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Please read this section first

The HPCSA and the Med Tech Society have confirmed that this clinical case study, plus your routine review of your EQA reports from Thistle QA, should be documented as a "Journal Club" activity. This means that you must record those attending for CEU purposes. Thistle will not issue a certificate to cover these activities, nor send out "correct" answers to the CEU questions at the end of this case study.

The Thistle QA CEU No is: MTS 18/059

Each attendee should claim ONE CEU point for completing this Quality Control Journal Club exercise, and retain a copy of the relevant Thistle QA Participation Certificate as proof of registration on a Thistle QA EQA.

DIFFERENTIAL SLIDES LEGEND

CYCLE 52 SLIDE 5

Plasmodium Falciparum

Plasmodium falciparum is a protozoan parasite, one of the species of Plasmodium that cause malaria in humans. It is transmitted by the female Anopheles mosquito. This species causes the disease's most dangerous form, malignant or falciparum malaria. It has the highest complication rates and mortality. Around the world, malaria is the most significant parasitic disease of humans and claims the lives of more children worldwide than any other infectious disease.

Pathogenesis

P. falciparum works via sequestration, a distinctive property not shared by any other Plasmodium. Within the 48-hour asexual blood stage cycle, the mature forms change the surface properties of infected red blood cells, causing them to stick to blood vessel walls (cytoadherence). This leads to obstruction of the microcirculation and results in dysfunction of multiple organs such as the brain in cerebral malaria.

Complicated malaria occurs more commonly in children under age five and sometimes in pregnant women. Women become susceptible to severe complicated malaria if infected by P. falciparum during their first pregnancy even if they live in hyper endemic areas. Susceptibility to severe malaria is reduced in subsequent pregnancies due to increased antibody levels against variant surface antigens that appear on infected erythrocytes.

Life Cycle

Infection in humans begins with the bite of an infected Anopheles mosquito. Plasmodium sporozoites released from the salivary glands of the mosquito enter the blood stream during feeding, quickly invading liver cells. The immune system clears the sporozoites from the circulation within 30 minutes.

During the next 14 days the liver stage parasites differentiate and undergo asexual reproduction, producing up to 40 000 merozoites that burst from the hepatocyte. The process of bursting red blood cells does not have any symptoms, but destruction of the cells does cause anaemia. When red blood cells rupture, hemozin wastes cause cytokine release, chills and then fever.

P. falciparum trophozoites develop sticky knobs in red blood cells which then adhere to endothelial cells in blood vessels, thus evading clearance in the spleen. The adhering red blood cells may cause cerebral malaria by preventing oxygenation of the brain. Symptoms of cerebral malaria include impaired consciousness, convulsions,

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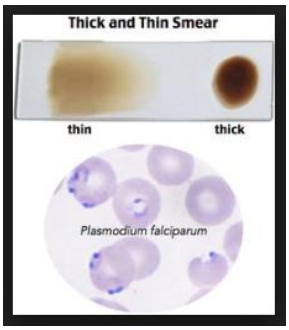
neurological disorder and coma. Additional complications from P. falciparum –induced malaria include advanced immunosuppression.

Individual merozoites invade red blood cells and reproduce, producing 12-16 merozoites within a schizont. The length of this erythrocytic stage depends on the parasite species - an irregular interval for P. falciparum.
The clinical manifestations of malaria, fever and chills are associated with the synchronous rupture of the infected erythrocytes. The released merozoites invade additional erythrocytes. Not all of the merozoites divide into schizonts, some differentiate into sexual forms, male and female gametocytes. These gametocytes are taken up by a female Anopheles mosquito during a blood meal. Within the mosquito midgut, the male gametocyte undergoes a rapid nuclear division, producing eight flagellated microgametes that fertilize the female macrogamete. The resulting ookinete traverses the mosquito gut wall and encysts on the exterior of the gut wall as an oocyst. Soon the oocyst ruptures, releasing hundreds of sporozoites into the mosquito body cavity, where they eventually migrate to the mosquito salivary glands.

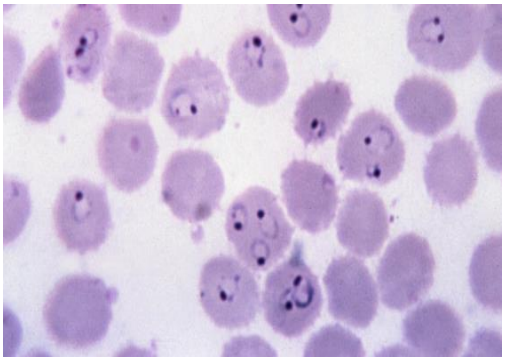
Because fusion of the gametes, zygote formation and meiosis must occur in the mosquito gut for the parasite to complete its life cycle, P. falciparum is an obligate sexual organism. It is often self-fertilizing. Its population structure appears to predominantly reflect inbreeding.

Microscopic Appearance

The preferred method to diagnose malaria and identify the species of Plasmodium is by microscopic examination of a blood film. Each species has distinctive physical characteristics. In P. falciparum, only early (ring-form) trophozoites and gametocytes are seen in the peripheral blood. It is unusual to see mature trophozoites or schizonts in peripheral blood smears, as these are usually sequestered in the tissues. The parasitized erythrocytes are not enlarged and it is common to see cells hosting more than one parasite. On occasion, faint, comma-shaped, red dots called “Mauer’s dots” are seen on the red cell surface. The comma-shaped dots can also appear as pear-shaped blotches.



Blood smears of P. falciparum



P. falciparum in erythrocytes

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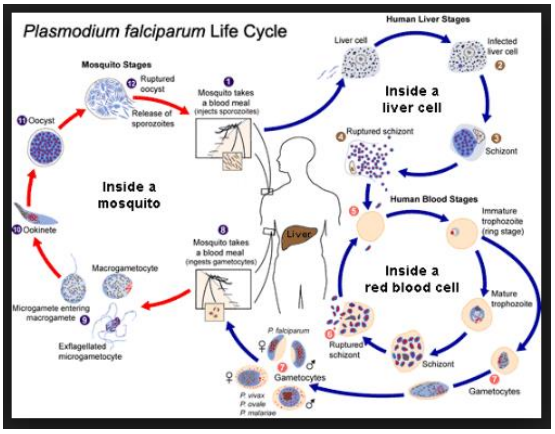

P. falciparum Life cycle

Treatment

Uncomplicated Malaria:

Artemisinin-based combination therapies (ACT's) are the first line antimalarial treatment for uncomplicated malaria caused by P. falciparum. The following ACT's are recommended:

- Artemether plus lumefantrine
- Artesunate plus amodiaquine
- Artesunate plus mefloquine
- Artesunate plus sulfadoxine-pyrimethamine
- Dihydroartemisinin plus piperaquine
-

The choice of ACT is based on the level pf resistance to the constituents in the combination. Artemisinin and its derivatives are not appropriate for monotherapy. As second-line antimalarial treatment, when initial treatment does not work, an alternative ACT known to be effective in the region is recommended such as:

- Artesunate plus tetracycline or doxycycline or clindamycin
- Quinine plus tetracycline or doxycycline or clindamycin

Severe Malaria:

In severe falciparum malaria, rapid clinical assessment and confirmation of the diagnosis is recommended followed by administration of full doses of parenteral antimalarial treatment without delay with whichever effective antimalarial is first available. Intravenous or intramuscular artesunate is recommended. Quinine is an acceptable alternative if parenteral artesunate is not available.

References

1. http://em.wikipedia.org/wiki/Plasmodium_falciparum

Questions

1. Name the mosquito that transmits P. falciparum
2. What are the symptoms of cerebral malaria?
3. What is the first line antimalarial treatment for uncomplicated malaria caused by P. falciparum?