

Visceral leishmaniasis in an Ethiopian patient with COVID-19: a case report

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Case Report

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Abstract

Background Coronavirus disease-19 (COVID-19) has dominated global health conversations within a short period of time. It can seem as if the hugely significant burden of infectious diseases, including visceral leishmaniasis, are no longer a public health issue. We discuss in this case the clinical and public health implications of COVID-19 and *Leishmania donovani* co-infection.

Case presentation An 18 years old male patient from Northwest Ethiopia diagnosed with COVID-19 and concomitant visceral leishmaniasis that ended in a fatal outcome. The rK39 rapid diagnostic test was positive, and the Giemsa stained bone marrow smears and culture confirmed the leishmanial infection.

Conclusion This young man's case demonstrated that the diagnosis and management of visceral leishmaniasis can be challenging in times of this pandemic. It is of crucial importance that clinicians have a high index of suspicion for a combination of COVID-19 and visceral leishmaniasis in endemic areas.

Background

Coronavirus disease-19, caused by *Severe acute respiratory syndrome coronavirus 2* (SARS-CoV-2), keeps claiming human lives while efforts to find vaccines have escalated. At the time of writing this manuscript (October 18, 2020), over 39.7 million cases and 1.1 million deaths have been reported globally (1).

Medical conditions associated with severity and death from COVID-19 includes diabetes, cardiovascular diseases, hypertension, pre-existing pulmonary disease and cancer (2). Little is known of co-morbidity from tropical infectious diseases.

Ethiopia is one of the countries with the highest burden of visceral leishmaniasis (VL), and the highest incidence of VL and HIV co-infection (3). The disease is widely distributed throughout the lowlands of the country especially in the north western, south western and south eastern regions.

Herewith, we report a case of COVID-19 with underlying VL in a patient from northwest Ethiopia. This is yet another co-infection of VL with a novel disease, that clinicians may find challenging to diagnose and treat.

Case Presentation

An 18 year old male patient presented with a 2 weeks history of recurrent high-grade fever with chills and rigors associated with extreme fatigue, loss of appetite and significant weight loss. He also complained of painful lower abdominal cramps and frequent loose stool. He showed no improvement with empiric anti-malarial and ceftriaxone treatment.

He had history of travel to leishmaniasis endemic area 6 months prior. He had no history of cough, hemoptysis nor tuberculosis. He never smoked cigarettes. His past medical history was unremarkable.

He tested positive for SARS CoV-2 rt-PCR from nasopharyngeal swab sample at the referring hospital where he first sought medical care. He was then transferred to Eka Kotebe covid-19 treatment center in Addis Ababa.

On admission physical examination, he was apathetic. His vital signs were: blood pressure 102/53 mmHg, pulse rate 110 beats per minute, respiratory rate 34, body temperature 38.4°C, and 90% oxygen saturation on room air. Conjunctivae were pale. He had shotty axillary lymphadenopathy and tipped splenomegaly.

Admission laboratory tests showed pancytopenia and hyperbilirubinemia. Serology for HIV, HBsAg and HCV Ab were negative. No hemoparasite was demonstrated on blood film. Peripheral blood smear showed normocytic normochromic anemia with no blasts (table 1 summarizes the lab tests).

While on care for severe COVID-19 (intranasal oxygen 3-4 liter per minute, dexamethasone 6 milligrams intravenously per day, prophylactic heparin and as needed paracetamol) and work up for the possible causes of cytopenia, he developed septic shock (fever with body temperature of 38.8 degree Celsius, change in mentation, tachycardia, hypotension and hyperlactemia). He was resuscitated, started cefepime and vancomycin, transfused with blood components, dexamethasone shifted to hydrocortisone 100 mg every 8 hourly, and vasopressor initiated together with other supportive care. Over 2 days, shock state was corrected. Pressor was de-escalated. He later required blood products transfusion and prophylactic antimicrobials due to the severe neutropenia. Plumpy'nut was also given for subjective global assessment C (severe) malnutrition. Over the subsequent days, he deteriorated with progressive liver dysfunction and bleeding.

As some of the clinical presentations was likened to VL, a request for leishmanial serologic test was made. The rK39 rapid diagnostic test (IT LEISH Rapid Test,4 Bio-Rad Laboratories) gave positive result. After obtaining verbal consent, bone marrow aspiration was performed. Examination of the Giemsa stained smear demonstrated amastigotes. Parasite density was very low (grade 1: 1-10 amastigotes/1000 fields of oil immersion). Culture of the bone marrow specimen in Novy-McNeal-Nicolle (NNN) medium grew promastigotes after 2 weeks of inoculation.

At the time, the diagnosis of VL presented a dilemma on treatment approach as the patient was already deteriorating. A difficult decision was made to use sodium stibogluconate (SSG) - the only anti-leishmanial available at the time. On point-of-care ultrasound examination, he was edematous with serosal effusions. He later became hypotensive. He was resuscitated, transfused with blood components, and antibiotics revised to meropenem for empiric coverage of hospital acquired infection. SSG was withheld after 2 doses. He unfortunately passed away from hemorrhagic bleeding and septic complications after 10 days of hospitalization.

Discussion And Conclusions

There are no specific clinical features that can reliably distinguish COVID-19 from other infections. The commonly reported clinical symptoms of COVID-19 infection includes fever, cough, chills and rigors, fatigue, diarrhea and abdominal pain. Lymphopenia and elevated liver enzymes are also common laboratory features (4). Most of these COVID-19 manifestations could also be a presenting feature of VL. Such diagnostic confusion could contribute to delayed diagnosis and treatment.

The literature on VL and HIV coinfection showing reciprocal impacts on pathogenesis, diagnosis and treatment is abundant. VL in HIV positive patients is an AIDS defining condition; and the co-infection is commonly found in endemic areas (5).

Even though this patient had some clinical features consistent with VL, parasitaemia was low. It is highly likely that the patient had asymptomatic *L. donovani* infection prior to SARS-CoV-2 exposure. One wonders if SARS-CoV-2 has the potential to reactivate latent *L. donovani* infections - reminiscent of what HIV does to asymptomatic infections of *L. donovani*. The corticosteroids used for covid-19 treatment could also contribute to immunosuppression resulting in VL reactivation.

The fact that this young patient with COVID-19 with no other co-morbidity, presented with VL and ended in a fatal outcome raises query about reciprocal impacts of the co-infection. In VL, plasma levels of cytokines and chemokines are high and contribute to cytokine storm (6, 7). Given this, it is conceivable that an underlying VL can exacerbate symptoms of COVID-19. Albeit anecdotal, it could suggest that VL could be added to the list of co-morbid conditions that predispose SARS-CoV-2 infected individuals to severe and fatal COVID-19.

This case illustrated that VL-COVID-19 co-infection could be challenging to diagnose and treat. In endemic regions, VL should be suspected in patients with COVID-19 infection. Like leishmania and HIV co-infection, SARS-CoV-2 and leishmania co-infection may prove to be a deadly gridlock. The incursion of SARS CoV-2 into VL endemic areas where HIV co-infection is also common can bring a profound immunopathological paradigm of triple co-infections. Epidemiologically speaking, the situation can turn dire in the face of the ongoing leishmaniasis control program.

Abbreviations

COVID-19: coronavirus disease 19

VL: visceral leishmaniasis

HIV/AIDS: human immunodeficiency virus/ acquired immunodeficiency syndrome

SARS CoV-2: severe acute respiratory syndrome coronavirus 2

rt-PCR: reverse transcription polymerase chain reaction

HBsAg: hepatitis B surface antigen

HCV Ab: hepatitis C virus antibody

NNN: Novy-McNeal-Nicolle medium

SSG: sodium stibogluconate

Declarations

Ethics approval and consent to participate: the IRB at the Eka Kotebe general hospital gave permission to publish the case report. Confidentiality has been maintained.

Consent for publication: Written informed consent was obtained from the patient's next of kin for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Availability of data and materials: All relevant data and materials are included in the manuscript.

Competing interests: the authors declare that they have no competing interests.

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Authors' contributions: MT, DK, HA, NG and HA: clinical diagnosis and management of patient. MT, DK and AH: parasitological diagnosis, designing, writing and editing of manuscript. All authors read and approved the final manuscript.

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Table

Table 1. *haematological and biochemical profile*

Test	Day 1	Day 2	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10
WBC (cells/ml)	2,700	2,100	1,900	870	1,500	1,070	2,020	2,500
Hgb (g/dl)	6.5	9.5	8.7	7.4	8.0	7.6	8.3	7.1
Platelet (cells/ μ l)	75,000	36,000	22,000	14,000	49,000	14,000	12,000	26,000
BUN (mg/dl)	13.0	16.0	11.0	-	-	-	15.0	15.0
sCr (mg/dl)	0.3	0.3	0.3				0.7	0.7
ALT (IU/L)	21.0	29.0	-	29.0	-	-	41.0	35.0
AST (IU/L)	113.0	214.0		166.0			307.0	299.0
ALP (IU/L)	247.0	273.0		368.0			372.0	234.0
Bilirubin [T/D], (mg/dl)	2.6/1.8	-		-			7.7/6.9	10.0/8.0
PT (sec)	16.0	-	-	-	64.0	20.0	-	-
INR	1.1				7.0	1.5		
aPTT (sec)	25.0				101.0	30.0		
Na (mEq/l)	130.0	132.0	-	133.0	-	139.0	129.0	127.0
K (mEq/l)	3.6	3.5		2.4		3.9	3.3	3.4
RBS (mg/dl)	109.0	71.0	64.0	58.0	54.0	47.0	120.0	110.0
Other tests	TSH = 2.5 mIU/L; Lipase 81 U/L; Amylase = 25 U/L; Uric Acid = 1.9mg/dl; LDH = 527 U/L; ESR = 60mm/hr; Urinalysis unremarkable.							

WBC = White Blood Cells; Hgb = Haemoglobin; BUN = Blood Urea Nitrogen; sCR = serum Creatinine; ALT = Alanine Transaminase; AST = Aspartate Aminotransferase; ALP = Alkaline Phosphatase; PT = Prothrombin Time; INR = International Normalized Ratio; aPTT = activated Partial Thromboplastin

*Time; Na = Sodium; K = Potassium; RBS = Random Blood Sugar; TSH = Thyroid-Stimulating Hormone;
LDH = Lactate Dehydrogenase; ESR = Erythrocyte Sedimentation Rate*