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Case Report

A Case of Imported Non-falciparum Malaria

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Abstract

A 27 year old male, native of Angola, where he was diagnosed with malaria, presents in our emergency department with headache, fever and myalgias. A diagnosis of severe *Plasmodium ovale* malaria with probable persistent hepatic forms was confirmed. He was started on a quinine and doxycycline scheme, later changed to atovaquone/proguanil due to concerns for resistance. Primaquine therapy was also administered. Despite clinical improvement and persistent elimination of parasitemia the patient developed significant antimalarial side effects.

Severe malaria can be associated with hemodynamic instability and serious organ dysfunction and requires prompt intravenous therapy. Malaria relapses are common with *ovale* parasites, which have dormant liver stage. Atovaquone/proguanil use is limited in endemic countries due to cost and resistance but can be used in developed countries for treatment of blood parasites. Anti-relapse therapy with primaquine is required for hynozoite elimination.

Most antimalarial drugs have serious adverse reactions that should be monitored cautiously.

Keywords: WHO; Malaria; *Plasmodium ovale*

Introduction

Malaria is an ancient infection that has existed for numerous thousand years. Still today, it is the most important parasitic disease of man [1]. According to the World Health Organisation (WHO), around 3.2 billion people are at risk of malaria infection and there were 214 million new cases of malaria in 2015 [1]. Antimalarial efficacy has been threatened by drug resistance which continues to emerge creating a major obstacle to malaria control [2].

Case Presentation

We present the case of a 27-year-old male, nahir of angola, university student who had moved from Luanda to Portugal 7 months before. The patient presents to the Emergency Department due to severe headache, fever, profuse sweating, rigors and myalgias reaching maximal within 48 hours.

He had been diagnosed with malaria during childhood and since then he had several similar episodes of fever, headache and myalgia annually, sometimes twice a year, that resolved with 4-6 days of malaria-targeted therapy. There were no complications or symptoms other than those described, and no need for hospitalization. Throughout his life the patient has had numerous anti-malarial treatments: in childhood, mainly chloroquine and quinine, after adolescence and adulthood, he was treated with regimens mainly based on Artemether and Lumefantrinar, and a single course of

sulfadoxine/pyrimethamine. Back in Angola, he had parasitemia identified by thick film during the episodes and was given treatment right away. The patient never knew the form of parasite and he was never tested for antimalarial resistance. He denied sexual risk behaviors, recent travel or sick contacts. He had no other relevant personal background, namely hemoglobinopathies or other hematological diseases.

Physical examination: Fever (38.3ºC) normal neurological evaluation. Normal cardiopulmonary auscultation, without hepato or splenomegaly apparent by palpation. No peripheral edema or cutaneous lesions.

In the emergency department the diagnosis of a non-falciparum Plasmodium malaria was confirmed (antigen identification), with parasitemia of 1.2%. There was evidence of clinical severity: acute renal injury (serum creatinine of 1.2 mg/dl), thrombocytopenia of 74,000/uL and mild coagulation dysfunction. Also, he had a slightly increased C reactive protein (27.7 m/L). There was no anemia, ionic changes or alterations in liver tests or signs of other organ dysfunction. The patient also had a renal ultrasound to exclude an obstructive cause for his acute kidney injury that came back normal.

It was decided to admit the patient for treatment and support of severe malaria with probable persistent hepatic forms. An endovenous quinine and doxycycline combination scheme was started in the same day, associated with oral primaquine 30 mg daily, after normal G6PD status has been confirmed.

Later a *Plasmodium ovale* was confirmed to be the causative agent.

The therapeutic scheme initiated in the Emergency Department was continued for 24 hours. Parasite density was then reassessed and confirmed to be below 1 percent. It was decided to switch to oral therapy as the patient remained afebrile and able to tolerate oral medication. Also, he reported significant side effects attributable to quinine: tinnitus and hearing loss. Given the many Chloroquine and Artemisinin-based courses that the patient did in the past and the associated risk of resistance, an atovaquone/proguanil 1000/400 mg (3 days) scheme was chosen, maintaining primaquine. The patient evolved favorably with persistent elimination of parasitemia and resolution of organ dysfunctions. Nevertheless, he developed important therapy side effects: anemia, leucopenia, hepatic cytolysis and peribuccal cutaneous lesions. These were attributed to toxicity of atovaquone/proguanil and subsided spontaneously with termination of therapy. The patient was discharged after 6 days, maintaining follow-up in internal medicine consultation. Three months later, he remained asymptomatic with no relevant analytic changes.

Discussion and Conclusion

There are four Plasmodium species that commonly cause illness in humans: *falciparum, vivax, ovale,* and *malariae*. *Plasmodium falciparum* and *Plasmodium vivax* cause the majority of morbidity worldwide with nearly all malaria-related deaths being caused by *falciparum*, which is also the most drug-resistant of all. *Plasmodium vivax* comes next, with a wider geographical spread and also with the ability to cause severe disease, it is becoming increasingly resistant to chloroquine [2].

Malaria relapses are common with *vivax* and *ovale* parasites, which have dormant liver stages (hypnozoites) that can reactivate months or years after the acute infection. *Plasmodium ovale*, and also *Plasmodium malariae*, remain sensitive to chloroquine but can also be treated effectively with Artemisinin-based Combination Therapies (ACTs). Atovaquone and proganile use is limited in endemic countries due to significant cost and high risk of resistance in some regions. However it is often used in developed countries for prophylactic and treatment purposes [3,4].

The majority of malaria infections in developed countries occur among people who have traveled to regions with ongoing malaria transmission [4].

We describe a non falciparum malaria with clinical severity criteria. Severe malaria can be associated with hemodynamic instability, pulmonary edema, hemolysis, severe anemia, coagulopathy, hypoglycemia, metabolic acidosis, renal failure, hepatic dysfunction, altered mental status, focal neurological deficits, or seizures.

Intravenous therapy should be initiated promptly, with one of two alternatives: the artemisinin derivatives (artesunate and artemether) or the cinchona alkaloids (quinine and quinidine) [5].

Parenteral artesunate (intravenous or intramuscular) is the preferred therapy for treatment of severe malaria. Intravenous quinine/quinidine remains the treatment of choice when the first

is not readily available and should be administered in conjunction with doxycycline, tetracycline, or clindamycin [5].

Our patient was treated with a combination of quinine and doxicicline due to lack of immediate access to artemisinin derivates.

During treatment of severe malaria, parasite density should be monitored regularly to confirm adequate response to therapy. Parasitemia below 1% has been used as a threshold for switching from parenteral to oral therapy [5].

The approach to malaria caused by *Plasmodium ovale* and *vivax* involves elimination of both the blood and liver stage, which is designation radical cure thereby preventing both recrudescence and relapse. Presumptive anti-relapse therapy with primaquine is required. Its efficacy for relapse prevention is documented as over 90%. Primaquine can cause severe hemolysis in individuals with G6PD deficiency, which is way it is contraindicated for patients deficient in G6PD [5].

This patient had probable recrudescent infections by *Plasmodium ovale* throughout his life due to inadequate treatment of liver forms, as he had never been medicated with primaquine. Nevertheless he had been exposed to several antimalarial since childhood, mainly Artemisinin-based Combination Therapies (ACTs). It was for this reason and the associated risk of selection of resistant parasites, that we decided to use atovaquone/proguanile, a therapeutic regimen to which it was never exposed and that is frequently used in Portugal for prophylaxis and treatment.

It is worth noting that there is great risk of adverse reactions to antimalarial drugs and this patient experienced several during treatment, mainly hematological (anemia, leucopenia), hepatic and cutaneous toxicity. It is important to be alert and monitor not only the response to therapy but also the manifestation and evolution of adverse effects.

Learning Points/Take Home Messages

- The majority of malaria infections in developed countries occur among people who have traveled to regions with ongoing malaria transmission.
- Malaria relapses can have several causes, such as resistance, inadequate dosage/duration of treatment, but are common with Plasmodium *vivax* and o*vale* malaria - adequate treatment requires primaquine to ensure elimination of liver forms that can reactivate after the acute infection has been treated
- During treatment of severe malaria, parasitemia can be used to monitor therapy response and as a threshold for switching from parenteral to oral therapy.
- Monitor not only therapy response but also antimalarial ad-

Bibliography

1. World malaria report 2017. Geneva: World Health Organization. Licence: CC BY-NC-SA 3.0 IGO (2017).
2. Yeung S. "Malaria—Update on Antimalarial Resistance and Treatment Approaches". *The Pediatric Infectious Disease Journal* 37 (2018): 4.
3. Tatem A., *et al*. "The geography of imported malaria to non-endemic countries: a meta-analysis of nationally reported statistics". *Lancet Infectious Disease* 17 (2017): 98-107.
4. Hanboonkunupakarn B and White N. "The threat of antimalarial drug resistence". *Tropical Diseases, Travel Medicine and Vaccines* 2 (2016): 10.
5. Guidelines for the treatment of malaria - 3ed edition. Geneva: World Health Organization (2015).

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