

A rare case of syncope triggered by atrial flutter in a hypertensive patient with malaria: a case report

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Abstract

Malaria is a parasitic disease that represents a serious public health problem in developing countries, especially *Plasmodium falciparum* malaria due to its severity and mortality. Cardiac involvement, although reported on few occasions, has been revealed to be more frequent and lethal than believed. Among the main cardiovascular manifestations of malaria are pericarditis, myocarditis and arrhythmias. We report the case of a 66-year-old man, known to have hypertension, who was admitted to the emergency department of Luanda Medical Center for syncope and whose electrocardiogram revealed atrial flutter with rapid ventricular response, and was later diagnosed with malaria with hematological and hepatic dysfunction. The patient's history reveals some risk factors for the emergence of atrial flutter, which, associated with an infectious pathology in with an intense pro-inflammatory response, with have acted as a *trigger* for the emergence of atrial flutter.

Keywords: Syncope; Atrial flutter; Hypertension; Malaria.

Introduction

Malaria is a parasitic disease, caused by plasmodium and transmitted by the *Anopheles* mosquito, which

causes a serious disease that affects a large part of the world's population [1]. According to the latest WHO global malaria report, there were an estimated 241 million cases of malaria and 627 000

malaria deaths worldwide in 2020. This represents about 14 million more cases in 2020 compared to 2019, and 69 000 more deaths.

Approximately two-thirds of these additional deaths [47 000] were related to disruptions in malaria prevention, diagnosis and treatment during the pandemic, and 95% of cases and 96% of all deaths in 2020 occurred in sub-Saharan Africa. About 80% of deaths in the region occurred among children under 5 years old [2]. Angola is among the top 10 nations with the highest number of plasmodium falciparum malaria cases and deaths [3% of global cases]. Between 2016 and 2019, there was a 14.4% increase in the number of cases per 1000 population at risk, but mortality decreased by 7.3% [3,4].

Plasmodium falciparum malaria represents, therefore, an important problem, which requires the rapid establishment of adequate medical treatment to avoid serious complications and death [1,5]. Serious complications include central nervous system dysfunction, pulmonary involvement, renal failure, and severe hematologic changes, in addition to metabolic acidosis and hypoglycemia [1,5].

There have been reports since 1946 about cardiovascular [CV] involvement due to malaria, and this involvement is more frequent than it is

considered, but it has been reported on very few occasions, however, they constitute a significant risk for affected patients [6].

Complicated malaria can have specific cardiac complications, although there are very few published cases; conduction disorders/arrhythmias, myocarditis and pericarditis, cardiac tamponade, and heart failure, may be direct complications of malaria infection [7,8]. Myocarditis is the most frequently documented cardiac complication as a result of malaria. It is a potentially serious complication caused by plasmodium falciparum, but has also been reported in plasmodium vivax infection [7].

Sequestration of erythrocytes in cardiac capillaries with subsequent obstruction of blood flow can cause ischemic heart disease and left ventricular dilatation [7,8]. Patients with complicated malaria who progress to severe sepsis or septic shock have myocardial dysfunction with left ventricular dilatation and low ejection fraction [7,8]. The most frequent electrocardiographic changes reported in malaria are: ST segment changes and QT interval prolongation that can trigger serious arrhythmias [7,8].

The pathophysiological mechanisms related to CV involvement are not well understood. Possible theories include an imbalance between the pro-

inflammatory response with the release of cytokines and/or the sequestration of erythrocytes by increasing cytoadherence to the endothelium. Pro-inflammatory cytokines such as tumor necrosis factor, alpha factor and interleukin-1 beta are elevated in malaria due to massive disruption of erythrocytes and parasite release. Inflammatory cytokines can produce nitric oxide with subsequent energy depletion and cardiac muscle contractile dysfunction. The glycosylphosphatidylinositols produced by *Plasmodium* act as toxins capable of producing gene dysregulation and apoptosis of cardiomyocytes [5,9–11].

Pro-inflammatory cytokines can generate endothelial dysfunction as an additional pathophysiological mechanism. The increase in cytokines stimulates the adhesion of molecules, and infected erythrocytes tend to adhere to the endothelium of blood vessels. The mechanism that occurs specifically in small capillaries and venules, generating severe tissue hypoxia and metabolic acidosis. The correlation between pro-inflammatory cytokines and organ dysfunction, although discussed in a few case reports, appears to be primarily responsible for severe malaria symptomatology and CV involvement [5,10,11].

Atrial flutter (AFL) is a supraventricular cardiac arrhythmia and

represents about 10% of supraventricular tachycardia cases in the general population, with an estimated prevalence of 85:100 000 inhabitants [12].

The most frequent causes of AFL are mitral and tricuspid valve diseases, chronic obstructive pulmonary disease, cardiomyopathies, advanced age, obesity, heart failure, ischemic heart disease, systemic or pulmonary arterial hypertension, thyrotoxicosis, hypoxemia, acute pulmonary embolism, use of drugs [digoxin, quinidine], sequelae of cardiac surgery, and absence or interruption of treatment with beta-blockers or angiotensin-converting enzyme inhibitors [13]. It can occur in 15-20% of patients without previous heart disease [14].

Electrical cardioversion is considered the most effective way of reversing AFL to sinus rhythm and should be the technique of choice for patients with hemodynamic instability; it can be performed with loads of 25 to 50 Joules, however the use of larger loads (100 to 200 J) is more effective, in addition to reducing the need to repeat the shocks, if there is no reversal with the first one. The use of previous antiarrhythmics increases the rate of reversal, as well as facilitates the maintenance of sinus rhythm after cardioversion [16].

This paper reports the evolution of a known hypertensive patient, who was admitted to the Luanda Medical Center (LMC) emergency department for syncope and whose electrocardiogram (ECG) showed atrial flutter with rapid ventricular response and during the investigation it was discovered that he had malaria with hematological and hepatic dysfunction.

Case report

A 66-year-old black male, born and residing in Luanda, with moderate alcohol consumption, overweight, known to have hypertension for several years, irregularly medicated with amlodipine. He was taken to the emergency room (ER) of the LMC by his relatives for syncope. In the period before the loss of consciousness, he reported severe occipital headache, fever, myalgias, dizziness and two episodes of vomiting of food content.

Upon observation in the ER he was initially sleepy, disoriented, bradypsychic, uncooperative, without meningeal signs or neurological focus; Eupneic, SpO₂: 93%, vesicular murmur maintained without adventitious sounds; cardiac auscultation: arrhythmic and tachycardic sounds, heart rate: 139 bpm, BP: 120/80 mmHg, with sweating and cold extremities and slow capillary refill time.

The exams performed revealed the Computed Tomography of the skull without enhancement changes. Hb: 17.7 g/dL, WBC: 6.240/mm³, moderate thrombocytopenia of 69.000/mm³, Smear positive with parasitemia of 14.830p/mm³, Blood glucose (random): 166 mg/dL, C-Reactive Protein 180 mg/L, Creatinine: 1.1 mg/dL, Total Bilirubin: 4.28 mg/dL, COVID Ag test negative, Lactic Dehydrogenase: 283 U/L and D-Dimers: 926; The ECG showed atrial flutter with heart rate of 117bpm (Figure 1) and the following diagnoses were valued: malaria with hematological and hepatic dysfunction, Atrial flutter (with rapid response) and Arterial hypertension (referred diagnosis).

He was medicated with artesunate, bisoprolol, amiodarone and heparin, and later sent to the internment area, where an echocardiogram was performed, which revealed: Left ventricular hypertrophy (LVH), without cavities dilatation, Ejection fraction estimated at 50%. The patient showed clinical and laboratory improvement, with negative results in the blood smear and a decrease in inflammatory parameters.

Anticoagulation was maintained and he was discharged on the 4th day of hospitalization, medicated on an outpatient basis with bisoprolol, candesartan and dabigatran, and 3

weeks later he returned to the LMC and underwent electrical cardioversion, without complications. After 9 months, the patient remains asymptomatic and

in sinus rhythm (Figure 2), and an echocardiogram revealed an Ejection Fraction of 58%.

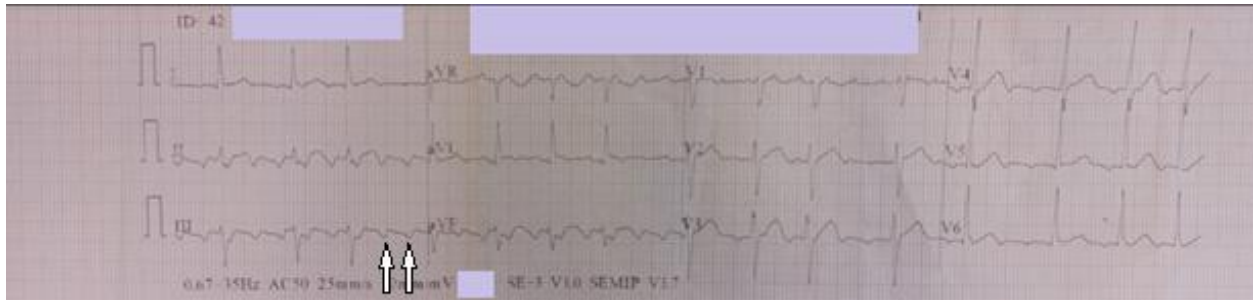


Figure 1. ECG: Atrial flutter, HR=117bpm (the arrows show flutters waves).

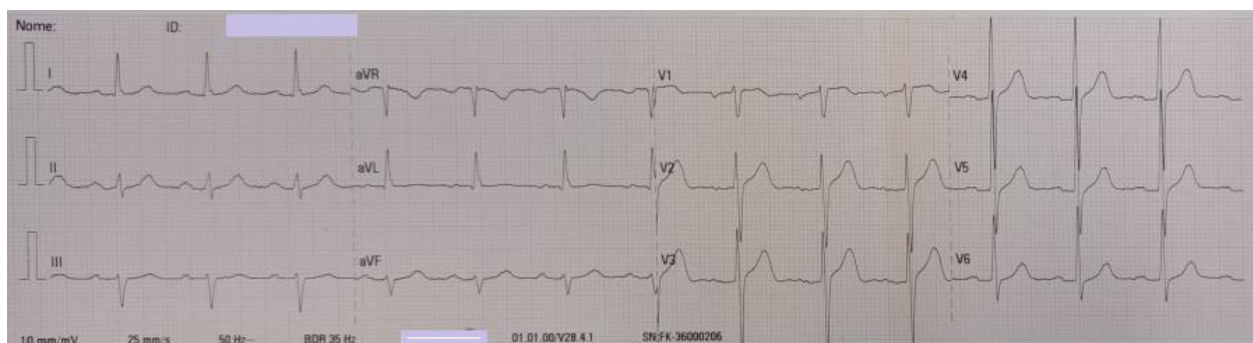


Figure 2. ECG: Sinus rhythm (after electric cardioversion).

Discussion and Conclusion

Complicated malaria can have specific cardiac complications, despite the small number of published cases, there are reports of conduction disorders/arrhythmias, myocarditis and pericarditis, cardiac tamponade and heart failure [7,8].

Atrial fibrillation and AFL are not common complications of malaria, and

from our research we did not find any case that related AFL to malaria.

Recent studies with endocardial mapping have shown that various forms of AFL represent forms of macro-reentry, mostly involving atypical isthmus in natural barriers, auricular incisions or tissue scarring, and even the cavotricuspid isthmus [16].

The patient's history reveals some risk factors for the development of AFL: hypertension, LVH and irregular

compliance with antihypertensive therapy. These risk factors associated with an infectious pathology in which there is an intense inflammatory response, with the release of cytokines, may have acted as a trigger for the emergence of AFL [5,10,11].

Treatment is based on heart rate control (calcium channel blockers, beta-blockers, amiodarone or digoxin) and then cardioversion, either pharmacological (with class Ia, Ic or III antiarrhythmics) or electrical. Electrical cardioversion should be immediate in the event of hemodynamic instability [14,17]. There are not many studies on anticoagulation, however, it is recommended that it be similar to the protocol adopted for atrial fibrillation. Immediate cardioversion should only be performed if the patient has an INR between 2 and 3 and if the flutter duration is less than 48 hours, or if the transesophageal echocardiogram excludes the presence of atrial thrombi [18]. Radiofrequency ablation to interrupt the re-entry circuit is increasingly used and may be an alternative for recurrent arrhythmias or those that do not respond to treatment [18].

In the case in question, the ECG revealed AFL, electrical cardioversion was successfully performed after 3 weeks with the patient anti-coagulated with dabigatran.

The importance of publishing this work lies in the fact that it addresses, in an unprecedented way, a rare association between AFL and an endemic and highly lethal pathology in our country, malaria, and draw attention to its possible cardiovascular complications.

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