Central Nervous System Involvement in Plasmodium falciparum Malaria:

By the end of this session the student should be able to :

1. List the main complications of malaria.
2. Define severe malaria
3. Define cerebral malaria.
4. Describe the main pathophysiological mechanisms underlying complications of severe malaria , including cerebral malaria.
5. Describe the main clinical features of cerebral malaria.
6. Outline the main steps in management of a case of cerebral malaria.

Severe malaria : is defined as symptomatic malaria in a patient with P. falciparum asexual parasitaemia with one or more of the following complications:

1. Cerebral malaria (unrousable coma not attributable to other causes).
2. Generalised convulsions (> 2 episodes within 24 hours)
3. Severe normocytic anaemia (Ht<15% or Hb < 5 g/dl)
4. Hypoglycaemia (glood glucose < 2.2 mmol/l or 40 mg/dl)
5. Metabolic acidosis with respiratory distress (arterial pH < 7.35 or bicarbonate < 15 mmol/l)
6. Fluid and electrolyte disturbances
7. Acute renal failure (urine <400 ml/24 h in adults; 12 ml/kg/24 h in children)
8. Acute pulmonary oedema and adult respiratory distress syndrome
9. Abnormal bleeding
10. Jaundice
11. Haemoglobinuria
12. Circulatory collapse, shock, septicaema (algid malaria)
13. Hyperparasitaemia (>10% in non-immune; >20% in semi-immune)

Cerebral malaria is the most common complication and cause of death in severe P. falciparum infection. In cases of falciparum malaria 80% of deaths are due to the CNS involvement.

Definition : A strict definition of cerebral malaria: the presence of P. falciparum parasitemia and the patient to be in unrousable coma , and other causes (e.g. hypoglycemia, bacterial meningitis and viral encephalitis) ruled out. To distinguish cerebral malaria from transient postictal coma, unconsciousness should persist for at least 30 min after a convulsion.

Pathophysiology: Cerebral malaria is the most important complication of falciparum malaria. However, its pathophysiology is not completely understood. The basic underlying defect seems to be clogging of the cerebral microcirculation by the parasitized red cells. These cells undergo changes on their surface that give them increased cytoadherent

properties, as a result of which they tend to adhere to the endothelium of capillaries and venules. This results in sequestration of the parasites in these deeper blood vessels. Also, rosetting of the parasitized and non-parasitized red cells and decreased deformability of the infected red cells further increases the clogging of the microcirculation. It has been observed that the adhesiveness is greater with the mature parasites. Obstruction to the cerebral microcirculation results in hypoxia and increased lactate production due to anaerobic glycolysis. The parasitic glycolysis may also contribute to lactate production. In patients with cerebral malaria, C.S.F. lactate levels are high and significantly higher in fatal cases than in survivors. The adherent erythrocytes may also interfere with gas and substrate exchange throughout the brain. However, complete obstruction to blood flow is unlikely, since the survivors rarely have any permanent neurological deficit.

Vascular permeability is found to be mildly increased, however, no definite evidence of cerebral edema has been found on imaging studies. 80% children with cerebral malaria have raised ICT, due to increased cerebral blood volume and biomass rather than increased permeability. The mechanism of coma is not clearly known. Increased cerebral anaerobic glycolysis, interference with neurotransmission by sequestered and highly metabolically active parasites have been blamed. Cytokines induce nitric oxide synthesis in leukocytes, smooth muscle cells, microglia and endothelium and NO is a potent inhibitor of neurotransmission.

Neurological signs in cerebral malaria:

As per the definition, patient should have in unarousable coma, not responding to noxious stimuli with a Glasgow coma scale of <7/15. Mild neck stiffness may be seen, however, neck rigidity and photophobia and signs of raised intracranial tension are absent. Retinal haemorrhages occur in about 15% of cases, exudates are rare. Pupils are normal. Papilloedema is rare and should suggest other possibilities. A variety of transient abnormalities of eye movements, especially
dysconjugate gaze, are observed. Fixed jaw closure and tooth grinding (bruxism) are common. Pouting may occur or a pout reflex may be ellicitable, but other primitive reflexes are usually absent. The corneal reflexes are preserved except in case of deep coma. Motor abnormalities like decerebrate rigidity, decorticate rigidity and opisthotonus can occur. Deep jerks and plantar reflexes are variable. Abdominal and cremasteric reflexes are not ellicitable. These signs help in distinguishing from behavioural problems due to fever of other causes. These patients may also have anemia, jaundice and hepatosplenomegaly. Investigations: Lumbar puncture and CSF analysis may have to be done in all doubtful cases and to rule out associated meningitis. **In malaria, CSF pressure is normal to elevated, fluid is clear and WBCs are fewer than 10/µl; protein and lactic acid levels are elevated.**

EEG may show non-specific abnormalities.

CT scan of the brain is usually normal.

Management:

1. Nursing care:

Meticulous nursing is the most important aspect of management in these patients. General measures for management of a comatose patient e.g. Maintain a clear airway. In cases of prolonged, deep coma, endotracheal intubation may be indicated. turn the patient every two hours , avoid soiled and wet beds ,semirecumbent position to reduce the risk for aspiration, naso-gastric aspiration to prevent aspiration pneumonia , maintain strict intake/output record. Observe for high coloured or black urine. Monitor vital signs every 4-6 hours. Changes in levels of sensorium, occurrence of convulsions should also be observed. If the temperature is above 39 C, tepid sponging and fanning must be done. Serum sodium concentration, arterial carbon dioxide tension, blood glucose, and arterial lactate concentration should be monitored frequently.

2. Urethral catheter can be inserted for monitoring urine output.

3. Seizures should be treated promptly with anticonvulsants, but their prophylactic use is still in dispute. Diazepam by slow intravenous injection, or intrarectally , or intramuscular paraldehyde are the drugs of choice.

4. Antimalarial treatment: Parenteral Quinine and Artemisinin derivatives have been proved to effective in treating cerebral malaria. For details see Treatment of Severe P. falciparum malaria in Reference number (3) below.

Prognosis:

Cerebral malaria carries a mortality of around 20% in adults and 15% in children. Residual deficits are unusual in adults (<3%). About 10% of the children (particularly those with recurrent hypoglycemia, severe anemia, repeated seizures and deep coma), who survive cerebral malaria may have persistent neurological deficits.

Key words:

Severe malaria ,Plasmodium falciparum , cerebral malaria , coma .

References:

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