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POST-COVID 19 HISTOPLASMOSIS: A CASE REPORT

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ABSTRACT

Pulmonary histoplasmosis is a common endemic pathology, caused by the fungus Histoplasma capsulatum, which can be found in chicken coops, hollow trees and mines. The infectious process occurs through the aspiration of conidia and the proliferation of the fungus in the organism. Most of histoplasmosis is an asymptomatic and self-limited lung infection, but it can present a picture similar to pneumonia, evolving with headache, dyspnea, fever and dry cough. Its diagnosis consists of suggestive imaging tests, associated with laboratory tests that confirm the suspicion. Treatment consists of prescription of antifungal drugs for a long time and serial follow-up. Another common lung condition today is that caused by SARS-Cov-2, a pandemic pathology, with different manifestations from mild symptoms to severe acute respiratory syndrome. Its diagnosis ideally consists of associating symptoms with RT-PCR and imaging tests. The therapy used is symptomatic medication, corticosteroids and prophylactic anticoagulation, but still under study.

KEYWORDS: Histoplasmosis; COVID-19; Histoplasma capsulatum; SARS-CoV-2.

INTRODUCTION

Pulmonary histoplasmosis is a common endemic mycosis caused by the dimorphic fungus Histoplasma capsulatum, first described in 1905 in Panama.[1] The fungus can be found in places such as hollow trees, chicken coops, mines, water tanks, abandoned buildings in its mycelial form and, in infectious processes, in its yeast form.[2]

The infectious process occurs when conidia are aspirated and, for the most part, infections are mild or subclinical. When inhaled, the body temperature allows conditions for the germination of the fungus to occur and, subsequently, of its yeast format, which the macrophages will phagocytize.[3] Subsequently, they will proliferate, causing bronchopneumonia and, via the lymphatics, reach the lymph nodes, causing new inflammatory foci.[3,4]

Acute pulmonary histoplasmosis appears, in most cases, weeks after contact with the fungus - less than 5% of people who have had brief contact with the fungus develop the disease - as a condition similar to pneumonia, coursing with dry cough, asthenia, headache, severe chest discomfort after deep inspiration - fever, myalgia and anorexia. Most symptoms improve after a few weeks, however asthenia, fatigue and dyspnea can persist for months, especially in patients with the most aggressive manifestation of the disease.[5,6]

Lung injury is characterized by bronchopneumonia due to neutrophilic infiltration and recruitment of defense cells such as macrophages and lymphocytes. Chest radiographs, as well as computed tomography scans of the chest, show enlarged hilar and mediastinal lymph nodes with local infiltration, measuring approximately one to four centimeters in diameter, with the possibility of pleural effusion in certain patients with an acute condition. It is also possible to maintain suspicion with reports of nodules, cavitations, pericarditis associated with mediastinal lymphadenopathy, arthritis and arthralgia, erythema nodosum, superior vena cava syndrome or obstruction of other mediastinal structures.[7,8]

The most used and recommended diagnostic methods are histopathological examination of the tissue of the pulmonary or mediastinal lymph node, respiratory fungal cultures (they have low sensitivity), detection of antigen in urine or serum and serology - immunocomplementary

fixation test, immunodiffusion test and enzyme immunoassay.[9, 10.11]

Treatment for H. capsulatum infection varies according to the patient's clinical condition, which can manifest itself in a mild and self-limited manner, without the need for specific therapy. However, patients with persistent symptoms and those who are immunocompromised require antifungal medication due to the likelihood of developing the severe form of the disease. The most used drugs, for about 4 weeks to 24 months, are Itraconazole, Fluconazole (in cases of intolerance), Amphotericin B, the former being chosen for moderate cases and the latter for more severe conditions.[12]

Another lung condition that has hit the population on a large scale today, since 2019, leading to a worldwide pandemic, is SARS-CoV-2 infection. This can manifest itself through symptoms such as cough, fever, myalgia, headache, dyspnea, dysphagia, diarrhea, nausea or vomiting, ageusia and anosmia (coronavirus) depending on the severity of the disease (mostly mild) and the individual's comorbidities bearer.[13]

The risk factors for serious diseases, despite having the possibility of occurring in healthy individuals of any age group, are: increasing age, comorbidities such as cardiovascular diseases, diabetes mellitus, obesity, smoking, hematological diseases - such as sickle cell anemia - and disease chronic obstructive pulmonary disease. In addition to these, there is still a correlation with male gender and it has been observed that in the ABO group, blood type O is the one that presented the least severe symptoms.[14]

The test of choice for detecting the virus is RT-PCR using a nasopharyngeal swab sample and, when positive, confirmation by additional tests is not required (response). On the other hand, in cases with a negative result, the RT-PCR can be repeated in 24 hours or serology collected, if the status remains negative with an informative character, in search of reagent IgG for the disease.[15,16]

The ideal therapeutic management for SARS-CoV 2 infection is still uncertain and widely discussed, however, it has been seen that in patients with mild syndrome, therapy with symptomatic medications has been resolving and, in patients with severe disease syndrome, there are evidence in the use of corticosteroids and prophylactic anticoagulation.[17,18]

The objective was to report a case of infection with H. capsulatum after infection with SARS-CoV-2 - even after applying the two doses of the Coronavac vaccine - in curative treatment, through the use of Itraconazole, highlighting the characteristics of the fungal infection soon after prophylaxis against and viral infection, as well as diagnostic and therapeutic procedures.

CASE REPORT

Patient N.S.O., 22 years old, female, from Valença, Brazil, started clinical condition on 02/28/2021, complaining of measured fever, varying between 38ºC and 39.6ºC, and generalized arthralgia. He attributed the condition to the vaccine reaction, as he had received the 2nd dose of the vaccine (Coronavirus) for COVID-19 five days earlier. He attended the Emergency Room (ER) of the Hospital Escola Luiz Gioseffi Jannuzzi (HELGJ), Valença, Brazil where screening was carried out for a possible infectious focus, which was not evidenced. Conducted then as a vaccine reaction, antipyretics were prescribed and instructed to return if signs and symptoms worsened or persisted, in addition to reporting the adverse effect. The following week, he returned to the hospital, as he maintained the clinic. After further tests, she was diagnosed with a urinary tract infection and treatment with Amoxicillin with Clavulanate was started. However, the fever still persisted, leading to hospital admission on 03/12/2021 for investigation of fever of unknown origin.

Upon admission to the Internal Medicine ward, she reported the condition described above, associated with diarrhea, since the beginning of antibiotic therapy, dyspnea on exertion and headache in the occipital region. In the anamnesis, he denied smoking, alcoholism, risky sexual behavior, comorbidities, use of continuous medication and previous surgeries. She referred to previous hospitalization for abortion in February/2020 and generalized myalgia after non-intense physical exercise associated with elevation of Creatinophosphokinase (9510 U/L), in June/2020, but no specific pathology was diagnosed. He also reported that he had symptoms (non-productive cough, anosmia and ageusia) of COVID-19 in January/2021, the diagnosis being confirmed on 01/11/2021 through a positive RT-PCR swab, for which he used Azithromycin 500mg (1x/day, for 5 days), Ivermectin 6mg (2 tablets, single dose) and Dexamethasone 6mg (1x/day, for 7 days). On physical examination, no noteworthy changes were observed.

During hospitalization, an investigation was carried out to clarify the persistent febrile condition, through laboratory and imaging tests. Abdominal tomography showed no alterations, but the thorax was described with the following report: “Irregular opacity, with an irregular triangular appearance, with soft tissue density and adjacent ground-glass opacity, measuring 2.4 x 2.0 x 2 .1 cm, in the upper segment of the right lower lobe with corresponding pleural thickening / Hilar lymph node enlargement / Consider fungal etiology.” Figure A.

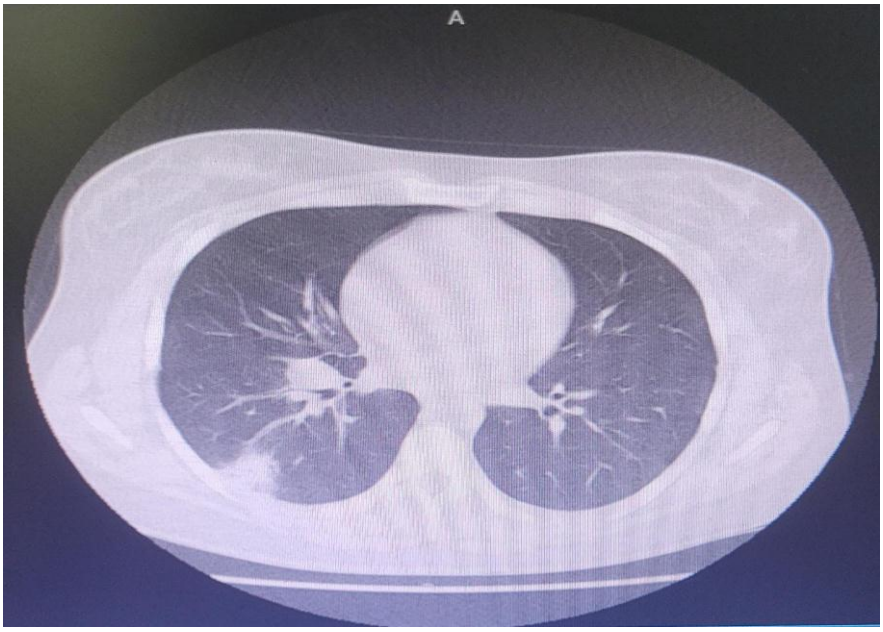

Figure A. Chest Tomography.

Laboratory tests showed normocytic and homochromic anemia (Ht 32.0%; Hb 10.5 g%; Hm 3.64 milh/mm3; HCM 28.85 pg; MCV 87.91 u3; CHCM 32.81%), elevation of Lactic Dehydrogenase (393 U/L) and Erythrocyte Sedimentation Rate (1st hour, 75mm, and 2nd hour, 115). In the serological investigation, it was seen Cytomegalovirus, Epstein BAAR and Toxoplasmosis, both, IgG reagents and IgM non-reactive, Total Anti-HBC non-reactive, Anti-HBs reactive, HBsAg non-reactive, Anti-HCV non-reactive, Antibodies HIV 1 and 2 non-reactive and Histoplasmosis (H. Capsulatum), by immunodiffusion of ouchterlony, with positive M band and undetectable H.

The treatment was symptomatic and, after discussion/infectologist's opinion, hospital discharge and outpatient investigation were chosen, since the patient maintained clinical stability, having had no fever for 6 days, not justifying her hospitalization at the time.

In outpatient follow-up, serologies were requested, using new methods, and other laboratory tests for diagnostic elucidation of the evidence of fungal infection seen on Chest Tomography and suspected Histoplasmosis. Tests for Cryptococcosis, Paracoccidioidomycosis, Aspergillosis, HTLV, Lupus Erythematosus, Syphilis and Brucellosis were negative. As for Histoplasmosis, they were positive by the enzyme immunoassay/Western blot and double immunodiffusion methods. An addendum was the positive result for the G6PD test, requested due to anemia and black family descent.

Treatment with itraconazole, orally, at a dose of 200mg, three times a day, for 3 days and then 200 to 400mg/day for 6 to 12 weeks was prescribed. The patient remains under clinical and therapeutic follow-up, remaining asymptomatic.

DISCUSSION

Infection by H. capsulatum is configured as an endemic mycosis since 1905, being common in environments with the presence of chicken coops, hollow trees, mines, water tanks and abandoned land.[1,2] Contact with the fungus is responsible for contagion with the fungus and is independent of the patient's age group, but immunocompromised patients - either due to the use of corticotherapy or associated comorbidity - are more likely to develop the disease. The vast majority of patients who have had brief contact with the fungus do not develop the disease. The patient described is female and aged 22 years. There are still few cases described in the literature of diseases caused by fungi after infection with the COVID-19 virus, making this case relevant due to the reduced number of similar reports. As for symptoms, most patients are asymptomatic, but a small number of individuals may manifest cough, headache, asthenia, chest discomfort, myalgia, fever and anorexia.[5,6] In the reported case, as a history of the current illness, persistent fever, generalized arthralgia, diarrhea and occipital headache were described. On physical examination, it was not possible to detect any noteworthy changes. Although numerous pathologies present with similar clinical manifestations, the hypothesis that the patient evolved with fever of unknown origin was maintained, due to the persistence of high temperatures during the use of antibiotic therapy and pulmonary symptoms. The condition was elucidated during hospitalization, through laboratory and imaging tests (Chest CT scan - Irregular opacity, with an irregular triangular appearance, with soft tissue density and adjacent ground-glass opacity with corresponding pleural thickening and hilar lymph node enlargement) which suggested strongly fungal infection.[7,8]

The most indicated therapeutic approach is the use of Itraconazole in high doses for 4 weeks to 24 months. Case studies have shown the effectiveness of the use of Itraconazole, to the detriment of the use of Fluconazole and even Amphotericin B. This treatment has been evaluated as the most efficient and with reduced side effects, compared to the use of Fluconazole – reserved for patients who present allergy to Itraconazole- and to Amphotericin B, used in severe manifestations of the disease.[12]

CONCLUSION

After the bibliographic review and the report, the reduced number of cases of fungal infection after vaccination and infection by COVID-19 was evidenced.

In short, the diagnosis is made due to findings during investigations of various pathologies involving fever of unknown origin. The patient is usually asymptomatic, but in some cases respiratory, gastrointestinal and pain symptoms may be present. Therapy consists of oral therapy for a long time and follow-up with laboratory and imaging tests. Only in asymptomatic patients or those with a self-limiting condition, watchful waiting is accepted.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal.

ETHICAL APPROVAL

Not applicable

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