Case Report: Relapse in Malaria With Cerebral Involvement

Alberto González R (albertojose1129@hotmail.com)
Hospital Militar Central
Silvia Juliana Duran
Hospital Militar Central
Estefania Barrios Chaparro
Hospital Militar Central

Short Report

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Abstract

Malaria is an endemic parasitosis in more than 80 countries and with a record of reported cases by 2020 of more than 200 million. Recent literature has been emphatic in increasingly demonstrating the economic impact and severity of disease caused by Plasmodium vivax. This case report decribes a A 19-year-old colombian male patient, active soldier, previously healthy, resident for 6 months in the city of Bogotá, reporting a clinical picture of 4 days of evolution characterized by quantified febrile spikes of up to 39 degrees, headache, arthralgia and several diarrheal episodes with non-dysenteric water content. Associated with the above, the patient presented a seizure of 3 minutes of duration with generalized tonic-clonic movements, superelevation of the gaze without relaxation of the sphincters, drowsiness and total amnesia of the event. He refers as the only relevant pathological history the presence of Malaria treated 6 months before while residing in the Amazon Department. In consideration of the referred history of malaria, it is decided to take a thick blood smear to search for haemoparasites whose result was positive for Plasmodium vivax. With the above findings, management began with intravenous artesunate under the consideration of complicated malaria by P. vivax with cerebral involment secondary to a relapse.

Introduction

Malaria is an endemic parasitosis in more than 80 countries and with a record of reported cases by 2020 of more than 200 million. The African continent remains the most struck by the disease. Countries such as Angola, Congo, Uganda, Mozambique, Burkina Faso and Nigeria account for approximately 55% of the total global registry according to the WHO data (1). Nearly four hundred thousand people die annually from the disease, representing a significant health burden for developing countries (1). *Plasmodium falciparum* is the predominant global species in up to 94% of the reports and is related to mortality in 70% of records. However, when we refer to America, a 71% of malaria cases are caused by *Plasmodium vivax*. Colombia, Brazil and the Bolivarian Republic of Venezuela add up to 77% of the statistics obtained (1). In this case report we will describe a relapse of a vivax malaria case with a severe and unusual presentation in which the neurological compromise is highlighted.

Case Report

A 19-year-old colombian male patient, active soldier, single, previously healthy, resident for 6 months in the city of Bogotá, reporting a clinical picture of 4 days of evolution characterized by quantified febrile spikes of up to 39 degrees, headache, arthralgia and several diarrheal episodes with non-dysenteric water content. Associated with the above, the patient presented a seizure of 3 minutes of duration with generalized tonic-clonic movements, superelevation of the gaze without relaxation of the sphincters, drowsiness and total amnesia of the event. He is admitted in the company of relatives who were witnesses and corroborate the story.

He refers as the only relevant pathological history the presence of Malaria treated 6 months before while residing in the Amazon Department.

The admission physical examination shows blood pressure: 115/67mmHg, temperature: 37 degrees, oxygen saturation: 99%, admission Glasgow: 15/15, heart rate: 98 per minute. In apparent good general condition, moist oral mucosa, sclerae with a slight icteric tint, no neck stiffness or lymphadenopathy. Non-aggregate breath sounds, tachycardia heart sounds no murmurs. Abdomen without pain and without palpation of visceromegaly. Limbs had no edema and distal pulses were present with good capillary refill. The patient responded to questioning adequately without evidence of neurological focus. He had the strength preserved in his limbs, normal reflexes present, no signs of Kernig and Brudzinski and the eye fundus examination performed by the neurology service did not show any relevant data.

Simple brain tomography is performed with no evidence of collections, bleeding or ischemia. Paraclinical tests document the presence of a hemogram with a leukocyte count of 5.3 x 109/L, neutrophils 80%, lymphocytes 10.3%, hemoglobin 12, 2 Gr/dl, hematocrit 36%, platelets 89,000, sodium 137 mEq/l, potassium 4.3 mEq/l, creatinine 1 mg/dl, CRP 4.07 mg/l, total bilirubin 1.7 mg/dl, normal transaminases, total abdominal ultrasound with mild splenomegaly. The urine exam was not suggestive of infection and an antigen and PCR test for COVID 19 taken on admission were reported as negative. Neurology proceeds to perform a lumbar puncture, obtaining clear liquid of rock crystal appearance, film array for cerebrospinal fluid negative for bacteria, negative for viruses and negative for fungi (cryptococcus). Cytochemical appearance normal and latex agglutination for cerebrospinal fluid negative with subsequent fluid culture equally negative, VDRL negative. Magnetic resonance imaging of the brain was performed with protocol for epilepsy with findings within normal limits and video telemetry evidence of epileptogenic foci. Prior consent of the patient, a sample for HIV is taken with negative result. A chest X-ray is performed, the result of which was normal. Could not get samples for stool given the disappearance of diarrhea since admission and the absence stools posteriorly. Serology is taken for dengue with a negative result and a rapid test for leptospirosis (lateral flow test) had a positive result. A second test is done seeking to corroborate the finding by the ELISA method which is reported as negative.

In consideration of the referred history of malaria, it is decided to take a thick blood smear to search for haemoparasites whose result was positive for Plasmodium vivax. The count yielded a parasitemia of 10320/UL (See figure in annex 1 at the end). With the above findings, management began with intravenous artesunate under the consideration of complicated malaria by P vivax with compromise secondary to a relapse. This conclusion was reached after having ruled out other diagnostic possibilities. The subsequent treatment was switched to the oral administration route at 48 hours as indicated in the management guideline. The patient evolves satisfactorily without new fever spikes, improvement in hyperbilirubinemia, without new convulsive episodes and a negative thick blood smear on the third treatment day. He was discharged in good general condition for continuity of outpatient care with primaquine until completing 14 days with indication of outpatient controls.

Discussion

Five species of Plasmodium are commonly associated with infection in humans. They are known as Plasmodium Vivax, Ovale, Malarie, Knowlesi and Falciparum (2). The parasite completes its cycle in 2 hosts: the Anopheles mosquito and the human (3). Once the Anopheles achieves to sting the human, it deposits the sporozoite present in his saliva which will pass into the blood stream, allowing its entry into the hepatocyte. After a maturation process, the parasite is released back into the blood in a form known as a merozoite that allows infection of red blood cells and their subsequent multiplication after various erythrocyte stages (4–5). It is widely known that the constellation of typical malaria symptoms are intensified in this part of the cycle.

For more than 100 years the phenomenon of relapse has been described. Patrick Mason demonstrated with the son of his volunteer that the mosquito harbored the plasmodium VIvax in the form of sporozoites. On his description, he mentions the recurrence of the disease nine months after the mosquito bite (6). Eighty years after this description, the dormant forms for P vivax were identified by Mr. Wojciech Krotoski, finding that, from that moment on, propose the explanation to infections that were documented after months of the primary infection by thousands of patients when these hepatic forms became active (7). Today, the concept of this latent form of the parasite is clearly demonstrated in practice and is known in the literature as

Hypnozoite. Its presence explains relapses in P vivax malaria and often offers a challenge in the disease control and management (8).

Two forms of sporozoites are assumed to invade the liver after a mosquito bite. These are known as tachysporozoites and bradysporozoites. These in turn have specific transcriptional responses with a unique molecular profile, with bradysporozoites being the ones that finally end up dormant (8).

Recent literature has been emphatic in increasingly demonstrating the economic impact and severity of disease caused by Plasmodium vivax. This species has been underestimated probably due to scientific biases in the literature and partly due to the highest known lethality associated with falciparum (9). Unlike years ago, the current evidence is incontrovertible and robust regarding the ability of P. vivax to cause severe disease (10, 11). Between the year 1998 to 2008, 234 P. vivax deaths were reported in Brazil (12). However, a requirement to speak of severity due to P. vivax or malaria complicated by P. vivax necessarily includes having ruled out co-infection by P. Falciparum, ideally with PCR, which is exotically found in studies. Such statement is suggested for any form of severity suspected P vivax, including cerebral malaria in which other comorbid Infectious and non-infectious conditions have been documented as coexisting (13, 14). The referred case highlights a late relapse due to P vivax in the city of Bogota in which there are no autochthonous records of the disease, so it is clearly assumed that the documented infection was related with the history of malaria in the Amazon 6 months earlier.

Although the original criteria described for cerebral malaria linking seizures require a number of convulsive episodes of 2 or more in 24 hours, the WHO has highlighted that a seizure episode that cannot be explained by another cause, in the presence of a confirmed parasitemia by plasmodium should be assumed as a "cerebral malaria prodrome" that requires to be consistent with the treatment strategy. The

foregoing justified our conduct for this case (15). It should be clarified that the criteria for complicated malaria that were previously only valid for P falciparum malaria are currently accepted for P vivax given the robust evidence of severe disease by this species (10, 11, 15).

Finally, we decided not to credit the positive rapid test for leptospirosis since the result could not be corroborated with the ELISA method with which the cross reactions are highly reduced. It was also considered, considering the probabilities and a logic medical reasoning, highly improbable that the patient attended simultaneously with both infectious pictures, so the rapid test was concluded as a false positive and a test was withdrawn and treatment directed at this condition was not considered.

Conclusion

Relapsing malaria is a condition that must be considered when approaching the patient with febrile syndrome in countries and areas endemic for the disease. The latency time of parasite such as hypnozoite can vary from weeks to months. Plasmodium vivax is a species capable of producing severe disease including brain involvement as demonstrated in this case.

Declarations

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Authors' contributions

The patient was treated under the supervision of AGR and SJD. Patient data were gathered by medical student EBC.

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Availability of data and materials

All the information used in this manuscript is available in the patient file at the Center

Conflicts of interest:

The authors declare no conflicts of interest

Ethics approval and consent to participate

Not applicable

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Author details

[1]Hospital Militar Central, Department of internal medicine Bogotá, Colombia.

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- Annex1.docx