ER-Infeciton combined meeting

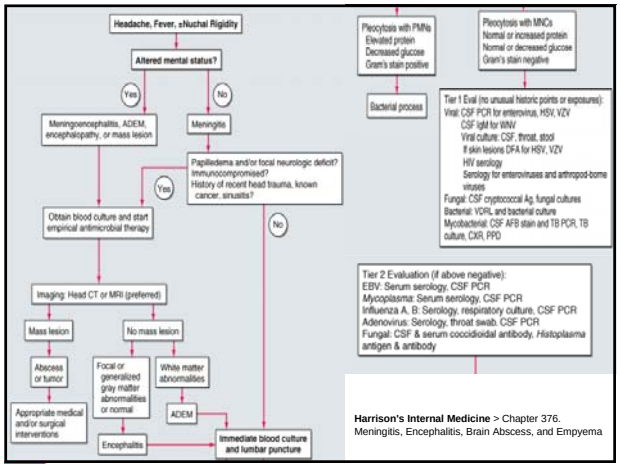
報告 :PGY 劉康懿
指導者: VS 洪世文
991016

Discussion

- Diagnosis of meningitis
- Role of steroid
- CNS tuberculosis

1.Meningitis

- Inflammatory disease of the leptomeninges, the tissues surrounding the brain and spinal cord,
- defined by an abnormal number of white blood cells in the cerebrospinal fluid (**CSF**)
- The meninges consist of three parts: the pia, **arachnoid, and dura maters**.



Harrison's Internal Medicine > Chapter 376. Meningitis, Encephalitis, Brain Abscess, and Empyema

Causes of Meningitis

- **Infectious Meningitis**
  Bacterial, Virus, Fungus
- **Noninfectious Meningitis**
- Drug-induced meningitis: NSAIDs, Trimethoprim, Isoniazid
- Carcinomatous meningitis
- Serum sickness
- Vasculitis
- Systemic lupus erythematosus
- Behçet's disease
- Sarcoidosis

Neisseria meningitidis	Nasopharynx	All ages	**Usually none, rarely complement deficiency**
Streptococcus pneumoniae	Nasopharynx, direct extension across skull fracture, or from contiguous or distant foci of infection	All ages	All conditions that predispose to pneumococcal bacteremia, fracture of cribriform plate
Listeria monocytogenes	Gastrointestinal tract, placenta	Elderly adults and neonates	Defects in cell-mediated immunity, pregnancy, liver disease, alcoholism, malignancy
Coagulase-negative staphylococcus	Dermal or foreign body	All ages	Surgery and foreign body, especially ventricular drains
Staphylococcus aureus	Bacteremia, dermal, or foreign body	All ages	Endocarditis, surgery and foreign body, especially ventricular drains
Gram-negative bacilli	Various	Elderly, neonates	Advanced medical illness, neurosurgery, ventricular drains, disseminated strongyloidiasis
Haemophilus influenzae	Nasopharynx, contiguous spread from local infection	Adults not vaccinated	Diminished humoral immunity

CLINICAL FEATURES

- Fever --95 % at presentation, most>38 degree
  --Exception : small percentage have hypothermia.
- Nuchal rigidity –
  88 % on initial examination
  persisted for more than seven days
- Altered mental status 78 %, Most were confused or lethargic
- Headache: 79 to 94 percent, severe and generalized
- Clinical triad: > *60 y/o : < 60y/o= 58% vs. 36%*, S.p (↑), Ca. (↓)
- 95 % presented with at least two of four symptoms

CLINICAL FEATURES

- Photophobia, nausea, and/or vomiting
- Skin manifestations, such as petechiae and palpable purpura
  -- rash was present in 11 and 26 %
  -- Mostly N. meningitidis.
  → rash was present in 64 %
  → characterized petechial in 91 % of patients, not specific
- Arthritis : 7%, (67% with N. meningitidis
- Caution: older adults, DM, CAD

CLINICAL FEATURES

- Neurologic complications :
  Coma
  Loss of airway reflexes
  Cerebral edema
  Seizures: 15 ~ 30 percent
  Focal neurologic deficits : 10 ~ 35 percent
  Hearing loss : late complication
  Papilledema is observed in <5 percent of patients at initial
- Fever, syndrome of rhombencephalitis (ataxia, cranial nerve palsies, and/or nystagmus) →Listeria meningitis

Physical Examination

- Examination for nuchal rigidity —
  -- inability to touch the chin to the chest,
  --Nuchal rigidity 30% Sensitivity, 70% specificity
  --Difficulty in lateral motion : less reliable finding

Signs of meningeal irritation	Maneuver	Positive test
Kernig's sign (5%Sensitivity, 95% specificity)	Place patient supine with hip flexed at 90 degrees. Attempt to extend the leg at the knee.	resistance to extension at the knee to >135 degrees or pain in the lower back or posterior thigh.
Brudzinski's sign (5%Sensitivity, 95% specificity)	Place patient in the supine position and passively flex the head towards the chest.	flexion of the knees and hips of the patient.
Jolt accentuation of headache sensitivity : 97 percent specificity : 60 percent	Patient rotates his/her head horizontally two to three times per second.	exacerbation of his/her headache with this maneuver.

Risk score for prognosis

TABLE 3. Components of the Risk Score for Prognosis in Bacterial Meningitis

Points	0	1	2	4	5	6	8	9	10	12	13	14	16
Age	20		30	40		50	60		70	80			
Tachycardia*	No								Yes				
Glasgow Coma scale	15	14	13	12	11	10	9	8	7	6	5	4	3
Cranial nerve palsy	No							Yes					
CSF leukocyte count†	High										Low		
CSF Gram stain	Gram−	No	Other							Gram+			

*The authors defined tachycardia as >120 beats/min.
†A low CSF leukocyte count was defined as <1000 cells/mm³.
CSF indicates cerebrospinal fluid.

TABLE 4. Risk of Unfavorable Outcome Based on Calculated Risk Score

Score	0	5	10	15	20	25	30	35	40	45	50	55	60	65
Percentage of unfavorable outcome	3.2	5.1	8.2	13	20	29	40	52	64	75	83	89	93	96

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LABORATORY FEATURES

- WBC elevated, with a shift toward immature forms
- Coagulation studies may be consistent with disseminated intravascular coagulation.
- Anion gap metabolic acidosis
- Hyponatremia
- Blood cultures —50 to 90 percent of patients (+)
  much less likely to be positive after antibiotics,
  particularly for meningococcus

LUMBAR PUNCTURE

- Screening CT scan is not necessary in the majority
- 2~4 hours delay in diagnosis and 1 hr delay in therapy

- 2004 Infectious Diseases Society of America (IDSA) guidelines
  ≥ 1 following risk factors then DO CT:

Immunocompromised state
History of CNS disease (mass lesion, stroke, or focal infection)
New onset seizure (within one week of presentation)
Papilledema
Abnormal level of consciousness
Focal neurologic deficit

Who couldn't have LP?

- Patient with clinical signs of impending herniation (ie, ↓ level of consciousness, GCS <11; brainstem signs including papillary changes, posturing, or irregular respirations; or a very recent seizure)

- If LP is delayed : blood cultures→ Dexamethasone (0.15 mg/kg IV every six hours) should be given shortly before or at the same time as the antibiotics →image study → re-evaluation of LP

- Prior administration of antimicrobials effect: 4~10hr, N.m

Analysis of CSF

Table 107-1 -- Analysis of Cerebrospinal Fluid

Test	Normal Value	Significance of Abnormality
Cell count	<5 WBC/mm[3] <1 PMN/mm[3] <1 eosinophil/mm[3]	Increased WBC counts are seen in all types of meningitis and encephalitis; increased PMN count suggests bacterial pathogen
Gram's stain	No organism	Offending organism identified 80% of time in bacterial meningitis, 60% if patient pretreated
Turbidity	Clear	Increased turbidity with leukocytosis, blood, or high concentration of microorganisms
Xanthochromia	None	Presence of RBCs in spinal fluid for 4 hr before lumbar puncture; occasionally caused by traumatic tap (if protein > 150 mg/dL) or hypercarotenemia
CSF-to-serum glucose ratio	0.6:1	Depressed in pyogenic meningitis or hyperglycemia; lag time if glucose given IV
Protein	15–45 mg/dL	Elevated with acute bacterial or fungal meningitis; also elevated with vasculitis, syphilis, encephalitis, neoplasms, and demyelination syndromes
India ink stain	Negative	Positive in one third of cases of cryptococcal meningitis
Cryptococcal antigen	Negative	90% accuracy for cryptococcal disease
Lactic acid	<35 mg/dL	Elevated in bacterial and tubercular meningitis
Bacterial antigen tests	Negative	>95% specific for organism tested; up to 50% false-negative rate
Acid-fast stain	Negative	Positive in 80% of cases of tuberculous meningitis if >10 mL of fluid

CSF, cerebrospinal fluid; PMN, polymorphonuclear; RBC, red blood cell; WBC, white blood cell.

Analysis of CSF

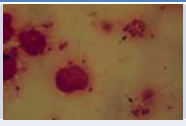
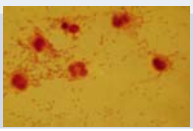
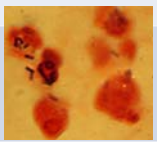
Infectious Diseases

CSF Findings in Meningitis

Condition	Appearance	Pressure (cm)	WBC/mm³ predom type	Glc (mg/dl)	TP (mg/dl)
Normal	clear	9-18	0-5 *lymphs*	50-75	15-40
Bacterial	cloudy	18-30	100-10,000 *polys*	<45	100-1000
TB	cloudy	18-30	<500 *lymphs*	<45	100-200
Fungal	cloudy	18-30	<300 *lymphs*	<45	40-300
Aseptic	clear	9-18	<300 *polys → lymphs*	50-100	50-100

• Additional CSF studies depending on clinical suspicion: acid-fast smear and culture, India ink preparation, cryptococcal antigen (CRAg), fungal culture, PCR (e.g., of HSV), cytology

Gram stain

Gram-positive diplococci suggest pneumococcal infection	Gram-negative diplococci suggest meningococcal infection
	
Small pleomorphic gram-negative coccobacilli suggest Haemophilus influenzae infection	**Gram-positive rods and coccobacilli suggest listerial infection**
	

2.Role of Steroid

- ↓ the rate of neurologic complications as well as mortality
- ↓ *the rate of hearing loss in children* *Cochrane Systematic Review from 2007 ,* The Evaluation and Management of Bacterial Meningitis, *Current Practice and Emerging Developments*
- 2004 Infectious Diseases Society of America (IDSA) guidelines recommended : adjunctive dexamethasone be initiated in ALL **adults** with suspected or proven pneumococcal infection.
- Timing: 15~ 20 minutes before or at the time of antibiotics
- Dose:

  0.15 mg/kg/dose 6 hourly for the first 4 days (European trial)

  0.4 mg/kg every 12 hours for four days (Vietnamese trial)

Role of steroid

- In the developed world:
  known, suspected pneumococcal meningitis, administration (1B);
  Others, not administering (2B)
- In the developing world:
  known or suspected bacterial meningitis
  with high HIV prevalence, not administering (1B)
  with low HIV prevalence, administering (2B)
- Reasonable to empirically administer adjunctive dexamethasone in patients in whom there is a suspicion for acute bacterial meningitis until results are available

3.CNS tuberculosis

- Include: meningitis, intracranial tuberculoma, and spinal tuberculous arachnoiditis.
- D/D:

Fungal meningitis (cryptococcosis, histoplasmosis, blastomycosis, coccidioidomycosis)
Viral meningoencephalitis (herpes simplex, mumps)
Parameningeal infection (sphenoid sinusitis, brain abscess, spinal epidural abscess)
Partially treated bacterial meningitis
Neurosyphilis
Neoplastic meningitis (lymphoma, carcinoma)
Neurosarcoidosis
Neurobrucellosis

Tuberculous meningitis

- Progress through three phases:
- The prodromal phase, lasting two to three weeks, characterized by the insidious onset of malaise, lassitude, headache, low-grade fever, and personality change.
- The meningitic phase with more pronounced neurologic features
- The paralytic phase, accelerates rapidly; confusion gives way to stupor and coma, seizures, and often hemiparesis.

- Outcome according as presentation:
  Stage I: lucid, no neurologic signs , stage II: lethargy, confusion , neurologic sign(+), stage III: advanced

Diagnosis of CNS TB

- CSF protein ranges from 100 to 500 mg/dL in most patients
- CSF glucose < 45 mg/dL in 80 % of cases
- CSF cell count is between 100 and 500 cells/microL

- AFB in the CSF remains the most rapid and effective means
- Three lumbar punctures be performed at daily intervals
- CSF for PCR testing
- MRI is superior to CT in defining lesions of the basal ganglia, midbrain, and brainstem and for evaluating all forms of suspected spinal TB

Treatment of CNS TB

- Initial two month period of intensive therapy, with four drugs (Grade 1B): INH, RIF, PZA, and either EMB or STM for fully sensitive isolates
- Then continuation phase lasting 7 to 10 months (INH and RIF)
- Glucocorticoid therapy for all patient with convincing epidemiologic or clinical evidence for TB meningitis. (1A)
- Mortality was reduced significantly in the dexamethasone-treated group (32 versus 41 percent)

Treatment of CNS TB

- There was no demonstrable reduction in residual neurologic deficits and disability among surviving patients evaluated by questionnaire at nine months follow-up.
- No mortality benefit from dexamethasone was evident in 98 HIV-infected patients included in the study.
- Dexamethasone— A total dose of 8 mg/day for children weighing <25 kg; 12 mg/day for adults and children >25 kg, for 3 weeks, then tapered off gradually over 3 to 4 weeks.
- Prednisone— A dose of 2 to 4 mg/kg per day for children; 60 mg/day for adults, for 3 weeks, then tapered.

Thanks for your listening!

- *Reference:*
- *Uptodate*
- *Rosen, 6th edition*
- *Harrison, 17th edition*
- The Evaluation and Management of Bacterial Meningitis, *The Neurologist* • Volume 16, Number 3, May 2010