Co-infection with syphilis and malaria: immune deterioration on CD4+

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Abstract

Syphilis is a well-known sexually transmitted disease found around the world. Malaria and syphilis are endemic in many regions of the world, and co-infection with the two pathogens is common. Here, the author used a new pathway ontology technology to predict the pathway of CD4+ suppression in an episode of co-infection. Of interest, the author found that there are some immune suppression processes that can be found both in syphilis and malaria. The mentioned processes are inhibiting interleukin-2 secreted by CD4+ and nitric oxide production. In the co-infection, the synergy to increase the immune suppression can be expected.

Keywords
Syphilis, Malaria, Function, CD4+ suppression

Introduction

Syphilis is a well-known sexually transmitted disease that can be detected around the world. Malaria and syphilis are endemic in many regions of the world, and co-infection with the two pathogens is common (1). The interaction between both infections within a co-infection episode is an interesting topic in infectious medicine and becomes a new interesting research topic. N’Gom et al found that HIV-2 infection that was co-infected with syphilis was associated with a further lowering of CD4+ count, suggesting a worse suppression of the immune system while co-infection with malaria is associated with a modest immune disturbance (2).

The hypothesis/Ideas

Indeed, syphilis poses the nature of immune suppression that leads chronicity (3). Similar, immune suppression by malaria is also noted (4). Long-term immunity to malaria infection may be affected by an IFN-gamma-mediated depletion of malarial-specific CD4+ T cells during infection (5). Due to the nature of cellular immunity suppression, there might be some common pathway between the two infections. During the co-infection, the synergistic effect between each other can be expected. However, there is no previous work to verify this hypothesis. A study on the expression pathway by creating of systemic network in an episode of co-infection is warranted.

Evaluation of the hypotheses/Ideas

To study the interaction between both infections, the new development in bioinformatics can be applied. Here, the author used a new gene ontology technology to predict the pathway of CD4+ suppression in an episode of co-infection. The author used Pubmed, Scopus, CAS, and Google
Scholar search databases to find the documents proposing the pathway for CD4+ suppression in both malaria and syphilis. Then the interactions among the pathways are searched. The creation of network map based on in silico systemic biology technique is performed. This technique is a standard and reliable in modern biology (6,7). The final resulted interaction map is then created.

**Experimental data**

Derived mechanisms (8-15) for CD4+ suppression in malaria and syphilis are presented in Table1. The final resulted interaction map is presented in Figure1. The common pathway for CD4+ suppression is presented in Figure2.

**Discussion/Conclusion**

New developments in medical science have forced a re-evaluation of our understanding on tropical infections. Both malaria and syphilis are important tropical infectious diseases. The co-occurrence between these two diseases can be expected. A large proportion of people with latent syphilis live in malaria-endemic areas, so co-infection with these two organisms is likely to be common. Aberration in pathogenesis of infection in an episode of malaria and syphilis co-occurrence is interesting and becomes a new focus in tropical medicine. The aberration in immunological process is believed to be important part in the pathogenesis of co-infection.

Here, the author studied the pathogenesis of CD4+ suppression in malaria-syphilis co-infection. The pathway ontology technique is used. This technique is a new concept and used in some recent molecular biological studies. Of interest, the author found that there are some immune suppression process that can be found both in syphilis and malaria. The mentioned processes are inhibiting interleukin-2 (IL-2) secreted by CD4+ (11, 12-13) and nitric oxide production (10, 11, 15). This common pathway implies the synergic effect to decrease CD4+ count. In this work, the author used the network mapping technique (6,7), which is an acceptable systemic biology method, to evaluate the hypothesis. In the co-infection, the synergy to increase the immune suppression can be expected. This is the first original report that co-infection with syphilis and malaria can lead to immune deterioration on CD4+ count. The finding in this study is not only supports the previous knowledge on malaria and syphilis but also gives the new view on the pathogenesis of co-infection.

<table>
<thead>
<tr>
<th>Diseases</th>
<th>Mechanisms</th>
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| Malaria  | Modulating dendritic cell function by hemozoin (8)  
Inhibit interleukin-2 (IL-2) secreted by CD4+ (9)  
Nitric oxide production (10,11)  
Inhibit interleukin-2 (IL-2) secreted by CD4+ (12,13)  
Impairment of mitogenic factor (13,14)  
Nitric oxide production (15) |
| Syphilis |            |
Figure 1. Pathway for CD4+ suppression due to syphilis and malaria co-infection (1= mechanism in malaria, 2= mechanism in syphilis)

CD = cluster of differentiation, IFN = interferon, IL = interleukin, MHC = Major Histocompatibility Complex, NO = nitric oxide, Th = T helper
Figure 2. The common pathway for CD4+ suppression (1 = mechanism in malaria, 2 = mechanism in syphilis)

CD = cluster of differentiation, IFN = interferon, MHC = Major Histocompatibility Complex, NO = nitric oxide, Th = T helper

References


