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Coronavirus Pandemic

Co-infection of COVID-19 and recurrent malaria

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Abstract

In tropical countries, endemic diseases such as malaria can be challenging to distinguish from COVID-19 because of the similarities in presenting symptoms. Here we reported a case of a young soldier with fever and myalgia six days before admission, with non-productive cough, chills, nausea and vomiting, dizziness, and headache for two days. Previously, he had experienced four times of malaria infection. He had a history of positive non-falciparum malaria rapid diagnostic test (RDT) two days before admission. Significant findings were epigastric tenderness, splenomegaly, and severe thrombocytopenia of 36×10^3 cells / μL. A naso-oropharyngeal swab examination revealed a positive SARS-CoV-2 infection. Consequently, he was hospitalized for 12 days, successfully treated, and discharged without sequelae. Thus, in light of a pandemic, physicians need to raise the suspicion of concurrent COVID-19 infection with other tropical diseases, especially at-risk patients, because malaria and COVID-19 may share similar manifestations. Moreover, further ancillary testing, such as RDT, may be warranted.

Key words: COVID-19; SARS-CoV-2; malaria; co-infection.

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Introduction

In tropical countries, due to spikes in the number of coronavirus disease of 2019 (COVID-19) cases, there is a sudden shift in public health focus from the ongoing war with tropical diseases like tuberculosis and malaria to this relatively novel respiratory disease. Consequently, this circumstance will undermine years of effort to curb the incidence of the aforementioned diseases. Furthermore, they can be difficult to distinguish from COVID-19 because of the similarities of presenting symptoms [1]. Also, they can present as a co-infection with COVID-19, which undoubtedly will negatively affect the patient's prognosis. Here we report a case of a patient coinfected with COVID-19 and malaria, which is successfully treated and discharged.

Case Illustration

A previously healthy soldier, a 24-year-old Indonesian male, came to the emergency department of a district hospital in Gorontalo with fever and myalgia six days before admission. He also complained of a non-productive cough, chills, nausea and vomiting, dizziness, and headache for the last two days. He recently travelled from an endemic region (Jayapura, Papua Province) and with a positive result of non-falciparum malaria rapid diagnostic test (RDT) two days before admission. He had a history of negative severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) rapid test, six days before admission, which is mandatory for inter-island travel. During his voyage on a ferry, he was exposed to his comrade who was having mild symptoms of upper respiratory tract infection and non-productive cough. His previous medical history was remarkable only for recurrent malarial infection (four times), with complete resolution of symptoms for each episode of infection. Moreover, he denied ever taking an antimalarial agent prophylactically.

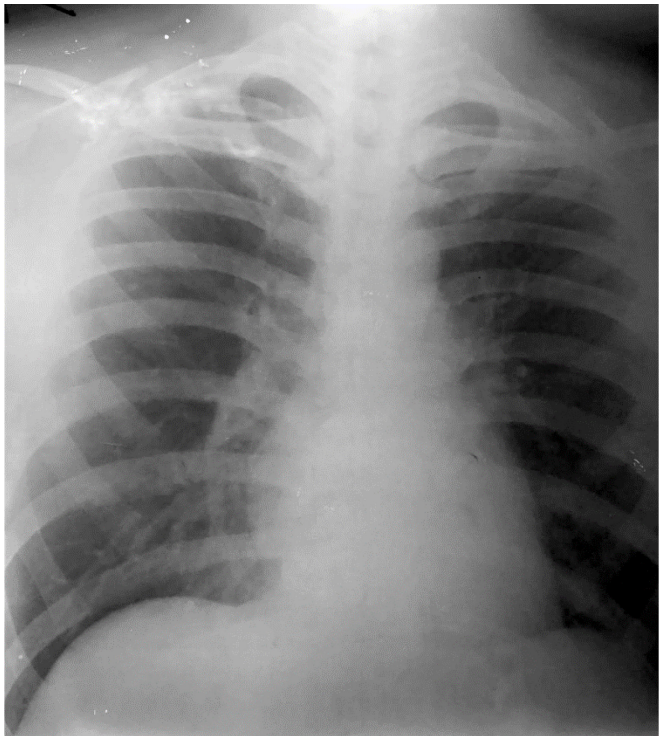
On physical examination, his body temperature on admission was 36.8 °C 2 hours after self-taking antipyretic medication. Other vital signs were within normal limits. The only remarkable physical examination was epigastric tenderness on palpation, with a numeric rating scale (NRS) of 4/10 and splenomegaly. His laboratory results on the first day of admission were significant for severe

thrombocytopenia with a count of 36×10^3 cells / µL. Other haematology indices were within normal limits (Table 1). Although the Widal titer for *Salmonella* Typhi was high, antityphoidal agent was not given as patient's clinical features did not reflect ongoing typhoid disease.

Chest X-ray revealed unilateral right paracardial infiltrates (Figure 1). He was managed as a case of recurrent non-falciparum malaria infection and a standard regimen of dihydroartemisinin + piperaquine (DHP) 4 tablets per day for three consecutive days and primaquine one tablet once daily (QD) for fourteen days were started, per the World Health Organization (WHO) guidelines for the treatment of malaria [2]. Based on the early warning score for COVID-19 screening, which is an amalgamation of scores derived from several studies, his score was 15 in total (highly suggestive) (Table 2).

The subsequent naso-oropharyngeal swab specimen examination with Xpert® Xpress SARS-CoV-2 (Cepheid, Sunnyvale, CA, USA) GeneXpert® revealed positive SARS-CoV-2. Consequently, he was admitted to the isolation ward and received oseltamivir 75 mg twice daily (BID) for ten days and azithromycin 500 mg QD for seven days to treat his respiratory symptoms and atypical pneumonia. During hospitalization, he had no episode of spike fever, nor dyspnea. Thick and thin blood smear were performed at the sixth-day of hospitalization showed polychromasia and low platelet count, without any stages of plasmodium were found. This was, presumably, because of the anti-malaria treatment being started since the day of admission. Repeated malaria RDT after seven days from the initial test was confirmed as negative.

Figure 1. Posteroanterior (PA) Chest X-Ray Film. The patient's PA chest x-ray showed right paracardial infiltrates.



Commensurately, after the course of treatment ended, the fever and the epigastric pain have entirely resolved. Upon discharge, complete blood count showed normalization of platelet count (Table 1; upon discharge). Follow-up PCR test for SARS-CoV-2 on the sixth day and eleventh day hospitalization were negative results. The patient was then discharged to a quarantine facility for twelve day isolation (Figure 2).

Table 1. Blood test (on the day of admission and discharge).

Test	Result (Day on admission)	Result (Upon discharge)	Reference values
Haemoglobin	14.9 g/dL	15.5 g/dL	13.5 - 18
Leukocyte	7,400/µL	7,100/µL	4,000 – 10,500
Neutrophil	55%	66.8%	35 - 70%
Lymphocyte	36%	23%	20 - 50%
NLR	1.5	2.9	
Thrombocyte	36×10^3/µL	171×10^3/µL	150,000 – 450,000
Hematocrit	44.9%	44%	40 - 50
SGOT	19 µ/L		< 31
SGPT	20 µ/L		< 31
Random Glucose	74 mg/dL		< 140 mg/dL
Widal Test			
Salmonella Typhi O	1/80		Negative
Salmonella Paratyphi O	1/160		Negative
Salmonella Typhi H	1/320		Negative
Salmonella Paratyphi H	Negative		Negative

Discussion

The ongoing COVID-19 pandemic is an additional challenge dealing with other tropical infectious diseases, including malaria. Both malaria and COVID-19 may share similarities of signs and symptoms consisting of fever, myalgia, difficulty in breathing, fatigue and acute onset headache [3]. Thus, others have warned the possibility of syndemics, i.e., the co-existing pandemic of both diseases [4]. In our case, the patient was admitted due to COVID-19 and concurrent malaria infection. The patient came from Papua Island. It is one of the notoriously known regions with the highest malaria prevalence in Indonesia [5].

A clinical diagnosis of malaria is based on the typical symptoms of fever (or history of fever in the last 48 hours and no other evident cause of fever), chills, headache, nausea, vomiting, myalgia, and malaise [6]. On the contrary, COVID-19 disease has the average time from exposure to symptom onset of 5 days, and 97.5% of people who developed symptoms do so within 11.5 days, after asymptomatic stage in 1-2 days. The most common symptoms are fever, dry cough, and shortness of breath [7]. A rapid diagnostic test is the main method for laboratory diagnosis of malaria infection, with subsequent blood smear examination to confirm it [8]. Similarly, SARS-CoV-2 infection can be easily detected through a rapid diagnostic test.

Nevertheless, these diagnostic tests may not be readily available in periphery district hospitals in non-endemic regions, like Gorontalo. Therefore, promotive and preventive efforts to curb the incidences of the diseases should be emphasized. Should hyperendemic occurs, pharmacological malaria prophylaxis and distribution of insect-treated bednets (ITNs) can be deployed [9]. Furthermore, the scarcity of rapid diagnostic tests underscores the importance of prioritization, which patients should be tested. Predictive models for COVID-19 diagnosis are promising regarding this; However, currently none is endorsed for this purpose [10]. Thus, we believe that thorough history taking, travel history in particular, and physical examination, compliment with knowledge regarding region's endemicity should guide the prioritization of whom to test for COVID-19 and malaria.

In our case, patients received standard regimen for malaria, oseltamivir, azithromycin and other symptomatics. The fever abates after 48 hours of DHP treatment. In most patients with confirmed SARS-CoV-2 infection, bacterial co-infection has been reported in

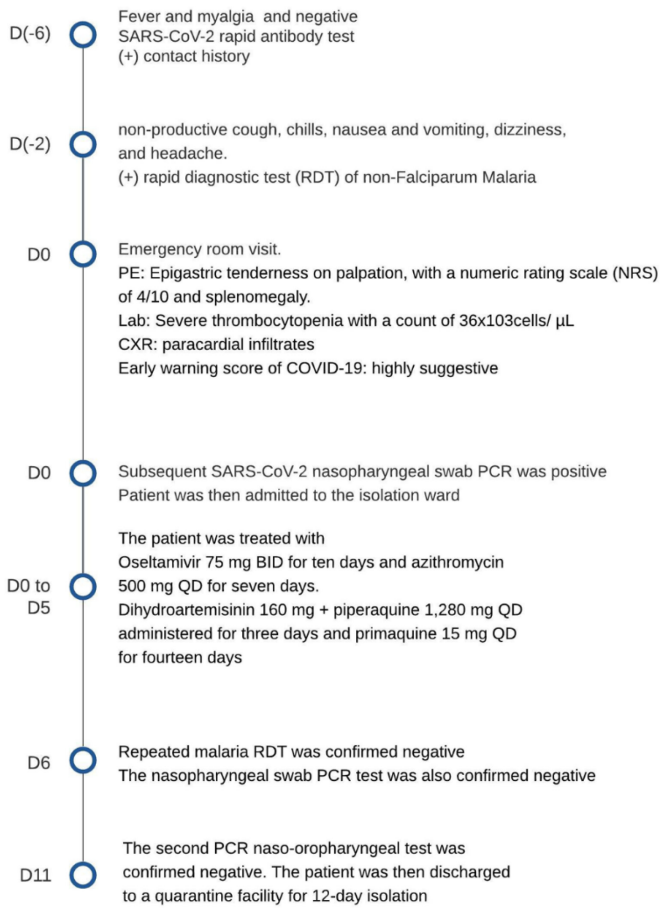
Table 2. Scoring System of Suspected COVID-19 at the Emergency Room.

Number	Parameter	Score	Other Additional Information	Status
	History			
1.	History of close contact or from endemic area of COVID-19 or	5	Evaluate one of the parameters	✓
	History going out without using mask more than 30 - 120 minutes	3	Evaluate one of the parameters	
2.	Fever / History of fever in the past 7 days	3	History of shivers or chiils	✓
3.	Cough	2		✓
4.	Dyspnea	1		
5.	Myalgia / fatigue / headache / odinophagia / nasal congestion / chest pain	0.5	0.5 for one of any symptom	✓
6.	Male gender	0.5		✓
7.	Age over 40 years	1		
	Physical Examination			
8.	Temperature > 38 °Celsius	1	Observe	
	Thorax ~ there's rhonchi on auscultation	-	Suggestion: Chest X-ray	
	Laboratorium			
9.	WBC / neutrophil normal - low count	1	Symptoms on less than 5th-6th day	✓
10.	Low lymphocyte < 10% or	2	Evaluate one of the parameters	
	Low lymphocyte < 15%	1	Evaluate one of the parameters	
11.	Neutrophil to Lymphocyte ratio (NLR) > 5 or	1	Evaluate one of the parameters (symptoms on the > 6th day)	
	NLR > 3.5	0.5	Evaluate one of the parameters (symptoms on the > 6th day)	
12.	Thrombocytes are slightly decreased (100,000 – 200,000)	1	Any signs of bleeding ?	
	Radiologic Findings			
13.	Abnormal Chest-X-ray (abnormal with bilateral patchy shadowing / local patchy shadowing / ground glass opacity)	3	More specific on bilateral patchy	✓
14.	Thorax-CT-scan (ground glass opacity -GGO- / bilateral patchy shadowing / local patchy shadowing)	5	More specific on GGO	

several patients affected by COVID-19 pneumonia [11,12]. Thus, azithromycin was given to the patient. In addition, azithromycin possesses putative beneficial effects, such as antiviral and immunomodulation [11,12]. Nonetheless, large randomized clinical trials in United Kingdom and Brazil have failed to show the benefit of azithromycin in addition to standard care [13,14]. Oseltamivir was also given to this patient. Although no positive outcomes have ever been reported, early oseltamivir administration can reduce the duration of fever and the time from peak to decline in temperature of COVID-19 patients [15,16].

Although the initial enthusiasm for antimalarial drugs to treat COVID-19 was high and proven to be useful in vitro, they did not translate well in the clinical settings [17]. Thus, with the regimen for COVID-19 is still developing, and with many ongoing clinical trials under the WHO SOLIDARITY Trial, possible cures are yet to be seen.

Figure 2. Timeline of Patient's Clinical Presentation.



SARS-CoV-2: severe acute respiratory syndrome-coronavirus-2; RDT: rapid diagnostic test; NRS: numeric rating scale; CXR: chest x-ray; COVID-19: coronavirus disease of 2019; PCR: polymerase chain reaction; BID: two times daily; QD: once daily.

Conclusions

In light of an ongoing pandemic, physicians need to raise the suspicion of concurrent COVID-19 infection with other tropical diseases, especially at endemic regions, because they may share similar clinical presentations. Moreover, further ancillary testing, such as RDT, may be warranted.

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Authors' contributions

AP: Investigation, Data Curation, Writing – Original Draft; JH: Writing – Original Draft, Visualization; AC: Writing – Review, Editing and Supervision.

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