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Post-Quinine Bilious Hemoglobin Fever in an 8-Year-Old Child Monitored for Severe Malaria at the Yalosase Health Center, Isangi, DR Congo

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Abstract

It has been known since March 2013 that Artesunate is considered the gold standard treatment for severe malaria [1] [2] [3]. However, in our regions, the drug of choice available to treat patients with severe malaria remains quinine until today. However, frequent and sequential use of quinine is associated with the occurrence of hemoglobinuria [2]. We report a probable case of bilious hemoglobin fever (BHF) in an 8-year-old child. This was an 8-year-old child with a history of frequent and recent treatment with quinine, received in consultation for coca-cola urine emission with rapid diagnostic test (RDT) positive. In search of a particular terrain, the retroviral and syphilitic serologies were negative. Considering the context, the diagnosis of post-quinine hemoglobin bilious fever (BHF) was retained and the patient had progressed well after administration of artemisinin and its derivatives. The child was followed, on an outpatient basis, without any sequelae. It would therefore be prudent for the time being to avoid them in prophylaxis and self-medication.

Keywords

Bilious Hemoglobin Fever, Severe Malaria, Quinine, Isangi

1. Introduction

Quinine is classically described as responsible for the occurrence of Bilious Hemoglobin Fever (BHF) [1] [2] [3] [4]. This is a serious and exceptional complication; it occurs during the treatment of malaria due to *Plasmodium falciparum*. The incidence can reach 7.13% population in some areas of Africa [1] [5] [6]. Although several etiological factors are frequently found during the onset of hemoglobinuria, the large number of cases of malaria encountered, the number of patients frequently taking quinine for self-medication and the relative rarity of hemoglobin bilious fever still seem to be attributed to the use of quinine in Africa [1] [2] [7]. In view of this observation made in African countries, and by situating ourselves in the Congolese context in this study, we summarize our concern with this question: What is the clinical aspect of bilious hemoglobin fever in the Democratic Republic of Congo (DRC) in general, and in Isangi in particular? Our observation is one of the rare cases reported in a child in rural areas.

2. Observation

It was an 8-year-old female, weighing 21 kg, treated with quinine for severe malaria in its algid form. The evolution was marked by the sudden onset, 48 hours after, of an emission of port red urine associated with intense physical asthenia without fever or vomiting (**Figure 1**). There was, moreover, no notion of pathological history or drug allergy reported in the child or in the family. No notion of taking herbal medicine. His mother also reports the notion of sequential and repeated intake of quinine. On physical examination, general condition was preserved, consciousness clear, mucous membranes pale and jaundiced (**Figure 2**).

Figure 1. Post-quinine coca_cola urine in an 8-year-old child monitored for severe malaria at the Yalosase Health Center, Isangi, DR Congo.

Figure 2. Yellowish coloration of the post-quinine bulbar conjunctiva in an 8-year-old child monitored for severe malaria at the Yalosase Health Center, Isangi, DR Congo.

The lymph node areas were free. The temperature was 37.1˚C, BP was not collected for lack of a pediatric cuff, pulse at 90 beats per minute and respiratory rate at 28 cycles per minute. The neurological and pleuropulmonary examination was unremarkable. The abdomen was flexible, painless with no collateral venous circulation and hepatosplenomegaly. On digital examination, the anal margin was clean and the finger cot was soiled with normal-looking stools. The urine was coca-cola-like. There was no edema of the lower extremities. At the paraclinical, there was moderate anemia at 8.4 g/l. RDT was positive while GE had come back negative as were HBsAg and anti-HCV antibodies. In search of a particular terrain, the retroviral and syphilitic serologies were negative. Hemoglobinuria was positive, but bile salts and pigments were negative on urine dipstick examination. There was no leukocytosis and kidney function was normal. The remainder of the classical biological and imagery assessment of coca cola urine and jaundice was not carried out for lack of a reduced technical platform. The diagnosis of quinine-induced bilious hemoglobin fever was the most probable and the patient had progressed well after stopping quinine. We prescribed and administered oral altermeter-lumefantrine. The patient was followed on an outpatient basis and had no sequelae.

3. Discussion

This study finds a case of post-treatment FBH of severe quinine-induced malaria at the yalosase health center (YHC), rural health zone of Isangi, Tshopo health province, DRC. It is associated with the intake of quinine, an aminoalcohol. Indeed, it has been constant that quinine is from time to time taken for prophylaxis and self-medication in settings where malaria is endemic. In this context, there is a development by the body of antibodies against the quinine salt; thus there will be an allergic reaction linked to the presence of anti quinine antibodies following the treatment of severe malaria caused by Plasmodium falciparum, treated with quinine, which will be responsible for the hemolysis. Little known, the latter can be fatal especially in rural areas where the technical platform and qualified human resources are lacking. The study by ALIOU *et al.* in Mali, in 2014 found a time to onset of 24 to 48 hours after the administration of antimalarial drugs such as quinine, halofantrine and mefloquine [1]. Our observation is one of the rare cases reported in a child in rural areas. The clinical picture is classically described in 2 phases. The first phase, characterized by signs of shock and intravascular hemolysis, is found in the majority of observations. We find the conjunctival pallor triad, jaundice and dark urine (coca-cola, dark beer. The second phase which is manifested by the occurrence of renal failure. In our study, the patient had presented a table of coca-cola urine associated with jaundice occurred 48 hours later. Our patient was successfully treated. We gave her the benefit of an artemisinin and its derivatives per os, "the artemeter lumefantrine association", combined with an oral antianemic agent. Our constant resembles the observation of Bumelu *et al.*, who notes that the most frequent call

sign is "coca-cola urine». Regarding the causal role of the drug, the molecule incriminated in our study is quinine. Several studies have had a similar result, including a study by the team of Assi LE *et al.* in 1999, Th.Daubrey-Potey *et al.* in 2004, Oumar A.A. *et al.* in 2007 observing BHF after treatment of Plasmodium falciparum malaria, treated with quinine [5] [6] [8].On the other hand, an FBH induced after taking the artemeter-lumefantrine combination was observed by the study by N. Aloni et all in 2020 in an 8-year-old Congolese child with a history of hemoglobinuria after treatment with quinine [9]. Therefore, the responsibility for this product of course remains to be verified. Indeed, there are many pathologies which can lead to acute intravascular hemolysis and it is therefore difficult to attribute this hemoglobinuria directly to quinine; Nevertheless, in our case, we believe that this is seen in the idea that the finding of a significant number of pharmacies without qualified personnel alongside a significant number of cases of malaria encountered in our regions, the number of patients taking quinine in self-medication and the relative rarity of FBH. The physiopathological mechanisms of FBH are multiple and are not fully understood. But the intense anaphylactic reaction to quinine has been suggested as a plausible explanation [6]. Intravascular haemolysis is either constitutional or linked to corpuscular abnormalities (pyruvate kinase deficiency, G6PD deficiency, Minskowski-Chauffart disease, etc.) or extra-corpuscular hemolyses where haemolysis of red blood cells is secondary to an extrinsic factor (an infectious agent, mechanical or toxic factor, immunological disorder ...). This study has the merit of documenting a case of post-therapeutic FBH which is rare. Its only limitation is that it has experienced methodological insufficiencies for financial reasons, we were unable to explore other causes of coca-cola urine. This shows the importance for the time being of avoiding quinine as a prophylaxis and of setting up a committee responsible for collecting information on the use and monitoring of patients treated with quinine, at the end of providing regular analyzes of those data.

4. Conclusion

The occurrence of hemoglobin bilious fever is currently a possible possibility in tropical countries, including the Democratic Republic of Congo: acute hemolytic episode of immuno-allergic origin linked to the recent and sequential intake in self-medication and/or prophylaxis of quinine or perhaps other antimalarials. A case of FBH has been observed following treatment with quinine. The benefit of aminoalcols is not compromised by episodes of acute hemolysis (rarely severe and usually moderate in intensity). Our results underline the need to avoid them in prophylaxis.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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