Chapter 9

PATHOLOGY OF MALARIA

M.G. Rajanandh,
 Dept. of Pharmacy Practice,
 SRM College of Pharmacy,
 SRM University.
OVERVIEW

- DEFINITION
- EPIDEMIOLOGY
- LIFE CYCLE
- PATHOGENESIS
- CLINICAL FEATURES
- COMPLICATIONS

- ORGAN CHANGES
  - Brain
  - Liver
  - Spleen
  - Kidneys
  - Heart
  - Lungs
  - GIT
  - Placenta

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- Liver
- Spleen
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- Placenta
DEFINITION

- This is an acute febrile illness caused by species of the genus *plasmodia*. This protozoan has 120 species.
- Infects about 100 million people at any one time globally.
- Causes 1 million deaths globally annually.
The most common pathogenic forms are:

- *P. falciparum*; is the most common specie accounting for about 95% of infections. (Tropics and subtropics)
- *P. malariae*; accounting for about 2-3% of infections (Tropics and subtropics).
- *P. ovale*; accounting for another 1-2% of infections. (rare except in West Africa)
- *P. vivax* (not seen in Africa due to lack of Duffy antigen.)
Epidemiology

- Infection by falciparum malaria - severe economic consequences.
- Globally about 1-2m death occurring annually due to falciparum malaria.
- 90% of deaths occur in sub-saharan Africa.
- Efforts to eradicate malaria has made Mosquitoes (Anopheles) resistant to DDT and plasmodium resistant to Chloroquine and Pyrimethamine.
- Manifestation of malaria varies with endemicity of the disease.
Endemicity

- The endemicity -measured by spleen rates in children <5 years of age, parasite rate and environmental features,

- Categorized as follows-

  - **Stable or holoendemic zone:** The SR is >75% and PR > 75%
  
  - **Hyperendemic/highly endemic zone:** SR & PR = 50 – 74%
  
  - **Mesoendemic zone:** SR & PR = 11 – 49%
  
  - **Hypoendemic zone:** SR & PR < 10%
Life cycle

Mosquito Stages

1. Ruptured oocyst
2. Mosquito takes a blood meal (injects sporozoites)
3. Schizont
4. Ruptured schizont
5. Human Blood Stages
6. Ruptured schizont
7. Gametocytes
8. Mosquito takes a blood meal (ingests gametocytes)
9. Microgamete entering macrogamete
10. Ookinete
11. Oocyst
12. Release of sporozoites

Sporogonic Cycle

A. Exo-erythrocytic Cycle

B. Erythrocytic Cycle

C. Human Liver Stages

- Liver cell
- Infected liver cell

- = Infective Stage
- d = Diagnostic Stage
Central to the pathogenesis and pathology of malaria is the shortening of the lifespan of the red cell.
Metabolic changes within the RBC

- Digestion of haemoglobin with utilization of glucose, oxygen and hemozoin formation.
- Hypoxia stimulating lactate formation.
- Free radical formation.
- TNF is major mediator of the changes seen in severe malaria.
Pathogenesis/Pathophysiology

- Alteration of the membrane transport system of the RBC
- Decrease deformability of the RBC and increase susceptibility to sludging and destruction
- Formation of knobs (from the rhoptery of mature schizonts) and protruberances on the RBC surface leading to formation of neo-antigens with increased immune stimulation and increased vascular stickiness (ICAM & ELAM) and cytoadherence.
- Presence of thrombospondin/CD46 which help in rosette formation.
Plasmodium falciparum

- It infects RBCs of all ages (P vivax and ovale – young, P malariae – old)
- Causes rosetting, sequestration – PfEMP1 binds to CD36, thrombospondin, VCAM-1, ICAM-1 and E selectin
- TNF, IFN-γ, IL-1 which suppress production of RBC etc
Antimalarial defence

- Evolutionary – Survival
  - Inherited alterations in RBCs-
    - HbS, HbC, lack of Duffy antigen
  - Others - βThalassaemia, G6PD, HLA Bw53 and HLA-DR
General mechanism of antimalarial defence
- Cellular and Humoral response
- Stimulation of immune response
  - Antibodies and T lymphocytes
  - Antigenic variation of PfEMP1
    - Parasite also reduces antigen presentation

Defence Mechanisms in Infants
- 1st 6 months is usually free of infection due to
  - Transplacentally acquired immunity
  - High conc of foetal Hb
  - PABA in breast milk
Clinical features

- Simple malaria
- Severe/complicated malaria
- **Severe normocytic anaemia (PCV <15%) and intense falciparum parasitaemia**
  - Rupture of erythrocytes
  - Phagocytosis
  - Complement mediated cytotoxicity
  - Raised Unconjugated Bil, Urobinogen, leukopaenia, monocytosis, thrombocytopaenia (DIC)
Complications
Splenic changes in Malaria

- Spleen is enlarged and weighs about 500g during acute attack. It is soft and diffusely pigmented.
- Upon repeated attacks the spleen is much larger and may exceed 1000g.
- Microscopically there is congestion and reticulo-endothelial hyperplasia.
- Increased phagocytic activity of macrophages
- Macrophage – engulfed parasites and RBC
- Haemorrhages and infarcts may be present.
- Spleen from patients with chronic malaria are fibrotic with foci of mineralization (Gandy-Gamna bodies)
- Brittle, thick capsule, fibrous trabeculae
Tropical Splenomegaly Syndrome (HIMSS)

- Characterized by large spleen >1000g
- Moderate anaemia,
- High IgM level
- Liver sinusoidal lymphocytosis.
- Chronic low-grade malarial infection
Liver changes in Malaria

- Liver is enlarged and has a slatey-gray appearance (hemozoin staining).
- Kupffer cells are enlarged and contain malarial pigment, parasites and parasitized RBC.
- Pigments are also found in parenchymal cells.
- The sinusoids and other vessels are usually congested. Focal areas of fatty change may be seen.
BRAIN

- Cerebral oedema/congestion with pink appearance of the brain.
- Petechiae in white matter
- Features of raised intracranial pressure (grooving of uncal gyrus).
Microscopic features

- Capillaries and venular congestion filled with parasitized RBC
- Blockage of blood vessels by parasitized RBCs
- Ring haemorrhages are characteristic.
- Durks granuloma.
Figure 3.19 is a low power view of the areas of haemorrhage.
Kidney Changes in Malaria

- Slightly enlarged
- Malarial pigments in the glomeruli.
- The cortico-medullary capillaries show parasitized RBCs and haemoglobin in tubules.
- Acute tubular necrosis and Acute renal failure.
- Quartan malarial nephropathy can occur in P. malariae infestation.
- Blackwater fever
Heart

- The heart may be dilated & flabby
- There is pericardial/endocardial petechiae and congested capillaries containing parasitized RBC.
- Focal hypoxic lesions
- Focal interstitial infiltrates of the myocardium
Lungs

- The lungs are congested and oedematous with occasional parasitized erythrocytes in pulmonary capillaries.
- Fibrin may be deposited in alveoli resulting in shock lung or ARDS.
GIT

- Oedematous
- Congested
- Focal/diffuse haemorrhage.
- Small vessels of the intestinal mucosa contain parasitized RBC
- Massive sequestration and parasitisation of the GIT is sometime associated with vasomotor collapse resulting in the clinical syndrome of Algid malaria.
Malaria and Pregnancy

- Malaria increases chances of foetal loss, pregnancy associated anaemia, IUGR and labour complications.
- The placenta bed is markedly parasitized.
- In active disease - massive parasitization of the intervillous space.
- Old infection - peri-villous fibrosis and hemozoin deposition. Hemozoin takes some weeks to clear.
Parasitized RBC in placenta (IVS)
Diagnostic Pathology

- Thick blood film helps in determining the density of infestation.
- Thin film for specie determination.
Other Issues in Malaria

- Congenital Malaria
- Chloroquine resistant malaria
- Control/eradication of malaria
- Newer diagnostic techniques
- National Policy on Malaria
- National treatment guideline