

Clinical Features of COVID-19 and Malaria Coinfection Based on Two Cases in Central African Republic

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Abstract

The aim of this manuscript is to bring our experience from Central African Republic (CAR), an endemic malarial area, during the COVID-19 pandemic. We present two cases treated at MINUSCA level 2+ hospital in Bangui, central African republic, during December 2021 and January 2022. COVID-19 and malaria infection were confirmed by appropriate tests. First case is man, 36 years old, who came to hospital, complaining about muscle pain, headache and fever. Second case is a man, 41 years old, who came to hospital due to fever, chills and malaise. Symptoms started to appear a day ago. We can conclude that in malaria endemic areas, in light of existing COVID-19 pandemic, based on similar symptoms characteristic of both diseases, it is essential to suspect both diseases and keep in mind the possibility of coinfection. Therefore a patient with uncharacteristic infectious symptoms should be tested for malaria, so as well for COVID-19 infection.

Keywords: Headache • World Health Organization (WHO) • COVID 19 • Coughing

Introduction

In malaria endemic areas, the COVID-19 pandemic brings additional challenges. The symptomatology of both entities is very similar, and there is a significant diagnostic challenge from the clinician, appropriate diagnosis, and accordingly appropriate therapy. There are 380,000 laboratory confirmed malaria cases in the Central African Republic (CAR) each year, reporting by World Health Organization (WHO), but the actual number is probably higher due to high rates of asymptomatic cases [1]. In the Central African Republic with estimated population of 4.8 million people, malaria is considered to be responsible for as much as 40% of all reported illnesses and 10% of all registered deaths, especially in the pediatric population [2]. The prevalence of asymptomatic cases in pediatric population in rural parts of CAR is 35.6% [3]. There were 14,358 confirmed cases of COVID-19 with 113 deaths in CAR, from January 2020 to May 2022, reported to WHO [4].

The aim of this manuscript is to bring our experience from Central African Republic (CAR), an endemic malarial area, during the COVID-19 pandemic. We present two cases treated at MINUSCA level 2+ hospital in Bangui, central African republic, during December 2021 and January 2022. COVID-19 and malaria infection were confirmed by appropriate tests.

Case Presentation

First case

First case is man, 36 years old, who came to hospital, complaining about muscle pain, headache and fever. Symptoms were accompanied with nausea, stomach discomfort and productive coughing. Symptoms started to appear two days before the visit to the doctor. He was vaccinated against COVID-19 with one dose Oxford-AstraZeneca COVID-19 vaccine. Also he denied allergies on some food and medications, and also denied other chronic conditions. On the admission patient had 37.7°C, with vesicular

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breathing, without pathological swishing. SpO₂ was 98% on room air, RR 12 breaths/min. He had sinus rhythm, normotensive, with HR 97 bpm. COVID-19 Ag test on admissions was negative. Malaria

infection was confirmed by antigen based Rapid Diagnostic Test (RDT) Care Startm Malaria (HRP2) Ag (ACCESS BIO, USA), and malaria SMEAR test (Table 1 and Figure 1).

COVID-malaria coinfection	Patient 1	Patient 2
Gender	Male	Male
Age	37	41
Symptoms	Mucle pain, headache, fever	Fiver, caught and malaise
Temperature	37.7°C	37.2°C
Auskultatorial findings	Normal	Normal
X-ray of the chest	Laterally patchy zones of GGO on both sides present	Normal findings
RDT test for COVID	Negative on admission positive after six days	Positive on admission
Malaria RDT test	Positive on admission	Positive on admission
Malaria SMEAR test	Positive on admission	Positive on admission
COVID 19 imunisation*	One dose	Two doses

*Oxford-AstraZeneca COVID-19 vaccine, codenamed AZD 1222

Table 1. Sociodemographic and clinical characteristics in both patients.

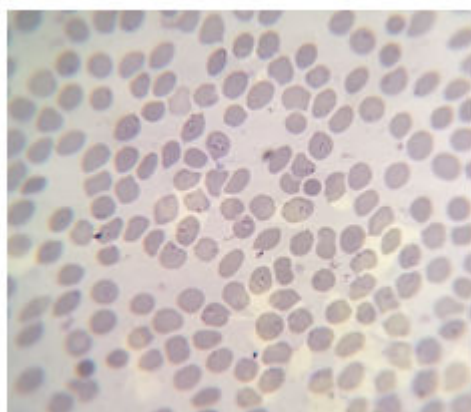


Figure 1. SMEAR test for patient 1.

Complete blood count, on admission: White Blood Cell (WBC) $9.5 \times 10^9/l$ (reference values from 4.0-10.0); Lymphocytes (Lymph) 14.3% (20.0-40.0%); mid cells 4.8% (3.0-15.0); Granulocytes (Gran) 80.9% (50.0-70.0); Red Blood Cell (RBC) $4.59 \times 10^{12}/l$ (3.50-5.50); Hemoglobin (HGB) 145 g/l (110-160); Hematocrit (HCT) 0.39 l/l (0.37-0.54); Platelet (PLT) $225 \times 10^9/l$ (100-380). After 10 days Complete Blood Count: WBC $25.3 \times 10^9/l$ (4.0-10.0); Lymph 9.3% (20.0-40.0%); Mid 5.8% (3.0-15.0); Gran 84.9% (50.0-70.0); RBC $4.95 \times 10^{12}/l$ (3.50-5.50); HGB 158 g/l (110-160); HCT 0.42 l/l (0.37-0.54); PLT $645 \times 10^9/l$ (100-380). Biochemistry Blood test on admission: Glucose 6.2 mmol/l (3.3-6.1); Urea 3.3 mmol/l (<8.1); Creatinine 88 mmol/l (<97); Aspartate Transaminase (AST) 94 U/l (<40); Alanine transaminase (ALT) 57 U/l (<40), Gamma Glutamyl Transferase (GGT) 46 U/l (10.0-71.0), C-reactive protein (CRP) 103.9 MG/L (0-6), potassium 3.3 mmol/l (3.6-5.0), Lactate Dehydrogenase (LDH) 630 u/l (105-245), Total Bilirubin (TBIL) 6.2 mmol/l (<21.0).

After six days of hospitalisation, and introduction of antimalarial therapy, since there was no improvement, we performed chest X-ray,

that showed laterally patchy zones of Ground Glass Opacity (GGO) on both sides of lungs, that can match the initial zones of COVID-19 pneumonia (Figure 2A). Therefore we repeated COVID-19 Ag test, and it was positive, so we induced anti-COVID therapy (corticosteroids and antibiotics). COVID-19 infection was confirmed by COVID-19 Ag test (SD Biosensor, S. Corea). X-ray of the chest, seven days after being hospitalized, showed on both sides laterally patchy zones of GGO. There were no signs of progression of previously findings (Figure 2B). Laterally patchy zones of GGO on both sides were seen on X-ray, 13 days after admission, but in regression (Figure 2C).



Figure 2. Chest X ray for patient 1: A) laterally patchy zones of GGO on both sides that can match the initial zones of COVID-19 pneumonia (6th day), B) laterally patchy zones of GGO on both sides without progression (11th day), C) laterally patchy zones of GGO on both sides in regression (14th day).

During hospitalization the patient was treated with antibiotics (Clindamycin 600 mg/8 h, Vancomycin 1 gr/12 h, Meropenem 500 mg/8 h), antimalarial drugs (Artemether amp. 3.2 mg/kg-1.6 mg/kg, tablets (Tbl.) Artemether/Lumefantrine 80/480 mg), gastro protection (Pantoprazole 20 mg/24 h) and low molecular weight heparin (Enoxaparin 0.6 ml/12 h), corticosteroids (Methylprednisolone 40 mg/12 h), rehydration and symptomatic therapy. This therapy improved his health condition.

Discharge medications: Tbl. pantoprazole 20 mg 2 × 1 30 minutes before meal for the following 10 days, Tbl. Levofloxacin 500 mg 1 × 1 for 5 days, Tbl. Doxycycline 100 mg 1 × 1 as malaria prophylaxis, caps probiotic 1 × 1 for the following 5 days, Tbl.

pronison 10 mg+5 mg for 3 days, 5 mg+5 mg for 3 days, 5 mg for 3 days. Follow up: This patient was discharged in good medical condition, with recommendation to be in self-isolation for another 7 days, and after that to do the PCR test for COVID-19.

Second case

Second case is a man, 41 years old, who came to hospital due to fever, chills and malaise. Symptoms started to appear a day ago. He was vaccinated against COVID-19 with two doses Oxford-AstraZeneca COVID-19 vaccine, and denied allergies on some food and medications, and also other chronic conditions. On admission the patient had 37.2°C, with vesicular breathing, without pathological swishing. SpO₂ was 95% on room air, RR 16 breaths/min. He had sinus rhythm, normotensive, with HR 76 bpm. RDT test for COVID-19 was positive on admission, as well as Malaria RDT test, and Malaria SMEAR test (Figure 3).

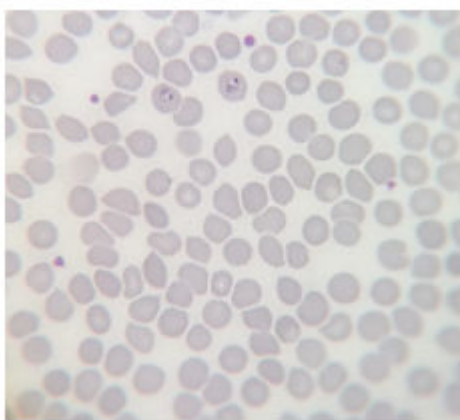


Figure 3. SMEAR test for patient 2.

Complete blood count, on admission: WBC $3.8 \times 10^9/l$ (4.0-10.0); lymph 24.8% (20.0-40.0); mid 5.9% (3.0-15.0); gran 69.3% (50.0-70.0); RBC $4.50 \times 10^{12}/l$ (3.50-5.50); HGB 137 g/l (110-160); HCT 0.37 l/l (37.0-54.0); PLT $125 \times 10^9/l$ (100-380). Biochemistry Blood test: Glucose 6.1 mmol/l (3.3-6.1); urea 3.3 mmol/l (<8.1); creatinine 87 mmol/l (<97); AST 62 U/l (<40); ALT 28 U/l (<40), GGT 46 U/l (10.0-71.0), LDH 222 U/l (105-245), Creatine Kinase (CK) 105 U/l (24.0-195.0); Creatine Kinase Myocardial Band (CK-MB) 4 U/l (0-5); potassium 3.4 mmol/l (3.6-5.0); amylase 82 U/l. X-ray of the chest: normal findings (Figure 4).



Figure 4. Chest X ray for patient 2: normal findings.

During hospitalization the patient was treated with antibiotics (Clindamycin 600 mg/8 h, Tbl. Levofloxacin 500 mg/12 h), antimalarial drugs (Artemether amp. 3.2 mg/kg-1.6 mg/kg, Tbl. Artemether/Lumefantrine 80/480 mg) gastro protection (Pantoprazole 20 mg/24 h) and low molecular weight heparin (Enoxaparin 0.6 ml/24 h), corticosteroids (Methylprednisolone 40 mg/24 h), rehydration and symptomatic therapy. This therapy improved his health condition.

Discharge medications: Tbl. Pantoprazole 20 mg 2 × 1 30 minutes before meal for the following 10 days, Tbl. Levofloxacin 500 mg 1 × 1 for 5 days, Tbl. Doxycycline 100 mg 1 × 1 as malaria prophylaxis, caps probiotic 1 × 1 for the following 5 days, Tbl. pronison 10 mg+5 mg for 3 days, 5 mg+5 mg for 3 days, 5 mg for 3 days. Follow up: This patient was discharged in good medical condition, with recommendation to be in self-isolation for another 7 days, and after that to do the PCR test for COVID-19.

Results and Discussion

In areas with endemic tropical diseases such as malaria, the COVID-19 pandemic brings additional diagnostic challenges. Due to similarity of the symptomatology of both entities, COVID-19 and malaria, it can be difficult for clinicians, in case of coinfection, to set proper diagnosis and start with appropriate therapy. Fever, myalgia, difficulty in breathing, fatigue and acute onset headache are the symptoms which are common for COVID-19 and also for malaria, so it is difficult to make a distinction based only on the clinical picture [5]. For physicians in areas with endemic tropical diseases, such as malaria, it is important to keep in mind possible co-infection [6]. This approach can be of great importance, because diagnosing co-infection will enable the inclusion of adequate antimalarial therapy, along with adequate symptomatic therapy, according to current recommendations. Since the malaria is a febrile illness with the most common symptoms of uncomplicated type such as fatigue, headaches, muscle aches, malaise, abdominal discomfort, fever, nausea and vomiting [7], definitive diagnosis can be established only by RPD test, PCR test and by the microscopic blood examination, which is a “gold standard” [8]. On the other hand, the most common symptoms COVID-19 are respiratory symptom such as cough, sputum, shortness of breath, and fever; a musculoskeletal symptom such as muscle and joint pain, headache, and fatigue; and digestive symptoms with abdominal pain, vomiting, and diarrhea [9]. Diagnosis can be definitely established by RPD and PCR test [10].

We presented two patients with a similar clinical picture who reported to the UN hospital in Bangui, CAR, in December 2021 and January 2022, respectively. Those were men, aged 37 and 41 years. The first patient came due to muscle pain, headache, fever (37.7°C). There were normal auscultatory chest findings. On chest X-ray, there were laterally patchy zones of GGO on both sides that could match the initial zones of COVID-19 pneumonia. On admission, RPD test for COVID-19 was negative, but positive after three days. RPD malaria test was positive on admission, also as SMEAR test. Laboratory findings on admission were: Lymph 14.3%, Gran 80.9%, glucose 6.2 mmol/l, AST 94 U/l; ALT 57 U/l, CRP 103.9 MG/L, potassium 3.3 mmol/l, LDH 630 u/l. After 10 days laboratory findings were: WBC $25.3 \times 10^9/l$; lymph 9.3%, gran 84.9%; PLT $645 \times 10^9/l$. During hospitalization, the patient was treated with antibiotics, antimalarial drugs, gastro protection, and low molecular weight heparin, corticosteroids, rehydration and symptomatic therapy. This therapy

improved his health condition, so after 13 days there were regression of chest X-ray findings. We discharged patient with antibiotics, corticosteroids and gastro protection therapy (Figure 5).

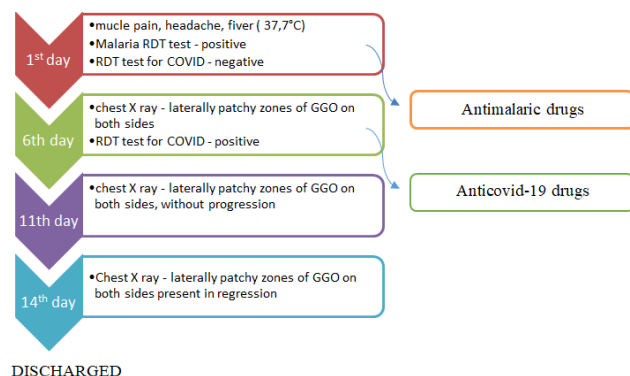


Figure 5. Timeline for first patient during the hospitalization.

The other one came due to caught, malaise and fever (37.2°C). There were normal auscultatory and X ray chest findings. On admission, RPD test for COVID-19 was positive, so as RPD malaria test. Laboratory findings were: WBC $3.8 \times 10^9/l$, AST 62 U/l; potassium 3.4 mmol/l. During hospitalization, the patient was treated with antibiotics, antimalarial drugs, gastro protection, and low molecular weight heparin, corticosteroids, rehydration and symptomatic therapy. This therapy improved his health condition, and he was discharged with antibiotics, corticosteroids and gastro protection therapy.

In both patients, we applied tests for both malaria and COVID-19 for admission, based on the general infectious picture, on the fact that we were in an endemic malarial area, because there was a COVID-19 pandemic. Therapy was antimalarial drugs, recommended antibiotics and symptomatic therapy for COVID-19, as gastro-protective therapy. This resulted in the complete recovery of both patients and their discharge.

Both patients denied chronic diseases as well as allergic reactions. The first patient, who developed a picture of pneumonia, characteristic of COVID-19 infection, received only one dose of vaccine against COVID-19 infection. On the other hand, the patient who did not develop pneumonia was immunized with two doses. In both cases, it was the same vaccine (Oxford-AstraZeneca COVID-19 vaccine, codenamed AZD 1222).

Conclusion

We can conclude that in malaria endemic areas, in light of existing COVID-19 pandemic, based on similar symptoms characteristic of

both diseases, it is essential to suspect both diseases and keep in mind the possibility of coinfection. Therefore a patient with uncharacteristic infectious symptoms should be tested for malaria, so as well for COVID-19 infection.

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