Malaria

Malaria is a parasitic disease spread by the Anopheles mosquito, resulting in a severe and potentially fatal illness that represents a major global health concern. Annually, approximately two billion individuals are at risk of contracting malaria, which affects populations in 90 endemic nations and 125 million travelers. The disease is responsible for an estimated 1.5 to 2.7 million fatalities each year. The Plasmodium parasite undergoes a complex multistage lifecycle, which is associated with distinct cyclical fevers. With appropriate and timely medical intervention, most patients can expect a swift alleviation of symptoms; however, serious complications may arise, such as cerebral malaria, severe malarial anemia, coma, or even death.[1] The choice of preferred antimalarial treatment and preventive measures is influenced by factors such as the specific species involved, geographical location, drug susceptibility, and the demographics of the patient. Additionally, latent or reactivated infections may occur years after initial exposure.[2,3]

Five species of Plasmodium are known to infect humans: P. falciparum, P. ovale, P. vivax, P. malariae, and P. knowlesi. The female Anopheles mosquito acquires gametes during a blood meal, which subsequently develop into sporozoites that multiply in the mosquito's gut. During later blood meals, these sporozoites are injected into the bloodstream of a human host through the mosquito's saliva. Within an hour, the sporozoites migrate to the liver, penetrate hepatocytes, and undergo rapid division to produce merozoites. In the course of an active infection, these organisms re-enter the bloodstream and invade red blood cells. Inside the erythrocytes, Plasmodium species consume hemoglobin and progress from immature trophozoites (ring stage) to either mature trophozoites or gametocytes. Mature trophozoites replicate, forming schizonts, which disrupt the integrity of the erythrocyte cell membrane, leading to adherence to capillary endothelium and subsequent cell lysis.[4,5,6]

The release of free heme into the peripheral blood triggers endothelial activation. If left untreated, malaria can persist for a duration of 2 to 24 months. Infections caused by P. vivax and P. ovale may exhibit a phenomenon known as "dormant schizogony," where inactive intrahepatic parasites (hypnozoites) remain dormant until they reactivate after months or even years. While hypnozoite development is not typically observed in cases of P. falciparum and P. malariae infections, there have been rare instances of resurgent P. falciparum infections occurring years after the initial exposure.[1,2]

The pathogenesis of malaria is associated with the secretion of toxins that induce IFN-gamma and TNF-alpha. The innate immune response is primarily characterized by the phagocytic activity of monocytes and macrophages within the splenic red pulp. The adaptive immune response is facilitated by the class switching of CD4-positive lymphocytes, induced by IFN-gamma and TNF-alpha. Additionally, TNF-alpha suppresses hematopoiesis, contributing to the development of anemia. The liver and spleen undergo enlargement, resulting in significant splenomegaly.[7] Reduced levels of arginine, diminished nitric oxide, and increased arginase activity have been noted in cases of severe malaria within peripheral blood. Research indicates that the arginase enzyme produced by the parasite may play a role in the depletion of arginine in critically ill patients, thereby hindering nitric oxide synthesis. A deficiency in nitric oxide can subsequently result in pulmonary hypertension and increased myocardial wall stress, particularly in pediatric patients. Consequently, treatments involving peripheral arginine or inhaled nitric oxide may be considered.[3,4,8] The degree of parasitemia influences the onset and intensity of symptoms: in naïve individuals, symptoms generally manifest at a parasitemia level of 0.002%, while previously exposed individuals may experience symptom onset at 0.2% parasitemia. Severe infections are typically characterized by parasitemia levels reaching 5%.[8]

References

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