Open Access Library Journal
2023, Volume 10, e9934
ISSN Online: 2333-9721
ISSN Print: 2333-9705

Coinfection: Malaria and Hepatitis, a Case Report and a Review of the Literature

Khadija Danaoui, Malika Idalene, Noura Tassi

Department of Infectious Diseases, Mohamed VI University Hospital of Marrakesh, Marrakesh, Morocco
Email: danaouikhadija@gmail.com

How to cite this paper: Danaoui, K., Idalene, M. and Tassi, N. (2023) Coinfection: Malaria and Hepatitis, a Case Report and a Review of the Literature. *Open Access Library Journal*, **10**: e9934.
https://doi.org/10.4236/oalib.1109934

Received: February 27, 2023
Accepted: April 8, 2023
Published: April 11, 2023

Abstract

In Africa, *Plasmodium falciparum* malaria and hepatitis A virus (HAV) are common infections, although concomitant infections of these two human pathogens are apt to occur, the awareness of their prevalence and eventual significance remains low. Given that both pathogens target the hepatocyte as a host cell for intracellular replication (mosquito-borne malaria parasites silently replicate in suitable hepatocytes before invading red blood cells), direct or immunologically mediated interactions in concurrent infections could potentially intensify or inhibit the spread of both infections. We report the case of a patient aged 29-year-old who worked in the catering trade in Côte d'Ivoire, and who had a history of malaria two years before his hospitalization, which was treated with Artemether-Lumefantrine, who was hospitalized in the Infectious Diseases Department of the Mohamed VI University Hospital of Marrakech having a co-infection with *P. falciparum* malaria and acute HAV revealed by an acute fever associated with jaundice, vomiting and diarrhea evolving since one week after his return from Côte d'Ivoire. Considering a high hepatic cytolysis (8 × normal), hepatic serologies (A, B, C) were realized and revealed the presence of positive antibodies anti hepatitis A type IgM. The patient was treated with Artesunate injection at 2.4 mg/kg at H0 H12-H24 then relayed with oral Artemether-Lumefantrine (Coartem) 4 tablets twice a day for 3 days. The clinical course was characterized by apyrexia with regression of jaundice, vomiting, diarrhea and disappearance of confusion. Biologically: an improvement of the infectious balance.

Subject Areas

Infectious Diseases

Keywords

Plasmodium falciparum Malaria, Hepatitis A Virus, Hepatitis B Virus, Hepatic Cytolysis

1. Introduction

In Africa, *Plasmodium falciparum* malaria and hepatitis A virus (HAV) are common infections [1], although concomitant infections of these two human pathogens are apt to occur, the awareness of their prevalence and eventual significance remains low. Given that both pathogens target the hepatocyte as a host cell for intracellular replication (mosquito-borne malaria parasites silently replicate in suitable hepatocytes before invading red blood cells), direct or immunologically mediated interactions in concurrent infections could potentially intensify or inhibit the spread of both infections.

Epidemiologically relevant interactions, though with contradictory findings, have previously been shown for *P. falciparum* malaria and hepatitis B (HBV). In a case-control study in The Gambia, the prevalence of HBV was significantly increased amongst children with severe *P. falciparum* malaria compared to matched controls [2]. In this study, we report the case of a patient whose consent was taken and who was hospitalized in the Infectious Diseases Department of the Mohamed VI University Hospital of Marrakech having a co-infection with *P. falciparum* malaria and acute HAV.

2. Clinical Presentation

A 29-year-old man who worked in the catering trade in Côte d'Ivoire, and who had a history of malaria two years before his hospitalization, which was treated with Artemether-Lumefantrine, was admitted to the infectious diseases department at the Mohamed IV University Hospital of Marrakech for acute fever associated with jaundice, vomiting and diarrhea evolving since one week after his return from Côte d'Ivoire. On admission, he was drowsy, tachycardic at 100 beats per minute, polypneic at 24 cycles per minute and normo-tensed at 11/6, febrile at 38˚C with a mucocutaneous sub-icterus, his capillary blood glucose was 1.2 g/L, but no hemoglobinuria on urinary strip. The other clinical examination was unremarkable.

The stay in an endemic region led to the suspicion of malaria first. The thick blood film and the blood smear revealed the presence of *plasmodium falciparum* with a parasitemia of 1.5%. Hemoglobin (Hb) was 13 g/dL, platelets 15,000/uL, white blood cells 16,430/mm^3, neutrophils 9340/mm^3, and lymphocytes 4820/mm^3. ALT level was 220 IU/L (5 × normal), AST level was 410 IU/L (8 × normal), alkaline phosphatase (ALP) level was 73 IU/L and gamma glutamyl transferase (GGT) level was 104 IU/L, a total bilirubin (TB) at 119.6 IU/L; a hyponatremia at 120 IU/L, a blood creatinine at 14.1 g/L and a blood urea at 1.17 g/L; a CRP at 178.68 IU/L (**Figure 1**).

Considering a high hepatic cytolysis (8 × normal), hepatic serologies (A, B, C) were realized and revealed the presence of positive antibodies anti hepatitis A type IgM. The patient was treated with Artesunate injection at 2.4 mg/kg at H0 H12-H24 then relayed with oral Artemether-Lumefantrine (Coartem) 4 tablets twice a day for 3 days.


PARASITOLOGIE–MYCOLOGIE

Parasitologie sanguine: Recherche de Plasmodium (Paludisme)

Recherche : (Examen du frottis sanguin coloré au MGG)	Positive
Parasitémie :	1.5 /100 GR
Espèce :	**Plasmodium falciparum**

Figure 1. Malaria parasite density measurements.

The clinical course was characterized by apyrexia with regression of jaundice, vomiting, diarrhea and disappearance of confusion. Biologically: an improvement of the infectious balance (WBC at 10,600/uL, PNN at 3960/uL, CRP at 21.34/uL), an increase of the platelets count 88,000, an improvement of the renal insufficiency (Urea at 0.17 g/L, creatinine at 5.2 g/L), as well as an improvement of the hepatic balance (ALT at 114 IU/L, AST at 92 IU/L, PAL at 47 IU/L, GGT at 43 IU/L, TB at 29.4 IU/L).

3. Discussion

The biological mechanism, if any, behind the observed temporal association remains unclear. For example, *P. falciparum* infections at the hepatic and/or blood stage could, through unknown immune mechanisms, promote HAV replication and thus increase the chances of detecting active HAV infections. Alternatively, coincident HAV infection could promote parasite survival at the hepatic stage, leading to an increased number of infective merozoites and an increased likelihood of subsequent pathogenic infection at the blood stage, in a similar way to the mechanism suggested for the observed association between malaria and hepatitis B virus (HBV). In the *Thursz* study, the increased incidence of severe malaria observed in chronic HBV carriers was explained by reduced expression of HLA class I molecules by hepatocytes during chronic HBV infection [3]. HLA class I molecules are important for the recognition and subsequent lysis of *P. falciparum*-infected hepatocytes by cytotoxic T lymphocytes (CTL). Thus, lysis of parasite-infected hepatocytes by CTL may have been impaired in HBV carriers, leading to increased susceptibility to severe malaria. Whether similar mechanisms play a role in the association between acute HAV and falciparum malaria is yet unclear.

An overestimation of the association of hepatitis A with malaria may be obtained if anti-HAV IgM remains positive (for a long time) after HAV viral particles have been cleared from the liver. However, the anti-HAV IgM response usually becomes undetectable within 6 months, but HAV RNA can be detected for more than 400 - 600 days after the ALT peak [4]. Thus, even if anti-HAV IgM remains positive for a long time after an acute infection, HAV viral particles will reside in hepatocytes during this period, perhaps increasing the likelihood of finding a concomitant infection between acute HAV and malaria [3]. *Peter et al.* found that nine out of ten cases of acute HAV infections occurred concurrently

with *P. falciparum* malaria infections and that HAV infections were a frequent cause of elevated plasma concentrations of an established biomarker of liver cell damage (ALT) in these patients. Children in Kilifi district with *P. falciparum* malaria and elevated ALT concentrations (100 U/L) had a 53% (8/15) risk of being co-infected with HAV, indicating that nearly 50% of the elevations could not be explained by HAV infections. This study did not reveal any adverse clinical consequences of the co-infections, except for a significantly lower hemoglobin level. This was not the case in our patient. Unlike *Plasmodium* infections, HAV is not known to affect hemoglobin levels. They hypothesized that *Plasmodium* infections in co-infected children were sustained and therefore caused a slight additional decrease in hemoglobin concentrations [5].

4. Conclusion

To conclude, we noted a time course association between falciparum malaria and HAV. Larger, prospective studies are needed to further elucidate the epidemiological interaction between these two important human pathogens.

Conflicts of Interest

The authors declare no conflicts of interest.

References

[1] Snow, R.W., Guerra, C.A., Noor, A.M., Myint, H.Y. and Hay, S.I. (2005) The Global Distribution of Clinical Episodes of Plasmodium Falciparum Malaria. *Nature*, **434**, 214-217. https://doi.org/10.1038/nature03342

[2] Thursz, M.R., Kwiatkowski, D., Torok, M.E., Allsopp, C.E., Greenwood, B.M., *et al.* (1995) Association of Hepatitis B Surface Antigen Carriage with Severe Malaria in Gambian Children. *Nature Medicine*, **1**, 374-375. https://doi.org/10.1038/nm0495-374

[3] Jacobsen, K.H. and Koopman, J.S. (2004) Declining Hepatitis A Seroprevalence: A Global Review and Analysis. *Epidemiology & Infection*, **132**, 1005-1022. https://doi.org/10.1017/S0950268804002857

[4] Klein Klouwenberg, P., Sasi, P., Bashraheil, M., Awuondo, K., Bonten, M., Berkley, J., Marsh, K. and Borrmann, S. (2011) Temporal Association of Acute Hepatitis A and Plasmodium Falciparum Malaria in Children. *PLOS ONE*, **6**, e21013. https://doi.org/10.1371/journal.pone.0021013

[5] Pasquetto, V., Guidotti, L.G., Kakimi, K., Tsuji, M. and Chisari, F.V. (2000) Host-Virus Interactions during Malaria Infection in Hepatitis B Virus Transgenic Mice. *Journal of Experimental Medicine*, **192**, 529-536. https://doi.org/10.1084/jem.192.4.529