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CASE REPORT

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A severe case of *Plasmodium falciparum* malaria imported by a French traveler from Cameroon to French Guiana despite regular intake of *Artemisia annua* herbal tea

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ABSTRACT

The use of herbal tea with *Artemisia annua* by travelers and traditional communities in Africa has increased in recent years as a supposed form of malaria prophylaxis, although its use is not recommended due to lack of efficacy. The risk of severe malaria complications that can lead to death is real regarding said behavior, and awareness needs to be raised. We report a case of severe *Plasmodium falciparum* malaria imported in the Amazon rainforest by a traveler returning from Cameroon who treated himself with *Artemisia annua* herbal tea.

KEYWORDS: *Plasmodium falciparum. Artemisia annua.* Prophylaxis. Amazonia. Severe malaria. Herbal tea.

INTRODUCTION

Malaria is a life-threatening protozoan disease caused by *Plasmodium* sp. which is transmitted by a mosquito vector and is present in tropical regions of the world, including the Amazon rainforest and sub-Saharan Africa. *P. falciparum* is the most dangerous of the species and can progress to a severe clinical case and death. There were 241 million cases of malaria in 2020[1].

Artemisia annua is a Chinese medicinal herb from the Asteraceae family that produces artemisinin, whose derivatives have been found to have antimalarial properties, such as artesunate, artemether and dihydroartemisinin. These artemisinin derivatives used in ACTs (Artemisinin-based combination therapies) have been WHO-recommended therapies for malaria since 2002[1,2]. Lately, it has been suggested that *A. annua* infusion or herbal tea could be used as a natural anti-malarial prophylactic and curative treatment. It is common to read on social networks that WHO and the so-called "Big Pharma" would implement all possible means to prevent the diffusion of this so-called "natural treatment". However, the dose of artemisinin absorbed when used in this way is inconsistent and there have been reports of treatment failures[3,4]. Furthermore, with the increase in artemisinin resistance in recent years, there is concern that the use of sub-therapeutic doses of artemisinin could create resistant parasites and accelerate global resistance to ACTs[5].

We report a severe case of *P. falciparum* malaria in a young French patient who traveled to Cameroon and then to French Guiana, in the Amazon rainforest, using *A. annua* herbal tea as prophylaxis.

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CASE REPORT

A 22-year-old student from Paris, France, with no previous medical history, was taken by local authorities to the health center in Saul (3°55'18''N, 53°18'02''W), a small village with around 100 inhabitants, located in the center of French Guiana, about 180 km southwest of Cayenne.

Saul is a popular tourist destination for hiking in the middle of the rainforest, which is only accessible by walking through the forest or by plane.

The patient was taken to the health center after he fainted during his walk. He was in poor general condition and manifested fever, vomiting and diarrhea

He had returned from a 4-month stay in Cameroon eleven days earlier, and was drinking *A. annua* herbal tea daily for malaria prophylaxis. He reported a first malaria episode in Cameroon which was treated with artesunate, and a second episode a month earlier which was treated with tablets that he could not identify. These malaria attacks occurred while he was taking an alternative treatment of *A. annua* herbal tea obtained from a local store in Cameroon. He strongly believed in the effectiveness of these tea infusions, and he associated these attacks with forgetting to take the decoction.

The symptoms started during his stopover in Paris, 5 days prior to the consultation at the Saul health center. He consulted a general physician 24 h later in Kourou (5°09'29." N, 52°38'33" W), a city located 60 km from the capital of French Guiana (Cayenne), where he was diagnosed through thick and thin blood smears that were positive for *P. falciparum.* However, the patient left for Saul, without taking the prescribed medicine. He continued drinking *A. annua* herbal tea. As soon as he arrived in Saul, he started a walk in the deep forest. Three days later, he was found by the local police several kilometers away from the village, in a poor clinical condition. He was febrile and couldn't walk anymore. The police carried him to the health center.

There, the physical examination showed no sign of sepsis, bleeding, hypoglycemia or dyspnea. His neurological examination was normal. The malaria rapid diagnostic test was positive with 2 bands, Pf and PAN. Treatment was started with artemether/lumefantrine (20/120 mg) and the patient was then transferred by helicopter to a hospital in Cayenne (Centre Hospitalier de Cayenne Andree Rosemon) (4°56'13.6"N, 52°19'32.9"W).

Thick and thin blood smears were positive for *P. falciparum* with a parasitemia of 1.62% of erythrocytes. Other laboratory tests showed: hemoglobin 12.7 g/dL, white blood cell count 8 G/L, platelet count 19 G/L, alkaline reserve 20.8 mmol/L, urea blood level 16.4 mmol/L (normal 2.8-8.1 mmol/L), creatinine blood level 135 µmol/L (normal 59-104 µmol/L), bilirubin 45.8 µmol/L (normal < 21 µmol/L) and CRP 205.4 mg/L (normal < 5mg/L).

He had watery diarrhea but no more vomiting (he had received metoclopramide in Saul).

A new blood draw showed worsening of the renal function with creatinine dosed at 325 µmol/L and urea at 26.1 mmol/L for an estimated glomerular filtration rate of 22 mL/min/1.73 m^2 (normal > 90 mL/min/1.73 m^2). A dosage of lactate returned normal at 1.6 mmol/L. There were no other signs of severe malaria apart from the acute renal failure, established by the severely reduced glomerular filtration rate.

The treatment with artemether/lumefantrine (20/120 mg) was continued for a total of 3 days as recommended by the French guidelines[6]. It was decided not to switch treatment for IV artesunate (recommended treatment in severe malaria)[7] because the patient's clinical state was already improving after the first dose of artemether/lumefantrine.

Parasitemia on day 3 was still positive but had diminished considerably (only the thick blood smear was positive). A new control on day 9 came back negative. Stool cultures as well as stool parasitology were screened and no pathogens were found.

Symptoms improved rapidly and the patient was discharged 5 days after the beginning of treatment. Renal function improved significantly with IV saline solution (0.9/1,000) but creatinine levels remained above normal values (121 µmol/L) on day 10. Follow up was done in outpatient consultations on days 9 and 28 post treatment.

Despite the severity of his clinical condition and the manifest lack of efficacy of this alternative treatment, he was still convinced the herbal tea could work as a malaria treatment.

DISCUSSION

To our knowledge, this is the first case reported in South America of a *P. falciparum* attack in a patient undergoing *A. annua* herbal tea prophylaxis. Although Brazilian researchers in the Amazon have already tested its effects *in vitro* and found some efficacy on *P. falciparum*, it's currently not supported by *in vivo* effects[8,9].

Treatment and eradication of *P. falciparum* malaria has always been a challenge because of parasite adaptation capabilities and fast emerging resistance to treatments. Since the discovery of artemisinin, ACTs have become the new standard drugs for malaria. But in 2009, artemisinin resistance started to appear in Southeast Asia and it is now spreading to Africa[10]. To prevent selective resistance from

developing too fast, artemisinin derivatives are always associated with another molecule in ACTs and these are not recommended as prophylaxis[2].

A few years ago, the use of *A. annua* herbal tea as malaria "prophylaxis" and treatment started to become popular as a supposed cheaper, more natural medication, with a very oriented argument against the resistance to "Big Pharma", the hegemony of WHO and the so-called Western countries. It's used in traditional communities in Africa and can be bought online, without prescription, by travelers who want to go to malaria-endemic regions and want to take a presumed more natural treatment rather than the recommended one. An article published a few years ago[11] encouraged this practice by bringing data that showed the efficacy of the infusion. This article gave power to the critics of Western medicine before it was retracted for data reliability and methodological reasons. In the same "natural medicine" movement, a curative effect of *A. annua* herbal tea for schistosomiasis and SARS-CoV2 was also evoked without proof[12,13].

The dose of artemisinin actually present in the herbal tea is inconsistent because artemisinin varies greatly in *A. annua* cultivars. In the same batch of seeds, one can find plants with a dosage of 0.3% all the way up to 1.9%[14]. There are also great variations in the percentage extracted when making the tea. It's often a sub-therapeutic dose which doesn't protect travelers from getting infected. However, it still exposes them to potential serious side effects, such as developing acute cholestatic hepatitis[15], as addressed in the case report from Switzerland. In addition, the spread of its consumption could probably lead to resistance selection in the long term, so it should be discouraged[5].

In this case report, the patient traveled from one malaria-endemic area to another, with only *A. annua* tea as prophylaxis. He was most likely infected in Cameroon as the symptoms started in Paris; the lag time (24 h) between his arrival in French Guiana and the first diagnosis of malaria is too short to be attributed to the South American journey. Also, *P. falciparum* cases have greatly decreased in French Guiana and are currently very low compared to *P. vivax* cases[16,17].

Such behavior may facilitate the transfer of resistant mutant strains from Africa to the Amazon, threatening the proposal to eradicate *P. falciparum* infections in this area. The burden and consequences of imported malaria cases may be greater than presumed in this region, where Anopheles spp. mosquitoes are endemic.

CONCLUSION

In this case report, the use of *A. annua* herbal tea as putative prophylaxis could not prevent the occurrence of a severe *P. falciparum* case imported from Cameroon and diagnosed in the Amazon. Artemisinin is currently the best tool we have against this deadly disease; unusual forms of *A. annua* products should not be used due to lack of proven efficacy and potential risk to public health.

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