

## COVID-19 in a Patient with Visceral Leishmaniasis

Antonio Marco Miotti<sup>\*</sup>, Aria Patacca, Carmela Grosso and Francesco Cristini

Operative Unit of Infectious Diseases, Hospitals of Forlì and Cesena-AUSL, Romagna, Italy

<sup>\*</sup>Corresponding author: Antonio Marco Miotti, Unità Operativa di Malattie Infettive, Ospedali di Forlì e Cesena - AUSL Romagna, Italy, E-mail: antoniomarcomiotti@virgilio.it

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### Abstract

Visceral Leishmaniasis is an infectious disease caused by protozoans of Leishmania genus and transmitted by the bite of infected sand flies. Its course is fatal in the absence of appropriate treatment.

Coronavirus disease 2019 (COVID-19) is a respiratory tract infection, first detected in Wuhan, China, in December 2019 and subsequently spread worldwide as a pandemic. It is caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). In its most severe forms, it proves to be life threatening.

Hereby we report, to the best of our knowledge, the first case of COVID-19 in a patient with Visceral Leishmaniasis. He was a 79-year-old Italian male seeking medical attention because of sub-chronic fever associated with asthenia, lack of appetite, weight loss and pancytopenia. After a series of routine tests, the man underwent a bone marrow biopsy, which led to the diagnosis of Visceral Leishmaniasis. He was thus given liposomal amphotericin B, with moderate improvement of clinical conditions and laboratory exams. However, the hospital stay was complicated by COVID-19, since the patient tested positive for SARS-CoV-2 and developed severe interstitial pneumonia, thrombosis of the pulmonary vessels and possible alveolar hemorrhage. Due to multiple comorbidities, the options for Coronavirus treatment were extremely limited and death followed.

**Keywords:** COVID-19; SARS-CoV-2; Coronavirus; Visceral Leishmaniasis

### Introduction

Visceral Leishmaniasis is an infectious disease caused by protozoans of Leishmania genus and transmitted by the bite of infected sand flies. Although endemic in the Mediterranean basin, this parasitic infection has a low incidence in Italy, approximately of 0.2/100 000 [1-3].

Its clinical features include fever, hepatomegaly, splenomegaly, pancytopenia, progressive anemia, and weight loss. The course is fatal in the absence of appropriate treatment [1].

Coronavirus disease 2019 (COVID-19) is a respiratory tract infection, first detected in Wuhan, China, in December 2019 and subsequently spread worldwide as a pandemic. Its etiologic agent is Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), mainly transmitted by droplets and contact [4,5].

As of 16 June 2020, 237500 cases of COVID-19 occurred in Italy, with 34405 deaths [6,7]. We describe one, observed in a patient with a confirmed diagnosis of Visceral Leishmaniasis. To our knowledge, no similar cases have been reported so far.

### Case Report

In March 2020, a 79-year-old Italian male was admitted to our hospital because of sub-chronic fever associated with asthenia, lack of appetite, weight loss and pancytopenia. He had several comorbidities, consisting of ischemic heart disease (with previous acute myocardial infarction), hypertension, interatrial septal aneurysm, aortic root ectasia, dilatation of ascending aorta, selective erythroid aplasia and

myasthenia gravis. For this last condition was regularly taking cyclosporin.

On physical examination: mild dehydration, slight bibasilar crackles. Vital signs: heart rate 120 bpm, respiratory rate 24, blood pressure 90/60 mmHg, body temperature 38.3°C.

Laboratory tests revealed these alterations: hemoglobin (Hb) 11.6 g/dl, white blood cells (WBC) 1800/mm<sup>3</sup>, neutrophils (N) 1100/mm<sup>3</sup>, lymphocytes (L) 300/mm<sup>3</sup>, platelets (PLT) 76000/mm<sup>3</sup>; glomerular filtration rate (GFR) 28 ml/mn, serum, glutamic pyruvic transaminase (SGPT) 52 U/L; c-reactive protein (CRP) 138 mg/L [cut-off:<5.0], lactate dehydrogenase (LDH) 459 U/L [reference range: 132 – 225].

No hyper eosinophilia observed. Electrophoresis normal.

Blood and urine culture was negative, as well for routine serologic tests.

Nasopharyngeal swab for SARS-CoV-2 was also negative.

Computed tomography (CT) thorax abdomen scan showed moderate splenomegaly, slight pleural, pericardic and pelvic effusion. Transthoracic ecocardiography ruled out valve lesions.

A bone marrow biopsy was performed, finding amastigote forms compatible with Leishmania genus within the cytoplasm of histiocytes. The polymerase chain reaction (PCR) assay on both blood and medullary tissue was positive for Leishmania spp, as well as serologic tests.

Visceral Leishmaniasis was therefore diagnosed, and the patient given liposomal amphotericin B (days 1-5, with subsequent doses scheduled for day 14 and 21).

It followed defervescence, with mild to moderate improvement of clinical conditions and laboratory exams. The alteration of renal function remained stable, with GFR around 30 ml/mn, since adequate hydration had been administered.

A few days after, for one of the bedmates testing positive for SARS-CoV-2, the man underwent a second nasopharyngeal swab, which showed presence of Coronavirus.

Because of his status, an antiviral therapy was soon begun. Unfortunately, neither cloroquine, nor hydroxychloroquine, nor azithromycin could be used, since controindicated in myasthenia gravis. We therefore fell back on darunavir and ritonavir, and suspended cyclosporin.

The clinical course was bad, with feverish recurrence, confusional state and progressive respiratory failure. High resolution computed tomography (HRCT) chest documented multiple ground-glass opacities compatible with severe interstitial pneumonia and conspicuous pleural effusion. This same examination, suggestive of COVID-19, showed also a massive vascular enlargement of the pulmonary vessels, interpreted by radiologists as a picture of thrombosis with possible alveolar hemorrhage. It seems likely that such alterations were also due to SARS-CoV-2.

Moreover, PLT dropped to 11000/mmc, WBC reached 700/mmc, N 390/mmc, L 220/mmc, Hb 6.9 g/dl and international normalized ratio (INR) rose from 1.1 to 1.7. Finally, D-dimer, N-terminal pro b-type natriuretic peptide (NT-proBNP), inteleukin-6, procalcitonin and fibrinogen were respectively 35000 ug/L FEU [cut-off:<500], 33046 ng/L [rule in:>1800], 388 pg/ml [cut-off:>5.9], 40 ug/L [cut-off:>0.5.] and 77 mg/dl [reference range: 150 – 400].

Due to severe thrombocytopenia and coexisting acute infection/sepsis, immunomodulatory drugs as tocilizumab and canakinumab were ruled out. We therefore started high dosage steroid regimen (desametasone mg 20/die) besides supportive treatment consisting of red blood cells, plasma and platelets transfusions plus granulocyte colony stimulating factor (G-CSF). Empiric antibiotic therapy with piperacillin/tazobactam and vancomycin was also given. Sadly the patient developed multiple organ failure and died in three days.

## Discussion

Despite being a rare disease in the Mediterranean area, Visceral Leishmaniasis should be considered in the differential diagnosis of FUO with systemic engagement [2,8]. COVID-19 is instead a newly discovered respiratory tract infection, quickly spread worldwide because of its high contagiousness. In its more severe forms, it proves to be life threatening [4,5].

To our knowledge, the association between these two pathologies has never been reported so far, making exceptional the aforementioned case. Definitely, the severity of comorbidities and the state of

immunosuppression of the patient contributed to the acquisition of these two infections and aggravated their course.

Nevertheless, amphotericin therapy was well tolerated and led to defervescence, with mild to moderate improvement of clinical conditions and laboratory exams. Unfortunately, the therapeutic options available for the treatment of COVID-19 were instead extremely limited: as a matter of fact, neither cloroquine, nor hydroxychloroquine, nor azithromycin could be used, since control indicated in myasthenia gravis. And due to severe thrombocytopenia and coexisting acute infection/sepsis, also immunomodulatory drugs as tocilizumab and canakinumab were ruled out. In addition to severe interstitial pneumonia compatible with COVID-19, high resolution computed tomography (HRCT) chest documented a massive vascular enlargement of the pulmonary vessels, interpreted by radiologists as a picture of thrombosis with possible alveolar hemorrhage. It seems likely that such alterations were also due to SARS-CoV-2 [9].

Finally, the clinical course was bad, with feverish recurrence, confusional state and multiple organ failure, culminating in patient's death.

## Conclusion

The concomitance of Visceral Leishmaniasis and COVID-19 had never been reported so far. In our case, burdened by several comorbidities, it resulted fatal.

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