Acute Infectious Encephalopathy

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Objectives

1. Discuss the etiology and pathophysiology of acute infectious encephalopathy.
2. Discuss the epidemiology of the condition.
3. Review the clinical presentation and the differential diagnoses for the condition.
4. Examine the diagnostic tests specific for this condition.
5. Determine treatment measures for acute infectious encephalopathy.
6. Analyze the outcomes associated with the treatments and other interventions.
7. Consider appropriate follow-up plans for patients.
Definition

• Presence of an inflammatory process of the brain associated with signs and symptoms of neurological dysfunction
• Often associated with evidence of meningeal involvement
• Most cases are unusual complications of common systemic viral infections
Epidemiology

- 3.5 to 7.4 per 100,000 persons per year
- 20,000 new cases each year in the U.S.
- Children (<12) and young adults are more commonly affected, disease severity greatest in infants and elderly patients
- Sex: Males > Females
- Transmission – inhalational, vector borne (mosquito, tick), blood borne, gastrointestinal, or genital
  - Etiology confirmed in ~30% of cases
Epidemiologic Clues

- To investigate for an etiologic diagnosis include the following in assessment:
  - Season of the year
  - Geographic locale
  - Prevalence in local community
  - Travel history
  - Recreational activities
  - Occupational exposure
  - Insect/animal contact
  - Vaccination history
  - Immune status of patient
Classification

- Infectious: viral (70%), bacterial (20%), prion (6%), parasitic (3%), fungal (1%)
  - Fungal, parasitic, or tuberculosis agents cause chronic disease
  - Host immune function critical for establishing an infectious differential diagnosis
  - Herpes simplex virus (HSV) – common cause of viral encephalitis
    - 2,000 cases in U.S. annually – as much as 28% mortality
  - Cytomegalovirus (CMV) and varicella-zoster virus (VZV) cause a more aggressive form of encephalitis in immunocompromised hosts
Common Etiologies

Viral
- HSV, VZV, EBV, CMV, Hepatitis, Mumps, Measles, Enterovirus, Adenovirus, Arboviruses (e.g. West Nile Virus, St. Louis Encephalitis, Eastern Equine, Western Equine), HIV, Influenza

Bacterial
- Mycoplasma, Legionella, Listeria, Mycobacterium tuberculosis

Parastic
- Toxoplasma, Trypanosoma, Echinococcus

Fungal
- Histoplasma, Cryptococcus neoformans
Pathophysiology

• Etiologies:

  1) Primary
     • Direct viral invasion vs. virus replicates outside of CNS → Gains entry to the CNS by hematogenous spread or by travel along neural pathways

  2) Immunologic Reaction
     • The immune system attacks CNS antigens that resemble proteins of the infectious agent
     • Occurs 1-3 wks later of a viral infection or vaccination
Pathophysiology

- Regional effect (i.e. HSV): neuron cell membrane receptors found only in specific portions of the brain leading to focal pathology
- Demyelination may follow the destruction of oligodendroglia
- Involvement of ependymal cells may lead to hydranencephaly
Pathophysiology

- Causing:
  - Meningitis
  - Cerebral edema
  - Hemorrhage
  - Apoptotic neuronal cell death
- End result: Inflammatory response with neurological symptoms
Clinical Presentation

- Dependent on site of infection
- Constitutional – fever, fatigue, myalgias, malaise
- Neurologic – headache, stiff neck, irritability, altered consciousness, incoherent speech, focal neurologic findings, seizures, stupor, coma
- Neuropsychiatric – mood alterations, hallucinations, depression
- Motor System – psychomotor hyperactivity, retardation, tremor, hyperreflexia
- Dermatologic – skin rashes (Lyme disease, typhus, rickettsial disease), skin lesions (VZV, HSV), bite-site paresthesias (rabies)
Clinical Presentation

- Cardiac – autonomic dysfunction (sympathetic overactivity), tachycardia, hypertension, diaphoresis
- Gastroenterologic – nausea, emesis (enteroviral), decreased appetite
- Pulmonary – cough, dyspnea (mycobacteria)
- Miscellaneous – incontinence, sleep/wake cycle disturbance (fragmented sleep)
Differential Diagnoses

• Stroke
• Seizures
• Vasculitis
• Autoimmune disease (most commonly systemic lupus erythematosus)
• Drug overdose
• Severe metabolic derangement (eg, metabolic acidosis, hyperglycemia)
• Malignancy – primary or metastatic
• Nutritional deficit
Laboratory Testing

• CBC
  o Leukocytosis – likely bacterial
  o Lymphocytosis – likely viral

• Peripheral smear

• Electrolyte panel (e.g. Chem 10)

• Liver and renal function studies (rule out metabolic encephalopathy); ammonia level

• Cerebrospinal fluid (CSF) studies
  o Culture and Gram stain or other special stains (eg, India ink for *Cryptococcus*, acid fast for TB)
  o Cell count with differential – usually have mononuclear pleocytosis
  o Protein – usually elevated
  o Glucose – low in bacterial, fungal, and mycobacterial infections
Laboratory Testing

- Cultures – relatively poor sensitivity
  - CSF fluid
  - Blood – 2-3 sets from separate venipuncture sites prior to the administration of antibiotics
  - Other site cultures based on other organ system involvement (sputum, urine, body fluid, tissue or gastric aspirate)

- Other tests:
  - Antibody titers for viruses – comparison of CSF and serum antibody loads
    - Ratio $\geq 20$ indicates intrathecal production
    - Intrathecal antibodies indicative of viral etiology
Laboratory Testing

- PCR of Fluids
  - Greater sensitivity during first week of symptom onset while viral agent present in CSF – yield decreases rapidly after the first week
  - False negatives most common during the first 2 days of symptoms
  - In undiagnosed, severe cases, PCR should be repeated after 3-7 days; Serology should be repeated in 4-6 weeks
- Sedimentation rate/C-reactive protein for suspected vasculitis
- For detailed lab tests for detection of specific organism, see handout attached
Imaging Testing

- Head imaging (CT/MRI) – rule out structural lesions, demyelination, and cerebral edema
- Temporal lobe enhancement suggestive of HSV-1
Diagnosis

• Correlate clinical findings with laboratory/imaging findings
• Brain biopsy – rarely performed
• Incorporate:
  1. Detailed patient history
  2. List of prescribed, OTC, herbal medications
  3. Environmental factors
  4. Immune system functionality of patient
Empirical Treatment

• Initiate treatment early to prevent serious sequelae (e.g. neurologic dysfunction, seizures, coma, death)

• Suspected viral encephalitis:
  - Acyclovir 10 mg/kg IV every 8 hrs for 10-14 days (e.g. HSV or VZV)
  - Ganciclovir 5 mg/kg IV Q 12 hrs for 14-21 days (e.g. CMV)
Empirical Treatment

- Initiate antimicrobials within 30 minutes if bacterial meningitis suspected
  - Vancomycin 1 g IV Q 12 hrs, Ceftriaxone 50 mg/kg IV Q 12 hrs, Ampicillin 2 g IV Q 4 hrs (if listeria suspected)
  - For rickettsial or ehrlichial infections, add doxycycline 100mg IV Q 12 hrs
  - Other antimicrobials on the basis of clinical factors
- Antifungal:
  - Metronidazole 500 mg IV Q 6 hrs
Specific Treatment

- Following identification of the causative microorganism, appropriate antimicrobial, antiviral, and/or antifungal may be required
- Most viruses are managed with supportive care
- Corticosteroids may be used as an adjunctive therapy
  - Methylprednisolone, 1 g IV daily 3–5 days
Management

- Management of hydrocephalus and increased ICP
- Treatment of systemic complications
  - Hypotension/shock
  - Hypoxemia
  - Hyponatremia
  - Exacerbation of chronic diseases
- Antipsychotics:
  - Haldol 0.5-5 mg IV
  - Risperidone 0.25-3 mg/day
  - Seroquel 12.5-100 mg/day
  - Lorazepam 0.5-2mg IV/PO
- Start with low dose and minimize benzodiazapine use, especially in geriatric population
Follow-up Care

- Monitor airway, breathing, circulation
- Frequent neurological assessments
- Monitor for seizures/subclinical seizures
- Monitor for cerebral edema/increased ICP
Prognosis

- Dependent on the virulence of the virus and the patient’s health status
- 40% of survivors have residual deficits: learning disabilities, memory impairment, neuropsychiatric abnormalities, epilepsy, fine-motor-control deficits, and dysarthria
- High mortality rates if not treated (50-100%); with treatment mortality ranges from 2-20%
- Poor outcomes with:
  - Extremes of age (< 1 y or >55 y)
  - Immune-compromised status
  - Preexisting neurologic conditions
Questions?
References


References


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