

Effects of Leishmania Species on Immune Response Against Malaria Parasite in Malaria Leishmania Coinfections

Abstract

Both Malaria and leishmania are most widespread protozoan parasitic diseases, certainly in tropical countries of the world. Malaria leishmania coinfection is common in leishmaniasis endemic areas which is mostly endemic to malaria too.

Researchers notice that in cases of malaria leishmania coinfection, leishmania species find to some extent the outcome of malaria infection, but also behavior of malaria parasite species play a significant role to figure the consequences of it. While *L. donovani* protect from severe malaria complications by suppression of major histocompatibility class II, so it diminishes the clinical severity of malaria but not malaria parasite density due to dysfunction of major histocompatibility class I, which is controlled by the suppressed one. In another side *L. mexicana* tends to sequester in macrophages and lead to severe clinical outcomes when it coexisted with malaria parasite at the same host.

Leishmania infection is excluded when studies aim to assess the immune response to only malaria parasite, experimental studies required involving different species of malaria and leishmania.

Keywords: Malaria, Leishmania, *L. donovani*, *P. falciparum*, *L. mexicana*, *P. yoelii*, Malaria leishmania coinfections.

Introduction

Malaria infection has an extremely changeable clinical phenotype, varying from a mild febrile sickness to life-threatening severe anaemia, acidosis and end-organ failure, even between persons with slight or no acquired anti-malarial immunity. In part this is clarified by heritable dissimilarities in vulnerability to malaria infection or parasite propagation recognized to be governed, among others, by red blood cell and haemoglobin polymorphisms.

Current data have also started to propose that there are variations in virulence among parasite genotypes which are clear as variable in vivo growth rates, with those that raise most rapidly being related with severe disease outcomes. But, it is also noticeable that quantitative and qualitative disparities in the nature of the anti-malarial immune response have deep influences on disease development and last outcome. A number of these discrepancies may turn out also to have a genetic basis, polymorphisms in a number of immune response genes have previously been hesitantly connected to vulnerability to malaria in humans and in rodent models, but it is also the case that environmental influences – linked to the occurrence and density of malaria infection; co-infection with viruses, bacteria and other parasites; dietary condition and so on –

may also considerably alter the immune response and thus the clinical outcome of malaria infection [1].

Leishmaniasis and malaria are between the most significant six diseases on the World Health Organization (WHO). There are two million fresh cases of Leishmaniasis diagnosed annually. While for malaria, 300–660 million people become infected annually with the *Plasmodium falciparum*, and 200–300 kids are dying each hour from it . Consistent with the world malaria report 2016, there were about two hundreds and twelve million cases of malaria and 429,000 mortalities.[2].

Cutaneous Leishmaniasis and Malaria (CL) are co-endemic in wide regions in tropical areas and co-infection may influence evolution of host-parasite interactions. Study done by Pinna Raquel A et al showed that ; In Malaria-Cutaneous Leishmaniasis Co-infection, reduced concentrations of IFN- γ , TNF, IL-6, and IL-10 noticed in the serum of co-infected groups, signifying modulation of Malaria immune response by *Leishmania* co-infections, noticed a strong thymic atrophy in Py single-infected and co-infected groups, which improved earlier in co-infected animals. The CD4 and CD8 T cell profiles in thymus, spleens and lymph nodes did not differ between Py single and co-infected groups, except for a diminish in CD4⁺CD8⁺ T cells which also augmented quicker in co-infected mice. Malaria ending distorted in proportion to the *Leishmania* specie concerned. Malaria infection reduced the harshness or postponed the onset of leishmanial lesions. These changes in Malaria and CL development seem intimately linked with alterations in the immune response as demonstrated by change in serum cytokine concentrations and thymus/spleens T cell phenotypes dynamics throughout infection [3].

In regions where malaria is co-endemic with visceral leishmaniasis (VL), co-infections with both diseases are frequent [4].

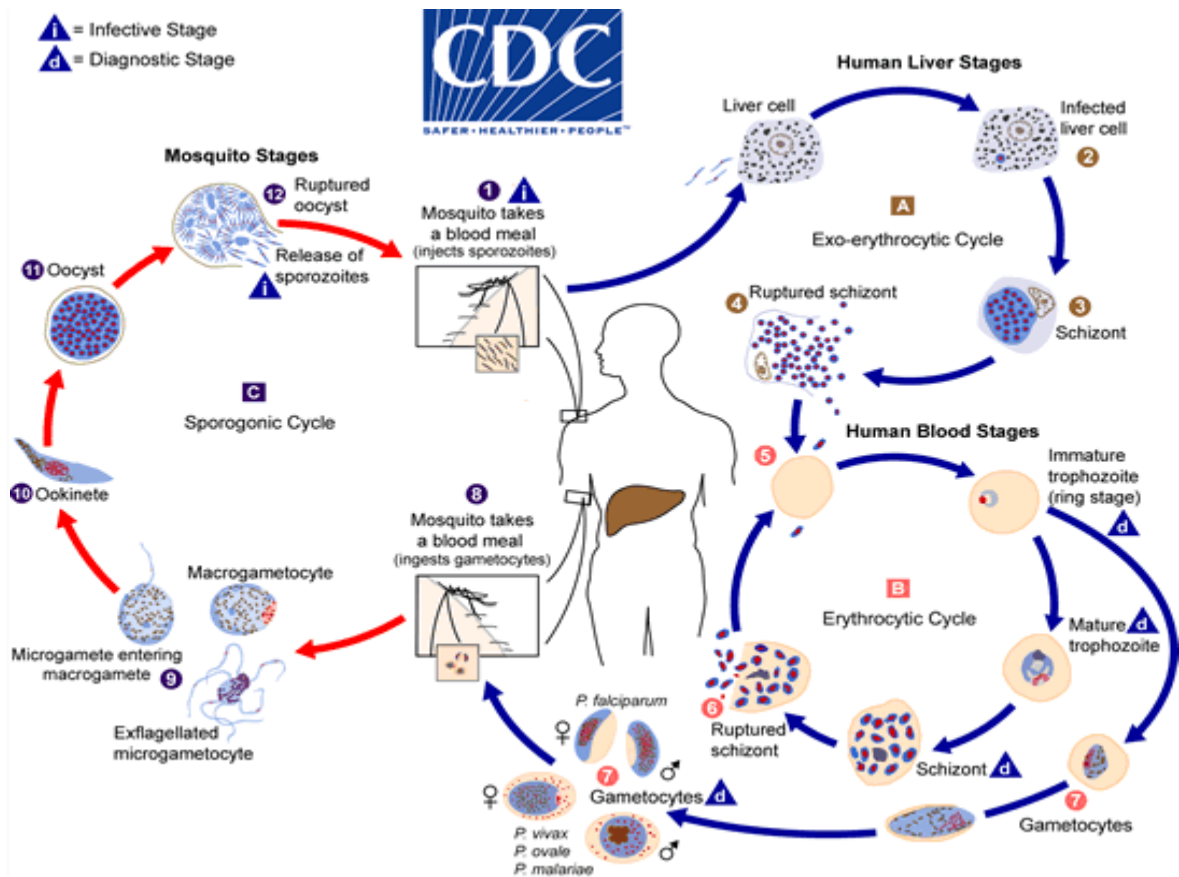


Figure (1): Shows life cycle of malaria parasite

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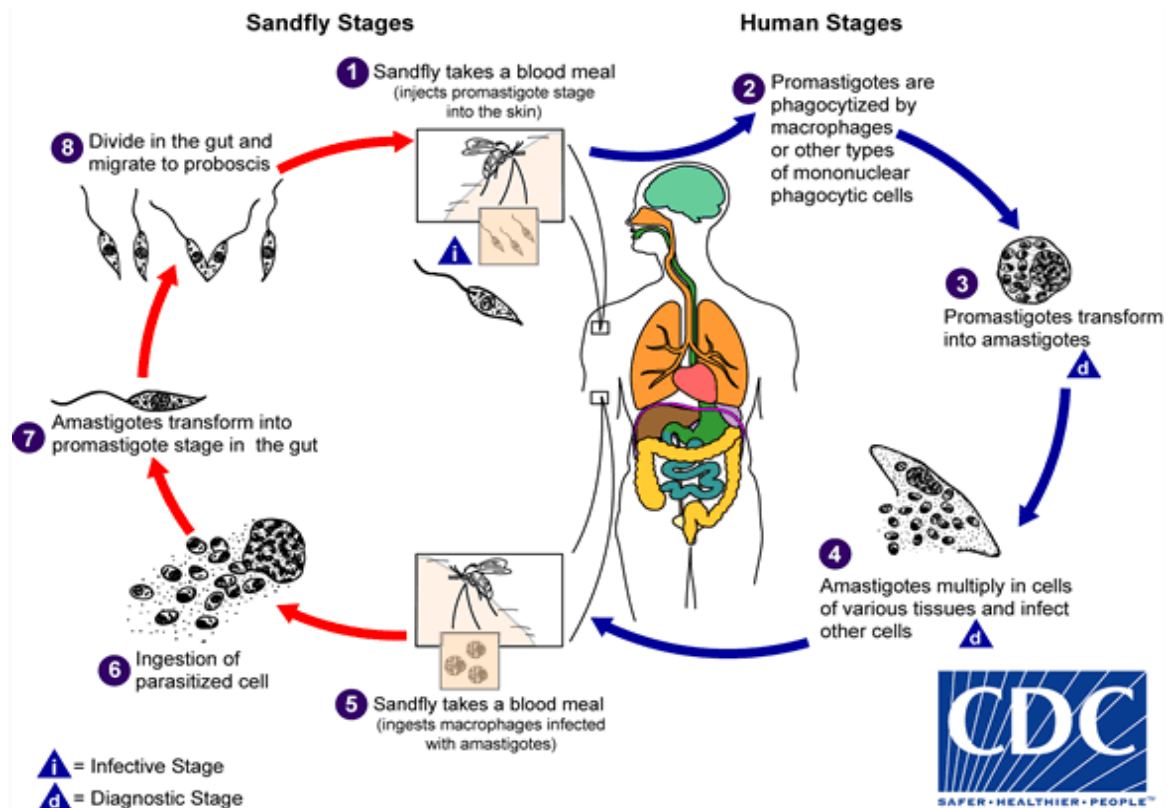


Figure (2): Life cycle of leishmania parasite

Discussion

Study done by van den Bogaart, E. Et al established that; The capacity of *L. donovani* and *P. falciparum* to jointly interrelate at the immunological point. Progressive polarization towards type-1 and pro-inflammatory cytokine models characterized the co-infected patients, whose response partially echoed the influence elicit by VL (IFN- γ , TNF) and malaria (IL-2, IL-13), and moderately resulted from a synergistic interface of the two diseases upon each other (IL-17A). Considerably decreased levels of *P. falciparum* parasitaemia were identified in the co-infected group as opposite to the malaria-only patients, suggestive of either a defensive or a non-detrimental effect of the co-infection against *P. falciparum* infection [5], signifying suppression of MCH class II expression by *L. donovani* [6]. Study done by Tania Gourley showed that; Class II transactivator (CIITA) recognized as a co-activator for MHC class II gene expression in antigen-presenting cells. Unexpectedly, when *CIITA*^{-/-} CD4 T cells were activated in existence of IL-12, they formed not only IFN γ but also high levels of IL-4. The IL-4 generation is owing to the buildup of IL-4 gene transcripts in Th1 cells. This transcriptional regulation is noticed in T cells differentiating to the Th1 but not Th2 lineage, reliable with induction of expression of the *CIITA* gene in T cells by IFN γ . Thus, as well as its role in transactivation of genes concerned in antigen presentation, CIITA has a significant task through the T cell differentiation by negatively regulating the IL-4 gene transcription [7]. Study done by Elhussein AB showed that; increase of serum IL-4 in Sudanese children suffering from *Plasmodium falciparum* malaria linked with severity of malaria hyperparasitaemia and not with severity of the disease [8], IFN-gamma up-controls

MHC class I expression and antigen processing and presentation on cells [9]. Owing to Class I MHC molecules span the membrane of about all cells (including erythrocytes) in an organism, while class II molecules limited to cells of the immune system named macrophages and lymphocytes [10]. consistent with the above mentioned details we can suggest the mechanism offered by *L. donovani* to give to induce protective action against severe falciparum malaria , also we suggest that tendency of *L. donovani* to sequester insides internal organs decrease sequestration of *P. falciparum* schizonts in capillaries of that vital internal organs.

Study done by Russell E. Coleman et al showed that; interfaces between *Leishmania mexicana* and *Plasmodium yoelii* tested in BALB/c mice. Percentage of erythrocytes infected with *P. yoelii* and width of footpad lesions reasoned by *L. mexicana* were the criterion accustomed to assess for disease severity. *L. mexicana* and *P. yoelii* infections were each considerably enhanced in dually infected mice when contrasted to mice infected with either parasite only. Death rates because of the normally nonlethal *P. yoelii* raised during concurrent infections [11], suggested owing to sequestration of leishmania amastigote antigens from presentation [6].

Conclusion :

Malaria and leishmaniasis co-infection is frequent , especially in leishmaniasis endemic area , and in case of research on evaluation of immune response against malaria parasite or studies aim to check the immunobiology of malaria among inhabitants of that areas , recommended to exclude leishmania parasite to get precise results.

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