Diagnosis of Neonatal Sepsis – Dr. Haidar

A- Laboratory studies

1. Cultures: blood and other normally sterile body fluids should be obtained for culture (blood, urine, CSF). Positive bacterial culture will confirm the diagnosis of sepsis. Results may vary because of number of factors, including maternal AB administered before birth, organisms that are difficult to grow and isolate and sampling errors. So clinical diagnosis is very important to decide the starting of AB.
2. Antigen detection tests: tests are available for GBS, N. meningitidis, H. influenza and Streptococcus pneumonia.
3. Gram stain of various body fluid.
4. Other lab tests: like WBC count with differential, platelets count and acute phase reactant (e.g. C reactive protein CRP, ESR, cytokines).

B- Radiological studies

1. Chest X ray: should be obtained in cases with respiratory symptoms.
2. Urinary tract imaging with renal Ultrasound examination, renal scan, or voiding cystourethrography.
3. Other studies: Like examination of the placenta and fetal membranes.

Management

- Initial therapy: in addition to the supportive therapy (like oxygen therapy, I.V. fluid, incubator, blood gas monitoring), treatment is most often began before a definitive causative agent is identified. It consists of penicillin, or usually ampicillin, plus an aminoglycoside such as gentamicin. In nosocomial sepsis, the flora of the NICU must be considered; however, generally, staphylococcal coverage with vancomycin plus either an aminoglycoside or a third generation cephalosporin is usually begun.
- Continuing therapy: is based on the result of culture and sensitivity. Monitoring for AB toxicity is important as well as following levels of aminoglycoside and vancomycin.

Congenital Infections (TORCH)

- TORCH represents a generic group of parasitic, bacterial and viral pathogens that produce congenital or perinatally acquired infections. TORCH stands for Toxoplasmosis, Others (hepatitis B, varicella, HIV, parvovirus), Rubella, Cytomegalovirus and Herpes simplex.
- Clinical Features: in TORCH manifestations are similar and include intrauterine growth retardation, nonimmune hydrops, anemia, thrombocytopenia, jaundice, hepatosplenomegaly, chorioretinitis and congenital malformations.
- Some of the unique manifestations may be noted in this table:

<table>
<thead>
<tr>
<th>Infection</th>
<th>Manifestations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toxoplasmosis</td>
<td>Hydrocephalus, abnormal spinal fluid, intracranial calcifications, chorioretinitis, jaundice or may be asymptomatic at birth.</td>
</tr>
<tr>
<td>Rubella virus</td>
<td>IUGR, microcephaly, microphthalmia, cataract, glaucoma, hepatosplenomegaly, jaundice, PDA, deafness, skin rash and thrombocytopenia.</td>
</tr>
<tr>
<td>Cytomegalovirus</td>
<td>Sepsis, IUGR, chorioretinitis, microcephaly, periventricular calcifications, anemia, thrombocytopenia, hepatosplenomegaly and jaundice</td>
</tr>
<tr>
<td>Herpes simplex type II virus</td>
<td>Intrauterine infection, chorioretinitis, skin lesions, microcephaly, encephalitis, skin vesicles and keratoconjunctivitis.</td>
</tr>
<tr>
<td>Varicella zoster virus</td>
<td>Microphthalmia, cataract, chorioretinitis, cutaneous and bony aplasia or atrophy or hypertrophy.</td>
</tr>
<tr>
<td>HIV</td>
<td>AIDS: symptoms usually develop between 3-6 m of age = failure to thrive, recurrent infections, hepatosplenomegaly and neurologic abnormalities.</td>
</tr>
</tbody>
</table>
Evaluation
• Any newborn suspected to have TORCH infections an attempt should be done to isolate the organism by culture (like in Rubella, CMV, herpes simplex II, gonorrhea) or to identify the antigen of the pathogens (like in hepatitis B, Chlamydia) or to identify specific fetal production of Ab (like IgM or increasing titer of IgG for toxoplasma, syphilis, parvovirus or HIV).

Treatment
• Is not always available, and may be not specific nor effective.
• For examples
  o In toxoplasmosis = pyrimethamine plus sulfadiazine.
  o In herpes simplex II = Acyclovir.
  o In Varicella zoster = Acyclovir.
  o In syphilis = penicillin.
  o Sometime the treatment is only symptomatic , and the prevention is more important

Neonatal convulsions
• Neonatal seizures defined clinically as a paroxysmal alteration in neurologic function (like behavioral, motor, or automatic function or all)
• Incidence: are not uncommon, the incidence range from 1.5 in 1000 to 14 in 1000 of live birth.
• Differential Diagnosis of Neonatal seizures:
  1. Perinatal asphyxia.
  2. Intracranial hemorrhage (subarachnoid, periventricular, ventricular or subdural hemorrhage).
  3. Metabolic abnormalities (hypoglycemia, hypocalcemia, electrolytes disturbances)
  4. Amino acid disorders.
  5. Congenital malformations.
  6. Infections (meningitis, encephalitis, cerebral abscess).
  7. Drugs withdrawal.
  8. Toxin exposure.
  9. Inherited seizures disorders (benign familial epilepsy, tuberous sclerosis).

Diagnosis
1. History: family history, maternal drug history and history of delivery.
2. Physical examination: thorough general examination, gestational age, blood pressure, presence of hepatosplenomegaly. In addition to that neurological evaluation and a notation of the seizures pattern.
3. Laboratory studies: serum biochemical studies, SCF studies, metabolic studies.
4. Radiological studies: Ultrasound of the head, CT scan of the head.
5. Other studies: like EEG, biopsy for histopathological studies.

Management
• Since repeated seizures may lead to brain injury, urgent treatment is indicated. The method of treatment depend on the cause. Hypoglycemia is treated by 2-4 ml /kg of 10% G.W. Hypocalcemia is treated by slow I.V. infusion of calcium gluconate, and if serum Mg level is low, so Mg should be given also.
• Anticonvulsants therapy: it is usually used when no underlying cause can be identified. Drugs like phenobarbital, phenytoin, diazepam, pyridoxine, lorazepam, IV medazolam or paraldehyde can be used according to the type of seizure and the underlying cause.
• In addition to the previous treatment, supportive therapy (like suctioning of the secretions, positioning of the patient, oxygen therapy...etc) should be started immediately.
*** Jitteriness is sometimes confused with seizures. In a jittery infant, eye movements are normal, the hand will stop moving if they are grasped and the movements are of a fine nature. While in infant who is seizing, eye movements may be abnormal (e.g. staring, blinking, nystagmoid jerks or tonic horizontal eye deviation), the hands continue to move if grasped and movements are of a coarse in nature, and finally EEG is normal in jitteriness while it is abnormal in seizures.

Neonatal screening tests

- These are tests performed during neonatal period for early detection of some inherited diseases, in order to diagnose them earlier and treat them as early as possible to prevent the possible complications and to improve the outcome.
- Screening tests are available for various genetic, metabolic, hematologic and endocrine diseases.
- Lab. testes performed on infants heel puncture blood samples include those for hypothyroidism, phenylketonuria, galactosemia, maple syrup urine disease, homocystinuria, biotinidase deficiency, adrenal hyperplasia, hemoglobinopathies, cystic fibrosis, tyrosinemia and other organic defects or aminoacidopathies.
- Tests for metabolic disease include the ferric chloride test (for PKU, tyrosinemia, and others). The dinitrophenylhydrazine test (PKU, maple syrup urine disease) and the cyanide-nitroprusside test (homocystinuria, cystinuria).
- Neonatal screening for Hyperphenylalaninemia effective and relatively inexpensive methods for mass screening of newborn infants have been developed and are used in the United States and several other countries.
- The bacterial inhibition assay of Guthrie, which was the 1st method for the purpose, has been replaced by more precised and quantitative methods (fluorometric and tandem mass spectrometry).
- All these methods require a few drops of blood, which are placed on a filter paper and mailed to a central laboratory for assay.
- Blood phenylalanine in affected infants with PKU may rise to diagnostic levels as early as 4 hr after birth even in the absence of protein feeding.
- It is recommended however, that the blood for screening be obtained in the 1st 24-48 hr of life after feeding protein to reduce the possibility of false negative results, especially in the milder forms of the condition.