MICROBIOLOGY
TEAM 432

Lecture (6)

cerebral malaria

Color guide:

- Very important
- Additional information
- Male doctor’s notes
- Female doctor's notes

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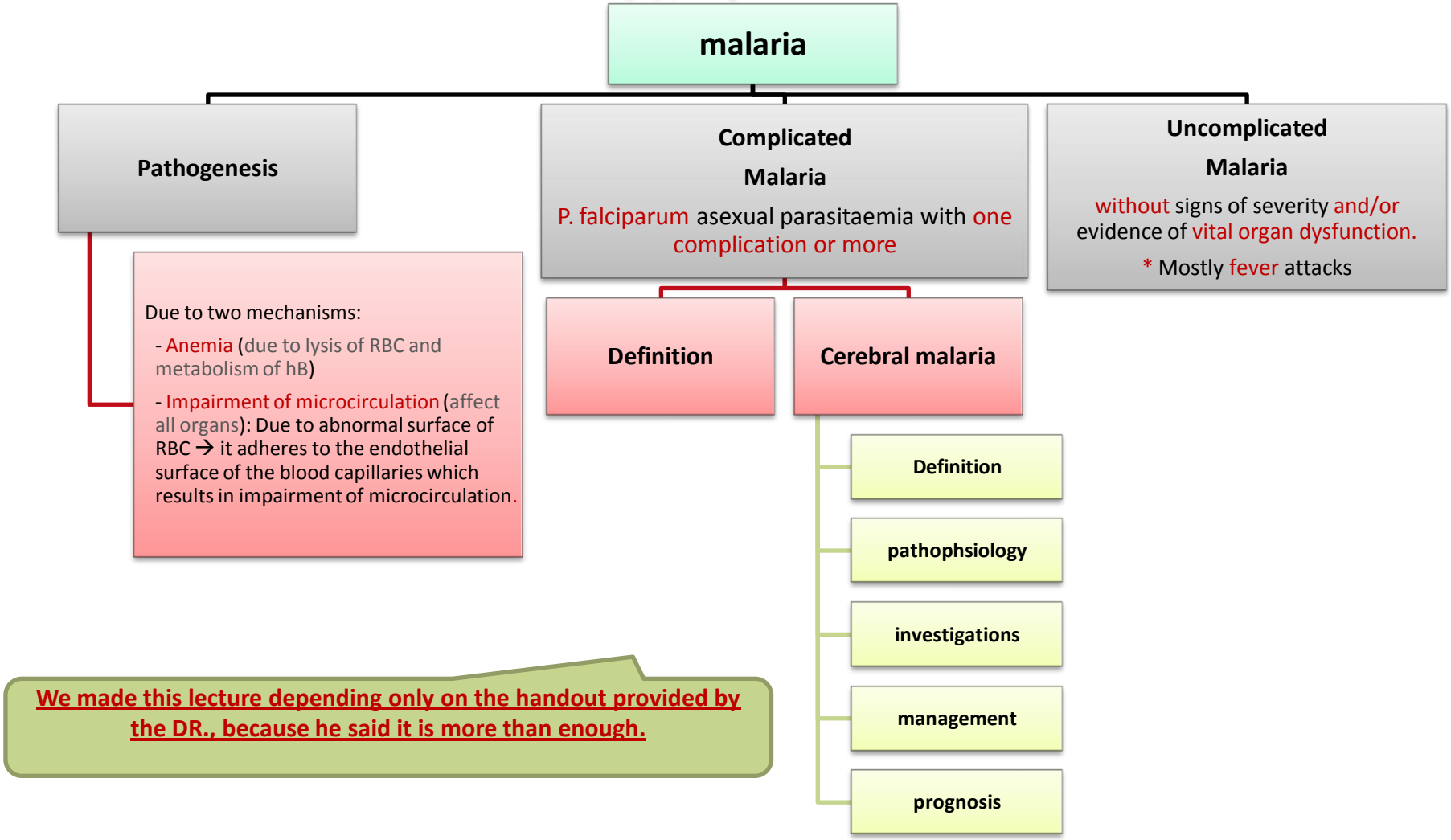
Objectives:

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.

Mind map



We made this lecture depending only on the handout provided by the DR., because he said it is more than enough.

Severe malaria (complicated) :

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

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

Cerebral malaria :

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 :

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.

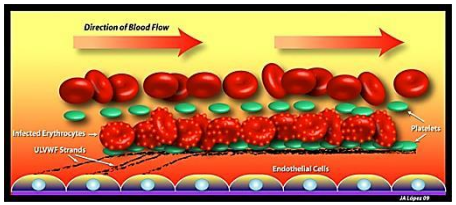
Pathophysiology:

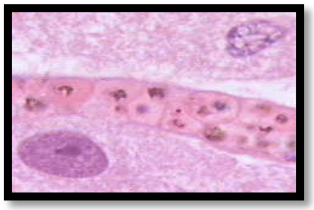
Cerebral malaria is the most important complication of falciparum malaria. However, its pathophysiology is not completely understood.

1- The basic underlying defect seems to be clogging of the cerebral microcirculation by the parasitized RBC.

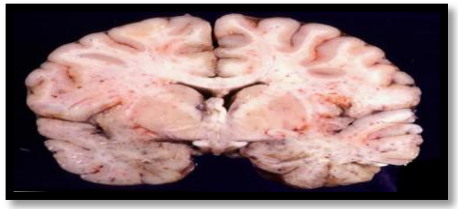
These cells undergo changes on their surface → that give them ↑cytoadherent properties, → they tend to adhere to the endothelium of capillaries and venules → sequestration of the parasites in these deeper blood vessels. Also, rosetting of the parasitized and non-parasitized red cells and decreased deformability of the infected RBC→ further increases the clogging of the microcirculation.

- It has been observed that the adhesiveness is greater with the mature parasites.
- 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.





Affected RBC adhere to endothelial lining due to their surface changes so they cause blood flow blockage



Small hemorrhages (petechial hemorrhages) in the capillaries

Pathophysiology .. Cont.

2- increased lactate production

Obstruction to the cerebral microcirculation → 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.

3-mild increased Vascular permeability

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

4- coma

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 NO 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 (muscle) 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.
•Convulsions are common before or after the onset of coma; they are significantly associated with morbidity and sequelae

Management: "NOT IMPORTANT"

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 2hrs , 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

Treatment important

consciousness	Impaired consciousness	Non impaired consciousness
	Supportive care	Treat complication
Drug route	Parentally	Orally. If not possible (patient can not swallow) → parentally.
Anti-Malarial drug	-Artesunate -Artemether -Quinine	

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.

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.

Dr. notes:

- **The a sexual stage (the blood stage) is the one responsible for the pathology of malaria.**
- **Severe falciparum malaria with coma (persisting for more than 30 minutes) after a seizure is considered to be cerebral malaria after other etiologies have been excluded (e.g. Hypoglycemia, Meningitis, etc.)**
- **In Sever malaria, there might be metabolic acidosis with respiratory distress due to impairment of the microcirculation**
- **It is particularly important to detect and treat hypoglycemia in any child with impaired consciousness.**
- **All children should have a lumbar puncture to exclude meningitis, If lumbar puncture is not possible patient should be treated for meningitis**
- **Convulsion is sign of severity**
- **Meningitis is a common co-infection of malaria**
- **Uncomplicated malaria has no organ involvement**

summary

- **Malaria can be complicated (with involvement of an organ) or uncomplicated (without involvement of an organ)**
- **Complications of malaria are caused by decreased oxygen supply to the tissues due to impairment of micro circulation and anemia**
- **Cerebral malaria is a complicated malaria caused by Plasmodium falciparum where unconsciousness should persist for at least 30 min after a convulsion after excluding other causes.**
- **The basic underlying defect seems to be clogging of the cerebral microcirculation by the parasitized RBC.**
- **other pathophysiological changes are coma, mild increase in the vascular permeability, and increased lactate production.**
- **Most cases will present in unurousable coma, abnormal eye movements, muscles abnormalities and convulsion.**
- **Hypoglycemia and meningitis have to be excluded.**
- **CSF analysis and Lumbar puncture is very important for diagnosis.**
- **Anti-Malarial dugs are used for treatment either parentally or orally.**

Questions

A. A patient came with cerebral malaria and has a positive blood film(thin blood smear test) , what examination would you perform ?

(this question was asked by the doctor)

1. CT. scan
2. Antimalaria AB .
3. MRI.
4. CSF analysis.

thick and thin blood smears to determine whether you have malaria.

- **Thick blood smears** → detecting the presence of parasites.
- **Thin blood smears** → discovering what species of malaria is causing the infection.

B. A patient was diagnosed with cerebral malaria, what is the causative organism ?

1. Plasmodium ovale.
2. Plasmodium falciparum.
3. Plasmodium vivax.
4. Plasmodium malariae.

C. Which one of the following is true about cerebral malaria ?

1. raised ICT, due to increased vascular permeability
2. the patient will remain unconscious for 15 min after a convulsion.
3. CT scan of the brain will be normal.
4. There will be decreased lactate production.

Qs	Answer
A	4
B	2
C	3
D	3

D. 10-year-old male presented with signs of cerebral malaria and he is suspected to have meningitis. If you can not do a lumbar puncture what would you do?

1. Blood culture
2. CT scan
3. Treat meningitis

For any problems and suggestions please contact:

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Thank you