SEMINAR ON ACUTE BACTERIAL MENINGITIS AND ANTI MICROBIALS IN NEURO SURGERY.

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ACUTE BACTERIAL MENINGITIS

• ABM is acute purulent infection in the subarachnoid space
• It is associated with a CNS inflammatory response that may result in decreased consciousness, seizures, raised ICP and stroke
• The meninges, subarachnoid space, brain parenchyma are frequently involved in inflammatory process.
ABM

- Community acquired meningitis vs. postoperative meningitis

- ABM Vs Aseptic meningitis
ABM : PATHO PHYSIOLOGY

ROUTES OF INFECTION

• Hematogenous spread
• Retrograde propagation from nasopharynx via infected thrombi in emissary veins
• Direct spread from contiguous foci of infection like orbital cellulitis, osteomyelitis of skull, basal skull fracture
• Direct inoculation following penetrating brain injury; in neurosurgical procedures
ABM : PATHOPHYSIOLOGY

• CSF is a moderately good culture medium as it contains very low concentration of Immunoglobulins and complement components
• Its opsonic activity is low
• It is devoid of PMN phagocytes
• Phagcytosis of bacteria is further impaired by fluid nature of CSF
Critical event in pathogenesis is **inflammatory reaction** induced by invading bacteria

- Many of the neurologic manifestations and complications are result of **immune response** to invading pathogens rather than direct bacteria induced injury

- As a result, neurologic injury can progress even after CSF has been sterilized by antibiotic therapy
ABM : PATHOGENESIS

- Elevated levels of CSF cytokines and chemokines (TNF, IL-1)
- These increase permeability of BBB
- Vasogenic edema
- Subarachnoid protenaceous exudates
- Obstructive hydrocephalus
- Intrrerstitial edema
  all these induce death of brain cells
INFLAMMATORY RESPONSE IN CSF

- CSF lactate increases
- CSF proteins increase
- CSF leucocytes increase
- CSF glucose decreases
POST OPERATIVE BACTERIAL MENINGITIS

EARLY:

• Within 7 days
• Direct inoculation of organisms

LATE:

• After 7 days
• Represents hematogenous or direct spread of organisms to infect damaged tissue or foreign bodies
• In many cases same organism can be isolated from elsewhere in the body
CAUSATIVE ORGANISMS

Varies with age in CAM

- **Neonates**: GNB
  - *Streptococcus agalactiae*
- **Children**: H influenzae, pneumococcus
- **Adults**: Pneumococcus, N meningitidis

In neurosurgical cases spectrum of organisms varies

- Following CSF leak: pneumococcus, H. influenzae
- Following VP shunt: *S. epidermidis*, *Propiobacterium acnes*
- Following craniotomy: *S. aureus*, GNB, Pseudomonas
CLINICAL FEATURES

• TRIAD: high grade fever (>100.4°F), severe headache, neck stiffness
• Prodromal features: like URTI, ASOM/CSOM, Pneumonia
• Signs of meningeal irritation:
  - photophobia
  - Kernig's sign
  - Brudzinski’s sign
CLINICAL FEATURES

Associated neurological signs:
  - impaired consciousness level
  - seizures
  - cranial nerve signs in 15% cases
  - sensory neural deafness in 20%
  - focal neurological signs in 10%

Non neurological complications: sepsis, shock, arthritis, ABE
Management protocol

Suspicion of bacterial meningitis

Pappiledema and / or focal neurological deficits

Absent

- Obtain blood cultures
  - Perform lumbar puncture

  CSF consistent with bacterial meningitis

  - Positive gram stain or bacterial antigen test
    - no
      - Empirical antimicrobial therapy
    - yes
      - Specific antimicrobial therapy

- Present

  Obtain blood cultures

  Empirical antimicrobial therapy

  CT scan of head

  - No mass lesion
  - Mass lesion
  - Consider alternate diagnosis
CSF ABNORMALITIES IN BACT. MENINGITIS

- Opening pressure: >180 mm H2O
- WBC: >500-1000/cu.mm
- RBC: Absent in non traumatic tap
- Glucose: <40 mg/dl
- CSF/Serum glucose: <0.4
- Protein: >45mg%
- Gram stain: positive in > 60%
- Culture: positive in > 80%
- Latex agglutination: may be positive in 70-80%
- Limulus lysates: positive in gram negative meningitis
- PCR for bacterial DNA: research tool
## D/D OF CSF PLEOCYTOSIS

<table>
<thead>
<tr>
<th></th>
<th>CELLS</th>
<th>PROTEINS</th>
<th>GLUCOSE</th>
<th>GRAM STAIN</th>
<th>CULTURE</th>
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<tbody>
<tr>
<td>ABM</td>
<td>20-20000 PMN</td>
<td>Increased</td>
<td>decreased</td>
<td>+/-</td>
<td>+/-</td>
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<tr>
<td>Para Meningeal infection</td>
<td>100-500</td>
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<tr>
<td>Post Op changes</td>
<td>100-500</td>
<td>increased</td>
<td>normal</td>
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NEWER TESTS IN CSF

• S.PROCALCITONIN > 0.5 ng/ml
  -Dubos et al. in J Paeds 2006

  TNF- ALFA in CSF
  -Adrian et al. in J of Paeds neurology 2005

Are useful markers for distinguishing bact. From aseptic meningitis.
Meningitis in neurosurgical settings

- Post head injury
- Post op meningitis
- Shunt infection
- Ruptured MMC
- Persistent dermal sinus
Post op meningitis

- Severe form of nosocomial infection
- Most common organism: staph aureus
- Seen in 0.5-0.7% of patients undergoing neurosurgical procedures if prophylactic antibiotics are given
Special considerations

• Signs of meningitis are marked /or confused with effects of operation itself or underlying CNS disease – hence delay in diagnosis

• Tempo of the disease is unpredictable acute vs. protracted course
Post op meningitis

- **AIIMS NEUROSURGERY**-year- 2006 experience:
  - Total no. of patients operated -3114
  - Total no. of CSF culture+ meningitis-70(2.2%)
  - Total cases of wound infection- 95(3.5%)
  - Total no. of patients affected- 165 (5.3%)
Microbial spectrum
AIIMS NEUROSURGERY-year- 2006 experience:

- Most common are gram negative bacilli
  Acinetobacter
  Pseudomonas

  Others- MSSA, MRSA. Klebsiella, Enterococcus

- About 80-90% of these GNB are ESBL+
  hence having resistance to conventional penicillins
Culture sensitivity pattern
AIIMS NEUROSURGERY-year- 2006 experience:

- Most cases are sensitive to carbepenems like meropenem/imipenems
  - cefoperazone+sulbactam
  - piperacillin+tazobactam
- Overall 20-30% of GNB are now showing resistance to carbapenems
ABM   Treatment Principles :

• Supportive care during critical phase
  - fluid, electrolyte management

• Eradicate causative organism with appropriate antibiotics

• Modify host's inflammatory response
  - role of steroids
Types of treatment failures:

- Recrudescence
- Relapse
- Recurrence
Prophylactic Antimicrobials in neurosurgery-Principles:

- Abs must be in tissues at time of contamination
- Repeat dose during prolonged surgeries
- Not cost effective in low infection risk surgeries
Role of Prophylactic Antimicrobials for specific neurosurgical procedures

• Craniotomy: role in prolonged microneurosurgical reopertive procedure

• CSF Shunt: role is established only if infection rate is high (>10%)
Empirical therapy in post op meningitis

- Should cover:

  - GNB: Ceftazidime (3rd gen. cephalosporin) + aminoglycoside
  - Anaerobes: metronidazole
  - GPC: Vancomycin +/- aminoglycoside
AIIMS NEUROSURGERY protocol for meningitis

- <2 years – fortum + netro + metro

- >2 years – cbactum + netro + metro
Antibiotic monotherapy- adv.:  
• Fewer superinfections  
• Smaller risk of toxic S/E  
• Lower cost  
• Smaller effect on host flora  

BUT STILL ANTIBIOTIC COMBINATIONS are used in serious infections- Rationale:  
✓ For synergistic action  
✓ To prevent development of resistance
• To treat polymicrobial infections
• To broaden coverage of empiric regimens
Emerging resistance of antimicrobial agents—a great concern

- Has led to closure of an ICU at Columbia, New York because of multiple resistant Acinatobacter
- Cephalosporin & Carbapenem resistant GNB
- Methicillin & Vancomycin resistant STAPH.aureus
Specific antimicrobials commonly used at AIIMS Neurosurgery deptt.

CHLOROMYCETIN:
- Good for G+ & G – cocci
- Excellent CSF penetration

AMINOGLYCOSIDES:
- Good for Staph. +GNB incl. Pseudomonas
- More rapid kill than B-lactums

METRONIDAZOLE:
- Good for anaerobes & micro aerophilic org.
- Readily crosses BBB
Specific antimicrobials commonly used at AIIMS Neurosurgery deptt.

CEPHALOSPORINS:

- Higher gen. are better for GNB & poorer for GPC
- Ceftazidime—best for pseudomonas
  - good csf penetration
  - dose: 1-2 gm I/V BD-TDS (max 6 gm)

MACROLIDE (VANCOMYCIN):

- doc. for staph.
  - 1 gm I/v BD-TDS
Drug fever:

- A non infectious cause of fever in neurosurgical patients
- Antibiotics / anticonvulsants
- Elevation of counts
- Temp. – pulse dieosonophilssosiation
- Defervesence on withdrawal of drug.