**CASE PRESENTATIONS**

**Otitis with *Aspergillus niger* in a patient with SARS-CoV-2 and multiple comorbidities**

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**ABSTRACT**

**Introduction.** COVID-19 is associated with a significant incidence of bacterial and fungal superinfections and with the exacerbation of pre-existing infections, representing a diagnostic and therapeutic challenge. 

**Case presentation.** A 64-year-old woman, confirmed with COVID-19 by the SARS-CoV-2 antigen test, is hospitalized accusing fatigue, nausea, watery stools, cough and vertigo started 10 days ago, aggravated 4 days before the presentation. It also reports recurrent episodes of otalgia and otorrheic pluriantibiotic treatment in the last 2 months. From the personal pathological antecedents we remember: hypothyroidism, dyslipidemia, hypertension, ischemic heart disease, history of deep vein thrombosis (DVT) and secondary pulmonary thromboembolism, in chronic anticoagulant treatment. Pathological clinical signs at admission: bilateral basal crackling rales. Biologically, inflammatory syndrome is detected, and radiologically, interstitial-alveolar infiltrates in the lower lung fields. On day 3 of hospitalization, the patient shows purulent secretion in the right external auditory canal and the ENT consultation confirms chronic suppurative otitis media in acute onset. Bacteriological examination of otic secretion reveals *Aspergillus niger*. Antiviral treatment with Remdesivir is initiated, antibiotic therapy initiated at home with Azithromycin is continued for one day, then escalated to Ceftriaxone i.v. (in the context of clinical-paraclinical aggravation), systemic corticotherapy, anticoagulation with Dalteparin in the prophylactic regime of DVT, systemic treatment with Voriconazole p.o. (according to the antifungal program) and topical (local) with a slow favorable evolution. 

**Conclusions.** The association of COVID-19 with otitis with *Aspergillus niger* is a rare and particular clinical picture.

**Keywords:** COVID-19, *Aspergillus niger*, otitis

**Abbreviations**

COVID-19 = coronavirus disease 2019  
SARS-CoV-2 = severe acute respiratory syndrome coronavirus  
DVT = deep vein thrombosis  
ENT = ear-nose-throat, otolaryngology  
Rt-PCR = real time polymerase chain reaction

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INTRODUCTION

With the appearance of atypical cases of pneumonia at the end of 2019, the new coronavirus (SARS-CoV-2) was identified, and the disease caused by it, COVID-19, spread rapidly worldwide, generating the COVID-19 pandemic, also present in 2021 (1-3).

In the management of COVID-19 disease, an important aspect is the occurrence of SARS-CoV-2 co-infection and other viruses, bacteria or fungi (4,5). Co-infection with fungi such as Candida, Aspergillus, Cryptococcus, Mucorales has been reported less frequently (4,6). Among fungi, co-infection with Candida and Aspergillus ranks first (7,8), with an increasing frequency, having a severe evolutionary potential, even fatal in some cases (7,9).

COVID-19 can lead to acute respiratory distress syndrome, and in the case of diffuse alveolar involvement with the appearance of inflammatory exudate, patients diagnosed with COVID-19 have a degree of immunosuppression by decreased CD4+ and CD8+ T lymphocytes (10). Patients with a critical form of the disease, admitted to the intensive care unit, requiring mechanical ventilation and a prolonged period of hospitalization have a greater predisposition to develop fungal co-infections (11).

These aspects suggest that patients, especially those with severe forms of the disease, may develop fungal infections in the middle of the disease course or in the more advanced stage (12).

AIM

The aim of the paper is to emphasize the importance of early diagnosis of a fungal infection in a patient diagnosed with SARS-CoV-2 infection. The informed consent of the patient was obtained.

CASE PRESENTATION

Presenting concerns

We present the case of a 64-year-old woman confirmed with COVID-19, who was hospitalized for chills, watery stools, fatigue, cough, started 10 days before and worsened 4 days prior the admission. She reports recurrent episodes of otalgia and otorrhea pluriantibiotic treated in the last 2 months.

The patient comes from a family outbreak and is known to have high blood pressure, hypothyroidism, dyslipidemia, ischemic heart disease, a history of deep vein thrombosis (DVT) and secondary pulmonary thromboembolism, in chronic anticoagulant treatment (Xarelto) and antihypertensive treatment (Nebilet).

Clinical findings

Clinical examination at admission revealed a patient with mediocre general condition, afebrile (36 degrees C), G = 82 Kg, normally colored skin and mucous membranes, post-thyroidectomy anterior cervical scar, left lower limb swelling, impalpable superficial ganglion system, system normotonous, normokinetic muscle, apparently intact morphofunctional osteo-articular system, dry cough, bilateral vesicular murmur present, bilateral crackling rales, rhythmic heart sounds, apparently without valvular murmurs, SpO2 = 96% in aa, AV = 85 bpm, TA = 125/71 mmHg, abdomen relaxed by volume through adipose tissue, mobile with breathing, painless spontaneously or on palpation, liver with lower edge at costal rim, impalpable spleen, intestinal transit present, watery stools, normal urination affirmative, bilateral negative Giordano, conscious, cooperative, temporally-spatially oriented, with no signs of meningeal irritation.

Diagnostic focus and assessment

Biologically, inflammatory syndrome is detected (CRP = 2.54 mg/dl, fibrinogen = 505 mg/dl) and radiologically infiltrated interstitial-alveolar in the lower 1/3 of the right lung field and in the lower 1/2 of the left lung field that associates small foci of condensation.

On day 3 of hospitalization, the patient presents with purulent secretion in the right external auditory canal and the ENT consultation confirms chronic suppurative otitis media in acute onset.

Otic secretion is taken and bacteriological examination and mycological examination are performed, being isolated in culture Aspergillus niger. Subsequently, antifungigram is performed. Biologically, on day 3 of hospitalization, leukocytosis (15,700/µl) and neutrophilia are detected (13,500/µl).

Therapeutic focus and assessment

During hospitalization he received antiviral treatment with Favipiravir 3.2 g/day on the first day po, then replaced with Remdesivir 200 mg iv on the first day, then 100 mg/day, iv on days 2-5, antibiotic treatment with Ceftriaxone (Cefort) 2 g/day, iv, for 8 days, systemic corticosteroids in decreasing doses, iv, anticoagulant treatment with Dalteparin (Fragmin) 5000 IU/day sc, antitussive (Bromhexin), anti-diarrheal (Tasectan), gastric protector (Famotidine), symptomatic and background treatment administered for known pathologies.

Because Aspergillus niger was isolated in the culture of otic secretion, treatment with Voriconazole 800 mg/day p.o. was instituted on day 1, then 400 mg/day, in the following days p.o., according to antifungigram. Under treatment the evolution was favorable with the progressive remission of the symptomatology.
Follow-up and monitoring

The patient was monitored by the family doctor and ENT doctor.

DISCUSSION

The COVID-19 pandemic is currently one of the most important health problems globally. The clinical picture is vast and includes asymptomatic, mild, moderate, severe and critical forms of the disease. The most common manifestations are fever, cough, dyspnea, rhinorrhea, myalgia, nausea, vomiting, watery stools, headache (13,14). Regarding the case presented, the patient had a disease-specific symptomatology.

In the literature, manifestations belonging to the ENT sphere have been described, such as the presence of acute otitis media, hearing dysfunction, altered taste and smell, oral manifestations, mumps (15). The SARS-CoV-2 receptor is known to be the angiotensin II converting enzyme (ACE II). The virus enters the body airborne and attaches to ACE II (16). This attachment is also mediated by cytosolic pH, which is reduced in the elderly and facilitates the production of a more severe form of the disease (16,17). The case presented is an elderly patient, known with chronic otitis, COVID-19 infection having a role in exacerbating otitis.

Aspergillus infection is more common with Flavus and Fumigatus species and can manifest as invasive aspergillosis. This is a serious complication of severe forms of pneumonia and has been present in the 2003 SARS epidemic. A series of autopsies performed on 20 deceased SARS patients showed that 10% of them (2/20) had an invasive infection suggestive of aspergillosis (18).

Most patients who develop severe forms of COVID-19 have at least one associated pathology such as diabetes, high blood pressure, chronic kidney disease, chronic obstructive pulmonary disease (19). In severe forms of COVID-19, the lungs are affected due to viral replication, cytokine storm and complex inflammatory processes, favoring the occurrence of fungal superinfections (20). A study conducted in France, on a group of 106 patients diagnosed with severe COVID-19, admitted to the intensive care unit, found the presence of Aspergillus in 19 cases (17.9%). Of these, Aspergillus fumigatus was isolated in 14 cases (21). In our case, although the patient was known to have high blood pressure, ischemic heart disease and was hospitalized on day 10 of evolution, she did not have a severe form of the disease. The isolated species of Aspergillus was Aspergillus niger, known in the literature for otic impairment. Early detection and established antifungal treatment allowed the control of otic fungal infection by preventing a possible spread of it, including lung.

CONCLUSIONS

Aspergillus-associated fungal infections associated with COVID-19 are more common in patients with severe forms of the disease and admitted to intensive care units. Although a less common species in SARS-CoV-2 infection, Aspergillus niger should not be overlooked.

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