Plasmodium falciparum

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Introduction

Plasmodium falciparum is a protozoan parasite that causes the most severe form of malaria and results in most Plasmodium fatalities in humans [1]. The female *Anopheles* mosquito is the main vector that can transmit this parasite to humans by penetrating the skin during a blood meal [2]. Distinct features of this organism can be examined under the microscope of a blood smear as it is the only *Plasmodium* species where its gametocytes take the shape of a banana. *Plasmodium falciparum* is responsible for causing cerebral malaria, severe anemia, metabolic acidosis, acute lung edema, acute kidney failure, and liver failure [1]. Malaria is most commonly

found in less developed countries around Africa, South East Asia, and the Pacific, which attribute to millions of deaths each year [3].

Appearance and Mode of Transmission

Plasmodium falciparum takes many forms during its life cycle and can be seen under the microscope in infected patient blood smears [4]. A common form this parasite takes while in the red blood cells is the ring form which has a cytoplasm stained blue with a red dot nucleus. The trophozoite form is similar to the ring form but is slightly larger and more vacuolated. Schizonts appear about two thirds the size of a red blood cell and contain many merozoites arranged in berry looking clusters in the cytoplasm. Gametocytes are almost twice the size of a red blood cell and are banana-shaped with spear ends. Sporozoites, the infective form to humans, are often crescent shaped and can move by peripheral fibers around it.

Transmission of *Plasmodium falciparum* malaria occurs when an infected female *Anopheles* mosquito with sporozoites bites a person [4]. Organ transplants, blood transfusions, and mother to fetus transmission can also spread this disease to healthy individuals. Once a person is infected with the sporozoites they travel to the liver cells and after a couple of weeks travel to the bloodstream [2]. The ruptured sporozoites release merozoites into healthy red blood cells where they turn into trophozoites and eventually schizonts. These schizonts eventually release merozoites when an infected red blood cell ruptures spreading to healthy red blood cells further spreading the infection.

Life Cycle and Symptoms

The *Plasmodium falciparum* life cycle is complex and involves a human intermediate host along with a mosquito definitive host [4]. The life cycle starts when a female *Anopheles*

mosquito takes a blood meal injecting sporozoites into the blood capillaries of a human. Inside the human, the sporozoites travel and infect liver cells where they asexually reproduce turning into trophozoites to eat on the cytoplasm. Within a couple of days, the trophozoites turn into schizonts that mature and rupture infective liver cells releasing thousands of merozoites into the bloodstream infecting old and young red blood cells. Inside the red blood cells, the merozoites turn into trophozoites that eat hemoglobin. The trophozoites proliferate and turn into schizonts that rupture red blood cells and spread to other healthy red blood cells. After a couple of erythrocytic schizogony cycles, the merozoites turn into female and male gametocytes. When a mosquito comes to take a blood meal again the gametocytes are ingested where the sexual reproduction cycle occurs. The male small gametocytes are attracted to the female small gametocytes within the mosquito where the male fertilizes the female to form zygotes. These zygotes eventually mature to form oocysts which contain sporozoites that eventually are released when the oocyst ruptures. The sporozoites migrate towards the salivary glands of the mosquito where they wait to be injected into a human to start its life cycle again.

Symptoms from severe malaria caused by *Plasmodium falciparum* can result in cerebral malaria, respiratory issues, kidney failure, and severe anemia [2]. In cerebral malaria, which accounts for the majority of deaths in infected *Plasmodium falciparum* patients can result in death if left untreated. It takes about two weeks for infected patients to feel symptoms of headaches, restlessness, muscle aches, and fever which can weaken the immune system. Some symptoms like diarrhea and vomiting are rare but can occur in more severe cases. A unique type of hemoglobinuria called blackwater fever can also be present in infected individuals as it makes urine appear black.

The Discovery of Blackwater Fever

During World War II fears of developing malaria in Greece were common [6]. One of the most severe types was developing blackwater fever which would cause renal failure and major hemolytic anemia in soldiers. Soon it was discovered that when quinine therapy was not available in Greece, then the disease would vanish. It was later discovered that the disease resulted from soldiers developing antibodies to the quinine drug, resulting in blackwater fever symptoms. Eventually, quinine was replaced with chloroquine leading to lower cases of this disease and overall improvement.

Statistics and Diagnosis of Malaria

In 2002, there were more than 515 million cases of *Plasmodium falciparum* malaria cases around the world [3]. Most cases of this disease occur in African countries; however, close to 25% of cases were reported in South East Asia. Regions with significant populations at risk include Africa with 521 million, South East Asia with 1,313 million, and Western Pacific with 142 million people. *Plasmodium falciparum* in sub-Saharan Africa is responsible for roughly more than 1 million deaths each year mostly in kids [2]. Interestingly, pregnant women are more at risk of developing life-threatening anemia from *Plasmodium falciparum*. This form of malaria can have fatal consequences on the fetus often resulting in death or birth defects.

Diagnosing malaria is usually accomplished by examining a peripheral thick and thin blood smear sample stained with Giemsa from an infective patient under a microscope [1]. Positive infections of malaria can be made when a lab tech can see ring forms of *Plasmodium falciparum* and the banana-shaped gametocytes on the peripheral of the blood cells [4]. It is important to view the *Plasmodium falciparum* blood smears between 24 and 48 hours and is crucial in identifying infective ring forms. It is generally considered a good procedure to view about 300 fields of the slide with an oil immersion lens to determine the severity of the infection

[2]. Other more expensive means of testing for malaria include nucleic acid sequence-based amplification and PCR testing. These molecular tests are more sensitive and reliable but are only available in wealthy countries. There is also the convenience of rapid diagnostic tests that look for specific antibodies produced by reactions with the *Plasmodium falciparum* parasite. The presence of antibody resistance to the lactate dehydrogenase and histidine-rich protein 2 of the parasite can indicate reliable positive infections. Chest X rays and CT scans may also help diagnose this disease if cerebral and respiratory issues are present. In addition to all of these tests, complete blood counts can be used to identify symptoms of severe malaria. For example, a low hematocrit result can often result from anemia caused by *Plasmodium falciparum*.

Treatment

The deadliest form of malaria, *Plasmodium falciparum* has built resistance to chloroquine making it more difficult to treat than other species [1]. People who do not take prophylactics when traveling to endemic areas may end up with a severe case of malaria. Antimalarial drugs used to combat this infection include quinine and derivatives of artemisinin such as artesunate. In the hospital, patients can be treated with these drugs through intravenous therapy, and patients can usually recover within two weeks [2]. Oral drugs may also be given when the patient is well enough such as quinine tablets to prevent relapse. In addition to treatments, prevention of this disease can be accomplished by taking prophylactic drugs before entering infective areas. Wearing pants and long-sleeved shirts along with using mosquito repellants during dawn and dusk can also help. An effective vaccine for malaria hasn't been developed yet, but with recent findings and development, one may soon be available.

Case of Sudden Splenic Rupture

A 74-year-old man came to the emergency department experiencing periods of fever along with nausea, vomiting, and body aches [5]. The patient noted that he lived in a region where malaria was endemic and had been infected before without issues and recovered. Upon examination of the patient a complete blood count was performed and revealed a low hemoglobin value of 11.5 g/dL. To check for malaria, a peripheral blood smear was ordered and the lab technicians identified the parasite as *Plasmodium falciparum*. High parasitemia was noted with over 1000 parasites per 200 white blood cells per high power field. As a result, the elderly patient was admitted to the intensive care unit to be treated. He was treated with an intravenous solution of an artesunate-based medicine on which he recovered within 3 days and was moved to a regular ward. Upon staying in the general ward over the next 5 days the patient experienced abdominal pain along with vomiting. A CT scan was ordered and images showed splenic lacerations and hematoma as a result of sudden splenic rupture. Splenectomy was performed on the patient and after 7 days he was discharged from the hospital recovered and well.

Conclusion

Not all patients such as this one recover well. As the deadliest parasitic disease in the world, malaria is responsible for millions of deaths each year. *Plasmodium falciparum* is the deadliest species that can cause severe malaria and results in most of the deaths contributed to the disease. The *Plasmodium falciparum* life cycle is complex and thrives by using the female Anopheles mosquito as a vector. This disease is serious and can cause cerebral issues with anemia resulting in a coma and death if left untreated. The resistance to traditional anti-malarial drugs for severe malaria is troubling and prevents current treatments from being effective. As technology and resources advance, the outlook for a vaccine for malaria is high and may prevent millions of deaths each year.

References

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