Syndromic Testing for Infectious Diseases
Part 3: Central Nervous System Infections

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Disclosures

- None

Utilization Message

- As you view this presentation, consider the following important points regarding testing:
  - How is the testing going to be used in your practice?
  - When should the tests be used?
  - How will results impact patient management?
Central Nervous System Infections

- Multiple categories of central nervous system (CNS) infection
  - Meningitis:
    - Inflammation of the meninges
  - Encephalitis:
    - Inflammation of the brain parenchyma
  - Meningoencephalitis:
    - Inflammation of both the meninges and brain
  - Myelitis:
    - Inflammation of the spinal cord
  - Encephalomyelitis
    - Inflammation of the brain and spinal cord

Meningitis vs. Encephalitis

- Symptoms are nonspecific and may overlap
- Causes of CNS infection may be bacterial, viral, fungal, or parasitic
- Noninfectious causes of CNS disease should also be considered

<table>
<thead>
<tr>
<th></th>
<th>Meningitis</th>
<th>Encephalitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fever</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Headache</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Nausea/Vomiting</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Photophobia</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Neck Stiffness</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Altered Mental Status</td>
<td>No</td>
<td>Yes</td>
</tr>
</tbody>
</table>
Common Causes of CNS Infection

Bacterial
- *S. pneumoniae*
- *N. meningitidis*
- *H. influenzae*
- *L. monocytogenes*

Viral
- CMV
- Enterovirus
- HSV
- WNV

Fungal
- Cryptococcus spp.

Diagnosis of CNS Infections

- Differential diagnosis can be narrowed by:
  - Careful clinical evaluation (eg, symptoms, exposure history and season, vaccination history, immune status)
  - Evaluation of cerebrospinal fluid

<table>
<thead>
<tr>
<th>CSF Findings</th>
<th>Infectious Causes of CNS Infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>Clear</td>
</tr>
<tr>
<td>Opening Pressure (mm H₂O)</td>
<td>100-180</td>
</tr>
<tr>
<td>Total White Blood Cells (cells/µl)</td>
<td>0-5</td>
</tr>
<tr>
<td>Protein (mg/dL)</td>
<td>≤30</td>
</tr>
<tr>
<td>Glucose (% of blood glucose)</td>
<td>≥60%</td>
</tr>
</tbody>
</table>

- Dedicated microbiologic testing necessary to establish definitive diagnosis
Diagnosis of CNS Infections: Traditional Laboratory Methods

- **Bacterial or Fungal Agents**
  - Gram and fungal stains
  - Culture
  - Antigen detection:
    - *Cryptococcus* species
    - *Streptococcus pneumoniae*

- **Viral Agents**
  - Culture
  - Singleplex molecular approaches (e.g., HSV I/II)
  - Serology (e.g., Neurotropic arboviruses)

Meningitis and Encephalitis Panel (MEP)

- Filmarray MEP (BioFire) FDA-approved in 2015
- Includes 14 targets:
  - **Bacterial**
    - *E. coli* KI
    - *H. influenzae*
    - *L. monocytogenes*
    - *N. meningitidis*
    - *S. agalactiae*
    - *S. pneumoniae*
  - **Viral**
    - Cytomegalovirus (CMV)
    - Human herpes virus 6 (HHV-6)
    - Human parechovirus (HPeV)
    - Varicella Zoster Virus (VZV)
    - Enterovirus
    - HSV-1
    - HSV-2
  - **Fungal**
    - *Cryptococcus* species
Case Studies

The Meningitis/Encephalitis Panel: To Use or Not to Use?

Case #1

• 20-year-old male presents with sudden onset fever, headache, neck stiffness and photophobia. He indicates that he recently returned from a mission trip to Mali. He is otherwise healthy, though he has missed all recommended vaccines after the age of 8.
• CSF was collected and was cloudy with elevated protein and 150 white blood cells (WBCs)/µL. CSF glucose was 20% of his blood glucose.
  • Should the MEP be performed in this patient?
HOT TOPIC / Syndromic Testing for Infectious Diseases Part 3: Central Nervous System Infections

Case #1 Resolution

- Findings are suggestive of bacterial meningitis
  - Travel to the ‘meningitis-belt’ in Africa
  - Incomplete vaccination against *N. meningitidis*; no booster for *S. pneumoniae*
- MEP would be appropriate as a first-line test for this patient as the differential for bacterial meningitis is broad

Case #2

- HIV-positive patient (105 CD4+ cells/µL) presents with photophobia, headache, fever, and progressive, unintentional weight loss. Patient indicates that he recently helped his local church clean the bell tower, which was covered with bird droppings.
  - *Should the MEP be performed in this patient?*
Case #2 Resolution

- Presentation, risk, and exposure suggestive of cryptococcal meningitis
- Perform *Cryptococcus* antigen (CrAg) test on CSF and serum first
  - CrAg detection is rapid, sensitive and inexpensive
  - MEP could be considered if the CrAg is negative.

Advantages of Syndromic Panel Testing for Meningitis and Encephalitis

- Broad panel
  - Inclusion of agent for which routine testing is not available (eg, HPeV)
- Rapid test-to-result turnaround time compared to standard methods (eg, culture)
- Potentially more sensitive in patients who received antibiotics prior to CSF collection
- Rapid assay with minimal technologist hands-on time
Limitations of Syndromic Testing for Meningitis and Encephalitis

- Cost
  - Targeted testing may be more appropriate in certain cases
- Broad, but not all inclusive!
- Interpretation of positive results may be challenging
  - HHV6 – Germline integration vs. genuine cause of CNS disease
  - *S. pneumoniae* – False-positive results have been reported
  - ≥2 targets detected
- CSF Gram and fungal stains and culture are still required
  - Susceptibility testing, public health laboratory requirements

References

Questions or requests…
Email to: MMLHotTopics@mayo.edu
For more information…
Visit MayoMedicalLaboratories.com
or call Mayo Laboratory Inquiry at 800-533-1710