Pandemic-related delay of falciparum malaria diagnosis in a traveler leading to cerebral malaria

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Running title: Cerebral malaria with CLOCC in a homecoming traveler

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Highlight

We report the case of a 29-year-old male in whom COVID-19 concerns led to a delayed diagnosis of falciparum malaria. The patient developed symptoms of cerebral malaria with cytotoxic lesions of the corpus callosum (CLOCC) in magnetic resonance imaging (MRI).

Case report

A 29-year-old man was admitted to our ward due to muscle weakness, fatigue, nausea, vomiting and recurrent febrile episodes. The patient arrived from Zanzibar three weeks earlier, where he visited his family. He did not seek pre-travel advice or took any malaria prophylaxis. His symptoms started two weeks after arrival in Vienna, but he remained at home for another week as he was afraid of the ongoing Coronavirus pandemic. The patient was born in Zanzibar, but stayed in Austria for the last 10 years.

Clinical examination at admission revealed diffuse abdominal pain, scleral icterus as well as a subtle impairment of consciousness. A dark discoloration of the urine was noticeable. Laboratory analysis demonstrated thrombocytopenia (31 G/L; normal range, 150 - 350 G/L), anemia (hemoglobin 9.9 g/dl; normal range, 13.5 - 18 g/dl), acute kidney injury (creatinine 1.5 mg/dl; normal range, 0.70 - 1.20 mg/dL), elevated bilirubin (4.2 mg/dl; normal range < 1.2 mg/dl), lactate dehydrogenase (892 U/L, normal range < 250 U/L) and elevated C-reactive protein (16.1 mg/dl; normal range < 0.5 mg/dl). Thick and thin blood smears revealed *Plasmodium falciparum* infection with high parasitemia (Figure1). Intravenous treatment with artesunate 240mg (b.i.d.) and clindamycin 900mg (b.i.d.) was initiated. Shortly after admission, the patient became hypotensive (blood pressure, 80/50mmHg) and consciousness continued to deteriorate. He was transferred to an intensive care unit (ICU). Neurological examination showed a bulbar dysarthria and sixth nerve palsy. MRI demonstrated a well-defined FLAIR- and T2-hyperintense, non-enhancing lesion in the splenium of the corpus callosum. The lesion showed restricted diffusion, consistent with the cytotoxic lesion of the corpus callosum (CLOCC) (Figure 2a, b and c). Under treatment the clinical condition and neurological symptoms of the patient improved quickly and he was discharged from the ICU 2 days later. Artesunate treatment was continued for a total of 3 days, Clindamycin was ended after 7 days. On follow-up MRI, performed 25 days after discharge, a complete resolution of the CLOCC was noted (Figure 2d, e and f).

Discussion

Today, around 5500 cases of malaria are imported to EU countries per year, of which 10% progress to severe malaria.[1] Zanzibar reported 5146 cases of malaria in 2018.[2] Hence, malaria prophylaxis is recommended for travelers to Zanzibar. The reported patient did not seek pre-travel advice or took malaria prophylaxis, which is a frequently reported problem in travelers visiting friend and relatives (VFR).[3] An increase of severe malaria cases associated with a delay of diagnosis and treatment during the COVID-19 pandemic was recently reported from France.[4] The increased time between the onset of symptoms and malaria diagnosis in our patient was clearly attributable to his concerns about COVID-19, resulting in progression to cerebral malaria with development of CLOCC in MRI imaging.

CLOCC are secondary lesions reported in a wide range of cerebral infections.[5] In a series of children with cerebral malaria from Malawi CLOCC was the second most common finding of white matter diffusion restriction in MRI, however, similar lesions were shown to be present also in uncomplicated cases of imported malaria.[6] Thus, whether CLOCC clearly represents cerebral involvement or even precedes clinical deterioration in malaria remains to be elucidated. In all, this case demonstrates that access and provision of pre-travel healthcare for travelers VFR still has to be improved and that awareness of classic tropical diseases remains essential in times of a pandemic.[7]

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Author statement

Authors contribution

KM, ST and SW were responsible for patient care, LS and SW wrote the manuscript; MT, was responsible for preparation of MRI images; all authors have seen and approved the manuscript.

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Conflict of Interest/Disclosure

The authors have declared no conflicts of interest.

Figure legend

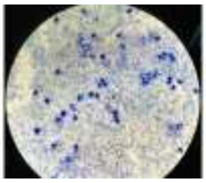

Figure 1: Thick blood smear demonstrates *Plasmodium falciparum* infection with high parasitemia. The black arrow shows a gametocyte of *Plasmodium falciparum*.

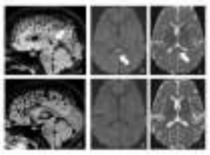

Figure 2: On sagittal FLAIR (a) a well-defined hyperintense lesion is detected in the splenium of the corpus callosum. Diffusion-weighted MR images (DWI) shows high signal on DWI (b) with corresponding low ADC (c), indicating diffusion restriction. The abnormality was consistent with cytotoxic lesion of the corpus callosum (CLOCC). Follow-up MRI 3 weeks later shows complete resolution of the abnormality (d-f).