International Journal of TROPICAL DISEASE & Health
18(1): 1-4, 2016, Article no.IJTDH.26995
ISSN: 2278–1005, NLM ID: 101632866

SCIENCEDOMAIN *international*
www.sciencedomain.org

Can Malaria Interfere with the Diagnosis of HIV Infection?

Martin E. Ohanu[1*] and Michael O. Iroezindu[2]

[1]Department of Medical Microbiology, University of Nigeria Teaching Hospital, Enugu, Nigeria.
[2]Department of Medicine, College of Medicine, University of Nigeria, Enugu, Nigeria.

Authors' contributions

This work was carried out in collaboration between the both authors. Author MEO did the study design and wrote the protocol. Authors MOI and MEO reviewed the clinical and laboratory management of the patient and conducted literature searches. Both authors read and approved the final manuscript.

Article Information

DOI: 10.9734/IJTDH/2016/26995
Editor(s):
(1) Siddharudha Shivalli, Department of Community Medicine, Yenepoya Medical College, Yenepoya University, Mangalore, India.
Reviewers:
(1) Anonymous, Baylor College of Medicine, Texas, USA.
(2) Adekunle Sanyaolu, St. James School of Medicine, Albert, Lake, Anguilla.
(3) Nkiruka Rose Ukibe, Nnamdi Azikiwe University, Nnewi Campus, Nigeria.
Complete Peer review History: http://sciencedomain.org/review-history/15392

Case Study

Received 14th May 2016
Accepted 28th June 2016
Published 14th July 2016

ABSTRACT

A 40 year old woman presented to the medical outpatient clinic of University of Nigeria Teaching Hospital Enugu with an acute febrile illness. She had blood film malaria parasitaemia of 2,400 parasites/µl, and tested positive to human immunodeficiency virus (HIV) 1 & 11 using rapid test kit. She was counseled and offered HIV confirmatory test which turned out indeterminate. She was treated for malaria using artemisinin-based combination therapy and advised to come back after three months for repeat HIV test. Three months later, the patient now asymptomatic with negative malaria parasite film was re-screened for HIV using enzyme linked immunosorbent assay (ELISA) technique which turned out negative. Our findings suggest that malaria may interfere with diagnosis of HIV infection especially when using the rapid test kit and hence give wrong epidemiological data – this also has grave implications for the individual patient. This observation is important in populations where both malaria and HIV are endemic.

Keywords: Diagnosis; HIV; interference; malaria; antibodies.

**Corresponding author: Email: ohanueke@yahoo.com;*

1. INTRODUCTION

Clinicians in tropical environments are frequently faced with the task of unraveling the cause of a febrile illness in order to administer prompt and effective treatment. Standard diagnostic tests for common infective conditions such as malaria and human immunodeficiency virus (HIV) infection are often available in developing countries. Laboratory diagnosis of malaria is based on either peripheral blood film microscopy, rapid diagnostic test or both [1]. On the other hand, laboratory diagnosis of HIV infection usually begins with antibody screening tests such as rapid tests or enzyme linked immunosorbent assay (ELISA) [2]. Despite the availability of these tests, diagnosis of febrile illness could be complicated by possibilities of co-infection and disease interactions.

The geographical overlap of malaria and HIV infection has sparked much interest in their potential interactions. Population-based studies have found that malaria episodes significantly led to transient increment in HIV-1 replication [3]. On the other hand, HIV-induced immunosuppression has been associated with increased malaria parasitaemia and more frequent/severe episodes of clinical malaria [4]. While there are concerns about overdiagnosis of clinical malaria in symptomatic HIV-infected individuals with incidental malaria parasitaemia [5], malaria episodes interfering with laboratory diagnosis of HIV infection may not have generated sufficient concerns in sub-Saharan Africa. We report a case of false positive HIV antibody screening test during a malaria episode in a Nigerian woman.

2. CASE

A 40 yr old woman presented to the medical outpatient clinic of University of Nigeria Teaching Hospital Enugu in 2010 with a three day history of intermittent high-grade fever associated with rigor, malaise and body aches. Review of system was unremarkable. She had a past history of three episodes of febrile illnesses in the past one year which were all treated as malaria using sulphadoxine-pyrimethamine without laboratory confirmation. Except for axillary temperature of 37.9℃, her physical findings were normal. Laboratory investigations revealed peripheral blood film malaria parasitaemia (*Plasmodium falciparum* of 2,400 parasites/µl), packed cell volume (PCV) = 36%, and total white blood cell (WBC) = 3,600/cm^3. Widal titres were insignificant. After pre-test counseling and obtaining informed consent, HIV I & II screening was done using Determine™ rapid test kit which turned out positive. She was then offered HIV confirmatory test (Western blot) which was indeterminate. Following antimalarial treatment with artemisinin-based combination therapy (ACT), her symptoms resolved. She was advised to come for a repeat HIV test in three months.

She turned up after three months and had remained asymptomatic. Repeat HIV I & II screening test was done using the enzyme linked immunosorbent assay (ELISA) test kit (DIALAB Diagnostics, Vienna, Austria) which turned out negative. Repeat blood film microscopy was negative for malaria parasite and full blood count was normal. Her laboratory findings are summarized in Table 1. She was diagnosed HIV negative, counseled and reassured. The lady has remained healthy till date.

3. DISCUSSION

We described an unusual case of a Nigerian woman who had a positive HIV screening test during an episode of acute uncomplicated malaria. The finding of indeterminate western blot confirmatory test warranted a repeat HIV antibody test three months later after successful antimalarial therapy which turned out negative.

Typically, ELISA or rapid tests are used for detecting anti-HIV antibodies for blood screening and/or surveillance purposes. While the former include third-generation ELISAs that utilize the antigen sandwich design for improved sensitivity, the latter are mainly immunochromatographic tests requiring less than 30 minutes of assay time [2]. Confirmatory tests such as the Western blot, indirect fluorescent antibody assay or the radioimmuno-precipitation assay are required to verify reactive screening test results [2].

In recent years, there have been growing concerns on the interaction of HIV infection and malaria in sub-Saharan Africa. Most of the available studies have focused on HIV-related immunosuppression predisposing to frequent or more severe malaria episodes or malaria infection being associated with transient increases in HIV viral load and some decline in CD4+ count [3,4]. So far, there is limited literature on malaria infection interfering with laboratory diagnosis of HIV infection in sub-Saharan Africa. The case we reported suggests possible cross-reactivity between antibodies to malaria parasite and HIV antibodies.

Table 1. Laboratory findings in the patient

	First visit (August, 2010)	Second visit (November, 2010)
Parasite count (*P. falciparum*)	2,400/ µl	0/ µl
Haemoglobin	12.6g/dl	13g/dl
Total WBC	$3.6x10^9$/l	$3.5x10^9$/l
PCV	36%	38%
Widal test titre (*S. typhi* somatic antigen)	1:80	1:40
HIV 1 &11 antibodies	Positive (Rapid test kit)	Negative (ELISA)
Western blot test	Indeterminate	------

HIV: Human immunodeficiency virus; ELISA: Enzyme linked immunosorbent assay; PCV: Packed cell volume; WBC: White blood cell

Few other studies have documented similar observations. Among 464 sera from adults in Cameroon, 56 (12.1%) gave inconclusive HIV serology out of which 25 (44.6%) were significantly associated with *Plasmodium*. All of the inconclusive sera were negative for HIV-1 RNA [6]. In Uganda, Gasasira et al. [7] found a prevalence of false-positive HIV ELISA of about 5% among acute uncomplicated malaria in children and adults. In that report, false-positive HIV test was more likely to be associated with younger age, which argues for the role of immune response to acute malaria. This interaction between malaria and HIV is thought to be driven by marked immunological stimulation, hypergammaglobulinemia, production of autoantibodies and circulating immune complexes, which are prominent features of malaria infection [7,8]. The authors postulated that younger individuals with a less developed immune response to malaria are more likely to exhibit non-specific B-cell stimulation, producing antibodies that cross-react with HIV-1 antigens in the absence of HIV infection [7].

Western blot remains the gold standard for confirming HIV screening test results. In contrast to ELISA or rapid tests that provide results reflecting the reactivities of antibodies to any or all of the antigens for screening purposes, Western blotting generates specific information on the reactivities of antibodies to individual proteins [9]. Any western blot reactivity that does not meet the requirement for being positive or negative must be considered indeterminate. Indeterminate Western blot may be due to HIV-related factors such as seroconversion in progress, advanced HIV disease with loss of antibody response or infection with HIV-2 [10]. It may also be related to assay conditions or performance of kits [10]. Once these have been excluded, indeterminate Western blot may result from other medical conditions such as autoimmune diseases, leprosy, other retroviral infections, post-measles virus infection, hyperbilirubinaemia, polyclonal gammopathies, hemodialysis, malignancies, sexually transmitted diseases, and multiple blood transfusions [10].

In the case reported, it would have been misleading to conclude that the patient had HIV infection, especially in the light of history of recurrent febrile illness within the past one year. Although test kit conditions could contribute to false positive rapid HIV tests, since Western blot was indeterminate, rather than negative, a case for cross-reactivity of malaria and HIV antibodies as explanation for the positive rapid HIV test is plausible. The negative ELISA test after successful malaria treatment further implicates malaria infection for the false-positive HIV test. The use of rapid test for HIV screening is common in resource-limited settings because it has a short turnaround time, obviates the need for trained manpower and reduces overall laboratory cost. However, ELISA was used for the repeat antibody screening in this patient because of its high sensitivity. According to Mehra et al. [11], RDTs fare poorly compared to ELISA as HIV screening assays. In their study, the sensitivity, specificity, negative and positive predictive values of RDT were 77.5%, 99.3%, 98.8% and 86.1%, respectively, taking ELISA as the standard test.

4. CONCLUSION

Acute malaria infection may interfere with HIV diagnosis using rapid HIV antibody screening tests. This observation is important in populations where both malaria and HIV are endemic, and cost and other considerations have promoted the scale-up of rapid HIV test kits. Despite resource constraints in developing countries, relying on two positive results using rapid HIV test kits could be misleading, especially for a patient suffering from malaria and could lead to overdiagnosis of HIV infection. This

emphasizes the need for positive HIV rapid test results to be repeated with ELISA or confirmed with the Western blot in selected patients.

CONSENT

The patient gave an informed consent for this case to be reported.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. World Health Organization. Universal access to malaria diagnostic testing- an operational manual; 2011. Geneva, Switzerland.
2. World Health Organization. Consolidated guidelines on HIV prevention, diagnosis, treatment and care of key populations; 2014. Geneva, Switzerland.
3. Kublin JG, Patnaik P, Jere C, et al. Effect of *Plasmodium falciparum* on concentration of HIV-1 RNA in the blood of adults in rural Malawi: A prospective cohort study. Lancet. 2005;365:233-40.
4. Laufer MK, van Oosterhout JJG, Thesing PC, et al. Impact of HIV-associated immunosuppression on malaria infection and disease in Malawi. J Infect Dis. 2006; 193:872-78.
5. Berg A, Patel S, Langeland N, et al. Falciparum malaria and HIV-1 in hospitalized adults in Maputo, Mozambique: Does HIV-infection obscure the malaria diagnosis? Malar J. 2008;7: 252.
6. Mbopi-Keou FX, Ndjoyi-Mbiguino A, Talla F, et al. Association of inconclusive sera for human immunodeficiency virus infection with malaria and epstein-barr virus infection in Central Africa. J Clin Microbiol. 2014;52(2):660-2.
7. Gasasira AF, Dorsey G, Kamya MR, et al. False-positive results of enzyme immunoassays for human immunodeficiency virus in patients with uncomplicated malaria. J Clin Microbiol. 2006;44(8):3021-4.
8. Wahlgren M, Berzins K, Perlmann P, et al. Characterization of the humoral immune response in *Plasmodium falciparum* malaria. Estimation of antibodies to *P. falciparum* or human erythrocytes by means of microELISA. Clin. Exp. Immunol. 1983;54:127–34.
9. Saah AJ, Farzadegan H, Fox R, et al. Detection of early antibodies in human immunodeficiency virus infection by enzyme-linked immunosorbent assay, western blot, and radioimmunoprecipitation. J. Clin. Microbiol. 1987;25:1605–10.
10. Guan M. Frequency, causes, and new challenges of indeterminate results in western blot confirmatory testing for antibodies to human immunodeficiency virus. Clin Vaccine Immunol. 2007;14(6): 649-59.
11. Mehra B, Bhattar S, Bhalla P, Rawat D. Rapid tests versus ELISA for screening of HIV infection: Our experience from a voluntary counseling and testing facility of a tertiary care centre in north India. ISRN AIDS; 2014.
Article ID 296840
Available:http://dx.doi.org/10.1155/2014/296840

Peer-review history:
The peer review history for this paper can be accessed here:
http://sciencedomain.org/review-history/15392