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Case Report

A pitfall of cognitive bias during the pandemic: Two cases of *Plasmodium falciparum* malaria coinfected or misdiagnosed with COVID-19

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ABSTRACT

We report two the cases of patients with imported *Plasmodium falciparum* malaria during the COVID-19 pandemic. One was coinfected with COVID-19 and the other was misdiagnosed with COVID-19; either way, the diagnosis of malaria was delayed. These cases suggest that physicians should beware of cognitive biases during pandemics and carefully evaluate febrile patients. Malaria should be considered in any febrile patient returning from a malaria-endemic area.

1. Introduction

The COVID-19 pandemic has greatly affected the epidemiology of other infectious diseases, especially imported infectious diseases [1,2]. In Japan, the number of cases of tropical diseases such as malaria and dengue reported each year has decreased because fewer people are traveling abroad and fewer travelers are visiting Japan [3,4]. As a result, physicians in Japan are less likely to encounter cases of these tropical diseases.

The COVID-19 pandemic has also had a significant impact on the diagnosis and management of febrile patients [5]. The diagnosis of COVID-19 in febrile patients has been prioritized, often resulting in other febrile illnesses being overlooked. Numerous cases that were initially misdiagnosed during the COVID-19 pandemic have been reported. Cognitive biases such as anchoring or premature closure have been shown to contribute to these misdiagnoses in some cases [6]. Diagnostic errors caused by cognitive biases during the pandemic could lead to fatal outcomes in patients with malaria because *Plasmodium falciparum* malaria needs to be diagnosed and treated as early as possible.

Here, we report two instructive cases of patients with imported *P. falciparum* malaria initially diagnosed with COVID-19 during the Omicron variant era.

2. Case report

2.1. Case 1

A 64-year-old Japanese woman with a medical history of diabetes mellitus, hypertension, spinal cord injury, and indwelling urinary catheter-associated pyelonephritis caused by extended-spectrum β-lactamase *Escherichia coli* returned to Japan from Nigeria four days before admission. She had been stayed in Nigeria for a month to visit her friends and relatives. The SARS-CoV-2 antigen test was negative on arrival, and she stayed in the designated hotel under the quarantine act. Two days before admission, she experienced general malaise and her polymerase chain reaction (PCR) test for SARS-CoV-2 was positive. She had a fever and hypotension and was transferred by ambulance to the Japanese Red Cross Narita Hospital. She had not taken chemoprophylaxis for malaria. She did not use repellents either and was occasionally bitten by mosquitoes. On admission, her vital signs were as follows: blood pressure, 94/62 mmHg; heart rate, 100 beats/min; body temperature, 36.2 °C; respiratory rate, 24 breaths/min; oxygen saturation on room air, 96%. Her physical examination was unremarkable. Laboratory tests revealed anemia (hemoglobin level of 10.4 g/dL), thrombocytopenia (platelet count of 40,000 cells/L), and elevated inflammatory marker levels (C-reactive protein level of 7.65 mg/dL). Urinalysis showed pyuria and bacteriuria. Her chest CT scan showed no evidence of pneumonia. Sotrovimab and meropenem were started for COVID-19 and

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possible pyelonephritis. On hospital day 2, she was started on remdesivir and dexamethasone for hypoxia. On hospital day 3, her fever persisted and her peripheral blood smear showed *P. falciparum*-infected erythrocytes with a parasitemia index of 0.5%. A rapid immune chromatographic test (BinaxNow Malaria Test; Abbott, IL, USA) for *P. falciparum* was positive. *P. falciparum* infection was later confirmed using PCR. Artemether/lumefantrine was administered for 3 days. On hospital day 5, meropenem was discontinued because the blood culture was negative, and the urine culture did not grow any significant pathogen. The parasitemia index decreased to <0.1% on hospital day 7. She made a full recovery and was discharged on hospital day 13.

2.2. Case 2

A 38-year-old man with no significant medical history returned to Japan from Togo and Nigeria, where he had stayed for two weeks for work, 18 days before admission. One week before admission, he developed a fever and went to a nearby hospital where he tested negative for SARS-CoV-2 PCR; however, he was clinically diagnosed with COVID-19 when he reported that several coworkers in his company recently had COVID-19. He was advised to stay at home in isolation under the observation system of the public health center. His fever continued and his consciousness deteriorated. The day he was admitted, a policeman found him unable to move in his room, and he was transferred by ambulance from another hospital to the Japanese Red Cross Narita Hospital. On admission, his vital signs were as follows: blood pressure, 126/82 mmHg; heart rate, 125 beats per minute; respiratory rate, 31 breaths per minute; oxygen saturation on room air, 98%; temperature, 40.2 °C. His physical examination revealed conjunctival icterus and jaundice of the skin. Laboratory tests revealed anemia (hemoglobin level of 9.4 g/dL), thrombocytopenia (platelet count of 26,000 cells/L), hyperbilirubinemia (total bilirubin level of 21.2 mg/dL), and elevated inflammatory marker levels (C-reactive protein level of 25.75 mg/dL). Malaria was suspected based on his travel history and symptoms. His peripheral blood smear showed *P. falciparum*-infected erythrocytes with a parasitemia index of 7.2%. A rapid immunochromatographic test (BinaxNow Malaria Test; Abbott, IL, USA) for *P. falciparum* was positive. *P. falciparum* infection was later confirmed using PCR. He was treated with intravenous quinine for three days, followed by artemether/lumefantrine for three days. He made a full recovery and was discharged on hospital day 8.

3. Discussion

These two cases suggest that the COVID-19 pandemic could significantly affect the diagnostic process of other fatal febrile diseases. Careful evaluation should be performed, especially in febrile patients with a recent history of travel to malaria-endemic areas. Malaria should be considered as a differential diagnosis because malaria, especially *P. falciparum* malaria, is fatal if not diagnosed and treated promptly. Obtaining a recent travel history for all febrile patients and identifying malaria-endemic areas are key clinical strategies for suspected malaria. This principle in travel medicine would be the same or even more critical in the COVID-19 era.

Case 1 suggests that concurrent conditions should be carefully evaluated in patients with known COVID-19. Concurrent infection with COVID-19 and malaria is common in malaria-endemic countries, and coinfection with COVID-19 and malaria has been reported to be associated with increased mortality compared to mono-infection with COVID-19 [7]. Furthermore, the clinical symptoms of COVID-19 such as fever, headache, respiratory symptoms and general weakness overlap with those of malaria, making it very difficult to differentiate between the two [8]. In case 1, the diagnosis was more challenging because the patient had an indwelling urinary catheter and a history of recurrent pyelonephritis. A confirmed diagnosis of COVID-19 and a possible diagnosis of pyelonephritis led to a premature closure bias that delayed the correct diagnosis of malaria. Finally, her thrombocytopenia reminded us to suspect concurrent malaria infection, suggesting that testing for malaria should be done immediately when any sign or symptom is inconsistent with the primary diagnosis.

Case 2 suggests that cognitive biases such as anchoring could lead to serious misdiagnosis during the COVID-19 pandemic. Anchoring bias is a type of cognitive bias that refers to the distortion of judgment by overemphasizing certain types of information. In the present case, the patient explained his travel history to Africa when he visited the medical facility, and the test for COVID-19 was negative. However, the patient's travel history was ignored and a fatal disease such as malaria was overlooked because the doctor was so focused on the possibility that he was in contact with COVID-19 patients.

Misdiagnosis has been reported not only during the COVID-19 pandemic but also during the 2009 H1N1 influenza pandemic. Lucy et al. reviewed 16 eligible studies and identified 686 misdiagnoses with 97 final diagnoses [6]. In their systematic review, respiratory infections accounted for the majority (72%), and nonrespiratory infections (14%) and noninfectious diseases accounted for the remainder (14%). They also found that cognitive biases directly affected diagnostic processes in four articles. This study suggests that physicians should be cautious about cognitive biases and carefully distinguish the suspected pandemic disease from other diseases that are differential diagnoses during pandemics.

In conclusion, we encountered two patients with *P. falciparum* malaria, one coinfected with COVID-19 and the other misdiagnosed with COVID-19. Physicians should beware of cognitive biases during the pandemic and carefully evaluate febrile patients. Malaria should be considered as a differential diagnosis of any febrile patient returning from a malaria-endemic area.

Ethical approval

Intravenous quinine (Quinimax®) was used in case 2 after obtaining informed consent to participate in the study "Efficacy and safety of injectable quinine in malaria patients (injectable quinine for malaria)" by the Development of Optimal Medical Care Network for the Diagnosis and Treatment of Tropical and Parasitic Diseases in Japan.

Written informed consent for the publication of this report was obtained from the patients.

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Authorship statement

All authors met the ICMJE authorship criteria; HM and RH conceived the study. HM, RH, HU, NT, MF, NM, EM, TK and YY were involved in the patients' care. HM and RH drafted the first manuscript. All authors critically reviewed the manuscript and approved the final version to be published.

Declaration of competing interest

None.

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