BACTERIAL MENINGITIS

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One of the most potential serious infections due to high rate of acute complications & long-term morbidity.

Etiology

The most common causes of bacterial meningitis in children older than 1 mo of age

- S. pneumonia.
- Haemophilus influenzae type b.
- Neisseria meningitides.

S. pneumonia and H. influenzae type b meningitis are much less common in developed countries since the introduction of universal immunization against these pathogens.
Anatomic defects or immune deficits increase the risk of meningitis from less-common pathogens such as (P. aeruginosa, S. aureus, coagulase-negative staphylococci, Salmonella spp., anaerobes, and L. monocytogenes).

Risk factor

- General: close contact (household, daycare centers, college dormitories, military barracks) with individuals having invasive disease caused by N. meningitidis or H. influenza type b, crowding, poverty, black race, male gender, and occult bacteremia.
- Immune deficiency.
- A congenital or acquired CSF leak across a mucocutaneous barrier, such as a lumbar dural sinus.
- CSF leakage through a rupture of the meninges as a result of a basal skull fracture into the cribriform plate or paranasal sinus.

Pathology

A meningeal purulent exudate of varying thickness may be distributed around the cerebral veins, venous sinuses, convexity of the brain, and cerebellum, and in the sulci, sylvian fissures, basal cisterns, and spinal cord. Ventriculitis with bacteria and inflammatory cells in ventricular fluid may be present, as may subdural effusions and, rarely, empyema.

Pathogenesis

It most commonly results from hematogenous dissemination of microorganisms from a distant site of infection. Bacterial colonization of the nasopharynx with a potentially pathogenic microorganism is the usual source of the bacteremia. Prior or concurrent viral upper respiratory tract infection may enhance the pathogenicity of bacteria producing meningitis.
Bacteria gain entry to the CSF through the choroid plexus of the lateral ventricles and the meninges and then circulate to the extracerebral CSF and subarachnoid space. Chemotactic factors then incite a local inflammatory response characterized by polymorphonuclear cell infiltration and this increase the neurologic damage.

Clinical Manifestations

The onset of acute meningitis has 2 predominant patterns:

- The more dramatic and, fortunately, less common presentation is sudden onset with **rapidly progressive manifestations** of shock, purpura, DIC, and reduced consciousness often resulting in progression to coma or death within 24 hr.
- More often, **several days of fever** accompanied by URTI or GIT symptoms, followed by nonspecific signs of CNS infection, such as increasing lethargy and irritability.

The signs and symptoms of meningitis are related to:

- Nonspecific findings: fever, anorexia, headache, photophobia, myalgias, arthralgias, tachycardia, hypotension, and various cutaneous signs, such as petechiae, purpura, or an erythematous macular rash.
- Meningeal irritation signs: nuchal rigidity, back pain, Kernig sign, and Brudzinski sign. In children, particularly in those younger than 12-18 mo, Kernig and Brudzinski signs are not consistently present.
- Additional sign: tache cérébrale

Increased ICP is a result of cell death (cytotoxic cerebral edema), increased capillary vascular permeability (vasogenic cerebral edema), and, possibly, increased hydrostatic pressure (interstitial cerebral edema) after obstructed reabsorption or flow of CSF.
SIADH may produce excessive water retention and potentially increase the risk of elevated ICP. Herniation does not usually occur because the increased ICP is transmitted to the entire subarachnoid space and there is little structural displacement. Furthermore, if the fontanels are still patent, increased ICP is not always dissipated.

Increased ICP is suggested by headache, emesis, bulging fontanel or suture diastasis (widening) , oculomotor or abducens nerve paralysis, cushnoid triad (hypertension, bradycardia, apnea or hyperventilation), decorticate or decerebrate posturing, stupor, coma, or signs of herniation.

Papilledema is uncommon in uncomplicated meningitis and should suggest a more chronic process, such as the presence of an intracranial abscess, subdural empyema, or occlusion of a dural venous sinus.

Focal neurologic signs usually are a result of vascular occlusion. Overall, approximately 10-20% of children with bacterial meningitis have focal neurologic signs.

Seizures (focal or generalized) caused by cerebritis, infarction, or electrolyte disturbances occur in 20-30% of patients with meningitis. Seizures that occur on presentation or within the 1st 4 days of onset are usually of no prognostic significance. Seizures that persist after the 4th day of illness and those that are difficult to treat may be associated with a poor prognosis.

Alterations of mental status are common among patients with meningitis and may be the consequence of hypotension, increased ICP, or cerebritis.

Hydrocephalus can occur as an acute complication of bacterial meningitis. Commonly a communicating hydrocephalus caused by adhesive thickening of the arachnoid villi around the cisterns at the base of the brain. Less often, obstructive hydrocephalus develops after fibrosis and gliosis of the aqueduct of Sylvius or the foramina of Magendie and Luschka.

DIAGNOSIS

The diagnosis of acute pyogenic meningitis is confirmed by analysis of the CSF, which typically reveals microorganisms on Gram stain and culture, a neutrophilic pleocytosis, elevated protein, and reduced glucose concentrations.

LP should be performed when bacterial meningitis is suspected.

Contraindications for an immediate LP include:
(1) Increased ICP (other than a bulging fontanel).
(2) severe cardiopulmonary compromise in whom positioning for the LP would further compromise cardiopulmonary function.
(3) infection of the skin overlying the site of the LP.
(4) Thrombocytopenia is a relative contraindication for LP.

Blood cultures should be performed in all patients with suspected meningitis. it reveals the responsible bacteria in up to 80-90% of cases of meningitis.

Elevations of the C-reactive protein, erythrocyte sedimentation rate, and procalcitonin have been used to differentiate bacterial (usually elevated) from viral meningitis.

CSF analysis:

The CSF **leukocyte count** in bacterial meningitis usually is elevated with neutrophilic predominance (75-95%). Normal healthy neonates may have as many as 30 leukocytes/mm3 (usually <10), but older children have <5 leukocytes/mm3 ; in both age groups there is a predominance of lymphocytes or monocytes.
pleocytosis may be absent in patients with severe overwhelming sepsis and meningitis and is a poor prognostic sign.
Pleocytosis with a lymphocyte predominance may be present during the early stage of acute bacterial meningitis and vice versa. The shift to other cell type invariably occurs within 8-24 hr of the initial LP.

The Gram stain is positive in 70-90% of patients with untreated bacterial meningitis.

Raised CSF protein levels are partly a result of increased vascular permeability of the blood–brain barrier and the loss of albumin-rich fluid from the capillaries and veins traversing the subdural space. Normal CSF protein 20-45 mg/dl.

Hypoglycorrhachia (reduced CSF glucose levels) is attributable to decreased glucose transport by the cerebral tissue. Normal CSF glucose is about 2 third of RBS before doing LP.

Partially treated meningitis: children who are received oral antibiotics when their CSF is obtained, will negative Gram stain and culture, but pleocytosis with a predominance of neutrophils, elevated protein level, and a reduced CSF glucose usually persist for several days, thus the presumptive diagnosis of bacterial meningitis can be made. Bacterial antigens(latex agglutination test) and polymerase chain reactions are useful such situation to identifying of causative organism.

A traumatic LP may complicate the diagnosis of meningitis affecting cell count and protein, but the Gram stain, culture, and glucose level may not be influenced. Repeat LP at a higher interspace may produce less hemorrhagic fluid, but this fluid usually also contains red blood cells.

TREATMENT

- A child whether presented with rapidly progressing disease of less than 24 hr duration or more protracted subacute course, in the absence of increased ICP and focal neurologic deficits, should receive antibiotics as soon as possible after an LP is performed.
- If there are signs of increased ICP or focal neurologic findings, antibiotics should be given without performing an LP and before a CT scan. CT scanning should be performed to determine the safety of performing an LP. Increased ICP should be treated simultaneously.

Initial Antibiotic Therapy

- Selected antibiotics should achieve bactericidal levels in the CSF.
- Although there are substantial geographic differences in the frequency of resistance of S. pneumonia to antibiotics, rates are increasing throughout the world.

The initial (empirical) choice of therapy

In immune-competent: The regimen should contain:

1- Vancomycin (60 mg/kg/24 hr, given every 6 hr): for S. pneumoniae
2- Third-generation cephalosporins: cefotaxime (300 mg/kg/24 hr, given every 6 hr) or ceftriaxone (100 mg/ kg/24 hr administered once per day or 50 mg/kg/dose, given every 12 hr): for S. pneumoniae, N. meningitidis, and H. influenzae type b.

— - Patients **allergic to β-lactam antibiotics** can be treated with chloramphenicol or combination of vancomycin and rifampin. Alternatively, patients can be desensitized to the antibiotic.

— - If **L. monocytogenes infection** is suspected: ampicillin or Intravenous trimethoprimsulfamethoxazole.

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— **<u>In immune- compromised patient</u>**

— Gram-negative bacterial meningitis is suspected: ceftazidime and an aminoglycoside or meropenem.

Duration of Ab:

3- Uncomplicated S. pneumoniae meningitis: 10-14 days.
4- Uncomplicated N. meningitidis meningitis: 5-7 days
5- Uncomplicated H. influenzae type b meningitis: 7-10 days.
6- Gram-negative bacillary meningitis: 3 wk
7- Partially treated meningitis: 7-10 days.

Corticosteroids

Rapid killing of bacteria in the CSF will releases toxic cell products after cell lysis (cell wall endotoxin) that precipitate the cytokine-mediated inflammatory cascade. The resultant edema formation and neutrophilic infiltration may produce additional neurologic injury. Therefore, agents that limit production of inflammatory mediators:

- IV dexamethasone, 0.15 mg/kg/ dose x 4 x 2 days, maximum benefit if given 1-2 hr before antibiotics are initiated, H. influenzae type b meningitis. In meningitis caused by other bacteria: still not proved.

Supportive Care

Assessment

- Medical: PR, BP, & RR should be monitored frequently.
- Neurologic: pupillary reflexes, level of consciousness, motor strength, cranial nerve signs, and evaluation for seizures, should be made frequently in the 1st 72 hr, when the risk of neurologic complicationsis greatest.
- Laboratory studies: BUN; s Na, Cl, K, and H2CO3; urine output and specific gravity; CBC; sometimes coagulation study (PT, PTT, fibronogin)

Therapeutic

- Nothing by mouth.
- If a patient is judged to be normovolemic, i. v. fluid should be restricted to one-half to two-thirds of maintenance, until ensuring that increased ICP or SIADH are not present.

- Patients with septic shock may require fluid resuscitation and therapy with vasoactive agents such as dopamine and epinephrine

- Signs of increased ICP should be treated emergently with endotracheal intubation and hyperventilation. Iv furosemide (Lasix, 1 mg/kg) and mannitol (0.5-1.0 g/kg).

- **Seizure:** Immediate therapy with benzodiazepines, careful attention paid to the risk of respiratory suppression. After immediate management of seizures, patients should receive phenytoin (15-20 mg/ kg loading dose, 5 mg/kg/24 hr maintenance) to reduce the likelihood of recurrence.

- Serum glucose, calcium, and sodium levels should be monitored.

Prognosis

- Appropriate antibiotic therapy and supportive care have reduced the mortality of bacterial meningitis after the neonatal period to <10%. The highest mortality rates are observed with pneumococcal meningitis.
- The most common neurologic sequelae include hearing loss, cognitive impairment, recurrent seizures, delay in acquisition of language, visual impairment, and behavioral problems.

Prevention

Neisseria meningitidis

Chemoprophylaxis is recommended for all close contacts of patients with meningococcal meningitis: rifampin 10 mg/kg/dose every 12 hr (maximum dose of 600 mg) for 2 days as soon as possible ,all contacts should be educated about the early signs of meningococcal disease and the need to seek prompt medical attention if these signs develop.

***Haemophilus influenzae* Type B**

- Rifampin prophylaxis should be given to all household contacts of patients with invasive disease caused by *H. influenzae* type b, if any close family member younger than 48 mo has not been fully immunized or if an immunocompromised person, of any age, resides in the household.
- The dose of rifampin is 20 mg/kg/24 hr (maximum dose of 600 mg) given once each day for 4 days

VIRAL MENINGOENCEPHALITIS

Viral meningoencephalitis is an acute inflammatory process involving the meninges and, to a variable degree, brain tissue.

Etiology

- **Enteroviruses:** the most common cause of viral meningoencephalitis.
- **herpes family: Herpes simplex virus** (HSV) type 1 is an important cause, temporal lobe usually affected.
- **Varicella-zoster virus** may cause CNS infection in close relationship with chickenpox.
- **CMV, Epstein-Barr virus**, **Human herpes virus 6**. **Mumps**.
- **Other viruses:** adenovirus, influenza virus, parainfluenza virus, rubeola, rubella, or rabies; it may follow live virus vaccinations against polio, measles, mumps, or rubella.

Pathogenesis and Pathology

Neurologic damage is caused by direct invasion and destruction of neural tissues by actively multiplying viruses or by a host reaction to viral antigens.

Clinical Manifestations

- The progression and severity of disease are determined by the relative degree of meningeal and parenchymal involvement.
- Some children may appear to be mildly affected initially, only to lapse into coma and die suddenly. In others, the illness may be high fever, violent convulsions interspersed with bizarre movements, and hallucinations alternating with brief periods of clarity, followed by complete recovery.
- The onset of illness is generally acute, although CNS signs and symptoms are often preceded by a nonspecific febrile illness of a few days' duration.
- All features of bacterial meinigitis may be presented.
- Exanthems often precede or accompany the CNS signs.
- Examination often reveals nuchal rigidity without significant localizing neurologic changes, at least at the onset.

Diagnosis

- Clinical: The diagnosis is usually made on the basis of the clinical presentation of nonspecific prodrome followed by progressive CNS symptoms. The diagnosis is supported by examination of the CSF.
- Neuroimagingmay show swelling of the brain parenchyma.
- Focal seizures or focal findings on EEG, CT, or MRI, especially involving the temporal lobes, suggest HSV encephalitis.

Laboratory Findings

- The CSF pleocytosis: contains from a few to several thousand cells per cubic millimeter. Early in the disease, the cells are often polymorphonuclear; later, mononuclear cells predominate.
- The protein concentration in CSF tends to be normal or slightly elevated, but concentrations may be very high if brain destruction is extensive, such as that accompanying HSV encephalitis.

- The glucose level is usually normal, although with certain viruses, for example, mumps, a substantial depression of CSF glucose concentrations may be observed.
- Isolating a virus is most likely early in the illness.
- *Detection of viral DNA or RNA by polymerase chain reaction is the test of choice*

TREATMENT

- With the exception of the use of acyclovir for HSV encephalitis, treatment of viral meningoencephalitis is supportive.
- Treatment of mild disease may require only symptomatic relief.
- Headache and hyperesthesia are treated with rest, non–aspirin containing analgesics, and a reduction in room light, noise, and visitors. Acetaminophen is recommended for fever.
- Intravenous fluids are occasionally necessary because of poor oral intake.
- It is important to monitor patients for complications.
- In prolonged states of coma, parenteral alimentation is indicated.
- SIADH is common in acute CNS disorders; monitoring of S. Na is required for early detection.
- glucose, magnesium, and calcium must be maintained normal to minimize the risk of convulsions.

Prevention

- viral vaccines for polio, measles, mumps, rubella.
- Domestic animal vaccine programs against rabies.