammation

Investigations

Whenever the diagnosis of meningitis is strongly considered, a lumbar puncture should be promptly performed. The opening pressure should be measured and the fluid sent for cell count (and differential count), chemistry (ie, CSF glucose and protein), and microbiology (ie, Gram stain and cultures). The CSF analysis can help clarify the underlying cause of meningitis (see table below).

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Bacterial</th>
<th>Viral</th>
<th>Neoplastic</th>
<th>Fungal</th>
</tr>
</thead>
<tbody>
<tr>
<td>OP (&lt;170 mm CSF)</td>
<td>&gt;300 mm</td>
<td>200 mm</td>
<td>200 mm</td>
<td>300 mm</td>
</tr>
<tr>
<td>WBC (&lt;5 mononuclear)</td>
<td>&gt;1000 / microL</td>
<td>&lt;1000 / microL</td>
<td>&lt;500 / microL</td>
<td>&lt;500 / microL</td>
</tr>
<tr>
<td>% PMNs (0)</td>
<td>&gt;80%</td>
<td>1 – 50 %</td>
<td>1 – 50 %</td>
<td>1 – 50 %</td>
</tr>
<tr>
<td>Glucose (&gt;40 mg/dL)</td>
<td>&lt;40 mg / dL</td>
<td>&gt;40 mg / dL</td>
<td>&lt;40 mg / dL</td>
<td>&gt;40 mg / dL</td>
</tr>
<tr>
<td>Protein (&lt;50 mg/dL)</td>
<td>&gt;200 mg / dL</td>
<td>&lt;200 mg / dL</td>
<td>&gt;200 mg / dL</td>
<td>&gt;200 mg / dL</td>
</tr>
<tr>
<td>RBC (&lt;5)</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Gram Stain (-)</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Cytology (-)</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Other workup would include: CBC, blood cultures, blood glucose and electrolytes, creatinine, liver function tests, coagulation studies, CXR (50% of patients with pneumococcal meningitis also have evidence of pneumonia on CXR). CT scans of the head and magnetic resonance imaging (MRI) of the brain generally do not aid in the diagnosis of meningitis. Some patients may show meningeal enhancement, but its absence does not rule out the condition.

Additional investigation may be considered depending on the clinical picture. For example:
- Pts who may have partially treated bacterial meningitis should have a latex agglutination test of the CSF.
- Pts who are immune compromised may be considered for an India ink stain or a serum cryptococcal antigen level.
- Pts who are at risk of tuberculosis meningitis should be considered for an acid fast stain and mycobacterial culture.
- Pts at risk for Lyme disease should be considered for measurement of Borrelia antibodies

Management Considerations

The Infectious Disease Society of America recommends using the following algorithm for treatment of bacterial meningitis.
For the dosing of dexamethasone use: 10 mg IV q 6 hrs for 4 days.

Begin empiric antibiotic coverage according to age and presence of overriding physical conditions (see chart below). Systemic complications of acute bacterial meningitis must be treated. These may include the following: hypotension and/or shock, hypoxemia, hyponatremia (SIADH), cardiac arrhythmias and ischemia, cerebrovascular accident (CVA) and exacerbation of chronic diseases. Also, remember to manage the fever and pain. During the treatment, it is also important to monitor for signs of hydrocephalus and increasing ICP and to treat if this occurs. Children should have a hearing test before being discharged from hospital.

**Pharmaco therapy**

<table>
<thead>
<tr>
<th>Age Category (most common organism)</th>
<th>Initial Antibiotic Regiment: To be adjusted when CSF cultures and gram stain reports available</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 – 1 Week (GBS, E.coli, L. Monocytogenes)</td>
<td>Cefotaxime IV @ 100 mg / kg / day divided q 12 h PLUS Ampicillin IV 200 – 400 mg / kg / day divided q 4 – 6 h</td>
</tr>
<tr>
<td>1 – 4 Weeks (GBS, E.coli, L. Monocytogenes)</td>
<td>Cefotaxime IV @ 150 mg / kg / day divided q 8 h PLUS Ampicillin IV 200 – 400 mg / kg / day divided q 4 – 6 h</td>
</tr>
<tr>
<td>1 – 3 Months (GBS, E.coli, L. Monocytogenes, S. pneumo, N. Meningitides, HIB)</td>
<td>Cefotaxime IV @ 200 mg / kg / day divided q 6 – 8 h OR Ceftriaxone IV @ 80 – 100 mg / kg / day divided q 12 h for first 2 days then q 24 h PLUS Ampicillin IV 200 – 400 mg / kg / day divided q 4 – 6 h</td>
</tr>
<tr>
<td>3 Mo. – 18 Years (S. pneumo, N. Meningitides, HIB)</td>
<td>Cefotaxime IV @ 200 mg / kg / day divided q 6 – 8 h OR Ceftriaxone IV @ 80 – 100 mg / kg / day divided q 12 h for first 2 days then q 24 h PLUS Vancomycin IV @ 10 – 15 mg / kg per dose q 6 hrs</td>
</tr>
<tr>
<td>18 – 50 Years (S. pneumo, N. Meningitides, HIB)</td>
<td>Ceftriaxone IV @ 2 g q 12 hrs for first 48 hrs then 2 24 hrs OR Cefotaxime IV @ 2 g q 6 hrs + / - Ampicillin IV @ 2 g q 4 hrs – q 6 hrs (add if possible L. Monocytogenes infection) + / - Vancomycin IV @ 500 mg q 6 hrs or 1000 mg q 12 hrs (add if possible S. Pneumo resistance to Cephalosporins)</td>
</tr>
<tr>
<td>&gt; 50 Years (S. pneumo, L. Monocytogenes, Enteric gram –ve, N. Meningitides) (includes adults with alcoholism and / or other debilitating illness)</td>
<td>Ceftriaxone IV @ 2 g q 12 hrs for first 48 hrs then 2 24 hrs OR Cefotaxime IV @ 2 g q 6 hrs PLUS Ampicillin IV @ 2 g q 4 hrs – q 6 hrs (add if possible L. Monocytogenes infection) + / - Vancomycin IV @ 500 mg q 6 hrs or 1000 mg q 12 hrs (add if possible S. Pneumo resistance to Cephalosporins)</td>
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Dexamethasone 10 mg IV q 6 hrs for 4 days has been shown to decreases mortality in patients with S. pneumonia meningitis and should be started 15 – 20 minutes before or concurrently with the first dose of antibiotics.

<table>
<thead>
<tr>
<th>Age Category</th>
<th>Treatment of Meningitis with a severe penicillin allergy</th>
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<tr>
<td>1 mo – 50 years</td>
<td>Chloramphenicol 12.5 mg / kg IV q 6 hrs PLUS TMP – SMX 5 mg / kg q 6 – 8 hrs PLUS Vancomycin IV @ 10 – 15 mg / kg per dose q 6 hrs</td>
</tr>
<tr>
<td>&gt; 50 yrs</td>
<td>TMP – SMX 5 mg / kg q 6 – 8 hrs PLUS Vancomycin IV @ 500 mg q 6 hrs or 1000 mg q 12 hrs</td>
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Dr. Michael Evans developed the One-Pager concept to provide clinicians with useful clinical information on primary care topics.
Prevention

All prevention recommendations from Anti-infective Guidelines for Community-acquired infections 2010 Edition

Vaccination and chemoprophylaxis are two means of preventing meningitis.

Chemoprophylaxis is recommended for:

- **H. influenzae type b infection**
  1. All home contacts (except those who are completely immunized against Hib) should be given Rifampin 20 mg/kg/day (maximum 600 mg/day) for 4 days.
  2. All children who are less than 5 years of age and who are unvaccinated or incompletely vaccinated should be brought up to date by administration of the recommended doses of a licensed Hib conjugate vaccine.

- **Meningococcal infection (choose one of the following)**
  1. Ciprofloxacin – Adults: 500 mg PO single dose, (contra-indicated for use in pediatrics)
  2. Rifampin – Adults: 600 mg q 12 hrs x 4 doses, Children > 1 mo 10 mg/kg (max 600 mg) per dose q 12 hrs x 4 doses, Infant < 1 mo: 5 mg/kg per dose q 12 hrs x 4 doses orally.
  3. Ceftriaxone – Adults: 250 mg IM x 1 dose, Children < 12 years 125 mg IM x 1 dose

For all other types of bacterial meningitis chemoprophylaxis is NOT indicated.

Vaccinations are used to induce active immunity against some of the pathogens responsible for meningitis. Currently available vaccines induce the production of antibodies against specific pneumococcal and meningococcal strains. For current vaccination recommendations from the Government of Ontario go to http://www.health.gov.on.ca.

Patient Resources

An excellent patient resource is www.aboutkidshealth.ca where the signs, symptoms, diagnosis and treatment of meningitis are discussed. Although this site is designed by the Hospital for Sick Children the information is mostly applicable to both children and adults. An alternate site for patient information can be found at www.meningitis.ca, the Meningitis Research Foundation of Canada.

Bottom Line

Meningitis is a medical emergency. When it is suspected an LP should be performed (provided there are no contraindications), blood cultures collected and empiric antibiotics started. Antibiotic choice is based on the patient's age and the most likely organisms causing the infection. When an LP is contraindicated the patient should have blood cultures collected STAT, be administered empiric antibiotics and have a head CT. If the head CT is negative then an LP may be performed and the CSF can be sent for analysis.

References can be found online at http://www.dfcm.utoronto.ca/programs/postgraduateprograme/One_Pager_Project_References.htm