

## Case Report

# COVID-19 in a Patient with Multisystemic Langerhans Cell Histiocytosis

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## Abstract

The Pandemic by the new coronavirus (SARS-Cov2) has brought the almost impossibility of state of art management due to its fast spread and little knowledge. Indeed patients with rare diseases already suffer from lack of evidence. The only way to spread information on those two conditions is at this point are case reports. So we report a SARS-Cov2 infection in a patient with Multisystemic Langerhans Cell Histiocytosis with Lung Involvement, and also discuss common features of those diseases and possible implications.

**Keywords:** Histiocytosis; COVID-19; Langerhans

## Introduction

Langerhans Cell Histiocytosis (HCL) is considered an inflammatory myeloproliferative neoplasm and characteristically, has its origin in myeloid progenitors (with phenotype similar to the Langerhans Cell) mostly presents with hyperactive activation of the Ras-Raf-Mek-Erk pathway (approx. 60% with mutated BRAF600E). This hyper activation in addition together with several other mechanisms, including oncogene induced senescence, evolves into a responsible for with anti-inflammatory storm', responsible for and much of symptomatology [1,2].

It is a very rare condition in adults (prevalence of 0.07-0.27/100,000) characterized by infiltration of one or more organs by Langerhans-type dendritic cells and systemic inflammatory process, with extremely polymorphic clinical presentation, mainly affecting bones, skin, pituitary, lung, central nervous system, lymphoid organs and more rarely the liver and digestive system. Its evolution is very variable. It has a heterogeneous clinical course, from a disease can be fulminant disease with multiple organ failure to lesions, evolve chronically, but also regress spontaneously with spontaneous regression [3].

Declared on March 11, 2020 by the World Health Organization (WHO), the pandemic by the new coronavirus (SARS-CoV2) already figures as one of the major catastrophes in history with the possibility of collapse of health systems in several countries. It is a disease with a clear predilection for pulmonary involvement. Benign mostly asymptomatic or oligopauci-symptomatic, some patients may develop respiratory insufficiency that comprises from a large majority of asymptomatic or pauci-symptomatic patients to patients with respiratory failure. Requiring mechanical ventilation. The death rate is around .... 1% (ref), and can be higher in elderly patients with co-morbidities [4]. The prognosis of COVID19 in oncology patients with onco-hematological malignancies is uncertain, is poor and it has been a matter of intense research and debate recently [5,6]. Thus, we report the first case of multisystemic Langerhans cell histiocytosis (with extensive pulmonary involvement) and infection by the new SARS-CoV2 [7-10].

## Case Report

In April 2015, Male, 27 years old, a 27-year-old male patient in April 2015, the patient reported complaints reported of polydipsia and polyuria (15 L/day) and was diagnosed with Pan-Hypopituitarism and Diabetes Insipidus. In July 2018, the patient developed hemoptysis and spontaneous pneumothorax. Chest CT scan (ou coloca computadorizada tomography) showed multiple cavitations and pseudocysts throughout lung parenchima. After performing conventional thoracic drainage with improvement and subsequent lung biopsy was done, through thoracotomy, showing evidencing histopathological findings of extensive histiocytoid and mixed inflammatory cellular infiltrate with frequent eosinophils, hemorrhage, congestion and positive immunohistochemistry for CD1a and S100 Langerin, compatible with the diagnosis of HCL, at CT were seen pulmonary parenchima with multiple cavitation and pseudo cysts. Analysis of the somatic BRAF mutation (V600E) was negative [10-13]. In December 2018, after final confirmed diagnosis of multisystemic HCL, chemotherapy with Vinblastine and Prednisone was started but after first initiated. Quando iniciou? After a few months of treatment first cycle, a second pneumothorax developed, together with ventilatory insufficiency and 35 days at ICU. severe sepsis? Due to worsening clinical features. After discharge, infusion he developed a second spontaneous Pneumothorax, and was submitted again to conventional chest drainage and two pleurodeses, with ICU time and hospitalization time of 35 days. After hospital discharge, in January 2019, a new treatment with CCcladribine was considered for second line therapy. The patient (4 cycles) received 4 cycles with was initiated resulting in radiologic partial response but with clinical rapid imaging (partial response) and clinical improvement and was kept in follow-up without new treatment is being followed without treatment since then. In May 2020, he presented with dry cough, fever, high-intensity headache and ageusia, where the hypothesis of COVID-19 was raised. On the 5th day of the disease, chest CT was performed [14-16], which showed ground glass pattern with pulmonary involvement smaller than 25% and nasal swab RT-PCR for SARS-CoV2 was positive. After discussion with the patient, treatment with Enoxaparin 40mg SC, Azithromycin 500 mg. Prednisone 20 mg daily was initiated. He showed no warning signs

(decreased saturation and/or dyspnea had no oxygen desaturation and dyspnea) and 14 days after initial symptoms there was total resolution of the condition and absence of consolidative opacity or in “ground glass” in a new chest CT performed on 05/25/2020 (16<sup>th</sup> day of disease). Patient remains stable and asymptomatic so far.

## Discussion and Conclusion

The present case, is the first description of SARS-Cov2 infection in patients with multisystemic HCL and pulmonary involvement (in partial response) and, aims to discussion about the possible implications of COVID-19 in this rare group of patients [17-19].

Several respiratory viruses have their pathophysiology described in the literature with particularities ranging from the cell receptor that internalizes it, the primarily infected cell (epithelial, endothelial cells, alveolar macrophages) and the type of immune response triggered. It is presumed that a disbalance of pro and anti-inflammatory immune response, where a continuous pro-inflammatory immune response of the patient against viral replication is responsible for the greater severity of cases, in the case of COVID-19 some recent publications have already showed the increase in levels of pro-inflammatory cytokines (IL-6, IL-1, TNF-alpha), some of them being prospectively studied as a therapeutic target [20].

HCL is recognized as a mixed nosological entity, with classic findings of cell proliferation (neoplasia) such as hyperactivation of the Ras-Raf-Mek-Erk pathway, mostly by somatic mutations and the evolution of an inflammatory disease, and is known, especially in severe cases, to have a systemic pro-inflammatory state. The mechanisms responsible for inflammation are still little known, but Oncogene-Induced Senescence is believed to play a key role in ‘cytokine storm’.

Given the absence of evidence of current effective treatment for COVID-19, prednisone with azythromycin and enoxaparin were chosen and administered for 7 days. Although Despite having achieving the case reported, given the partial response to the treatment of HCL performed in 2019 with Cladribine, the with persistence of a viable disease with pulmonary involvement and the possible interaction between inflammation caused by HCL and pulmonary infection by the new SARS-Cov2 and being immunosuppressed due to cladribine treatment, the patient evolved well in the absence of evidence of current effective treatment for COVID-19, was chosen to start prednisone 20mg/day for 7 days, enoxaparin 40mg/day and azithromycin 500mg/day for 5 days, after heavy risk/benefit and discussed possible side effects with the patient. The evolution was benign, with complete improvement resolution of pulmonary images related to COVID-19, with no possibility of correlation between the proposed treatment and the favorable outcome.

## Conclusion

This is the first documented description of infection by the new SARS-Cov2/COVID-19 in a patient with HCL with extensive pulmonary involvement and, in this case, with a favorable outcome. Without the need for hospitalization.

Further studies, including the dosage of IL-6 on a as a research subject may provide more data on the possibility of inflammatory overlap between both pathologies. There is no recommended

treatment for COVID-19, and each case should be discussed in the light of the results of future clinical studies.

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