

# Late complications of COVID-19 infection , Pulmonary embolism , Myocarditis and Fungal endocarditis : A case report

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## Abstract

Late complications of COVID -19 infection are as important as the acute phase problems . A young woman with a history of COVID-19 infection and concomitant visual problems was admitted with exacerbation of dyspnea . During the admission, pulmonary embolism , myocarditis and fungal endocarditis were detected .

Late complications of COVID-19 infection , Pulmonary embolism , Myocarditis and Fungal endocarditis : A case report

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## Abstract

Late complications of COVID -19 infection are as important as the acute phase problems . A young woman with a history of COVID-19 infection and concomitant visual problems was admitted with exacerbation of dyspnea . During the admission, pulmonary embolism , myocarditis and fungal endocarditis were detected and she underwent surgical replacement of the tricuspid valve and antifungal treatment .

Key clinical message :

Late complications of COVID-19 infection are still remained to be determined and the patients should have a long term follow up .

Key words : COVID-19 , myocarditis , endocarditis , pulmonary embolism

Introduction

Since the start of the COVID-19 pandemic, different reports have been published regarding the role of persistent inflammation in this disease (1) . Even after several months, the patients may struggle with late complications of the disease, which should be kept in mind in order to plan the management and follow-up strategy . We report a case of a young lady with late complications of COVID-19

### Case report

A 39 year-old woman was admitted with acute dyspnea from two days ago. Her past medical history was unremarkable, except for the history of severe COVID-19 infection 6 months prior ( prolonged intubation and one month ICU admission ) with concomitant decrease in the visual acuity of the left eye ( 2 meters finger count ) , for which she received oral prednisolone based on the initial diagnosis of vitritis and retinitis . She had previously received oral prednisolone 25 mg daily for 3 months for eye symptoms. In addition, the patient had been administered remdesivir and dexamethasone in her previous admission before she was discharged with nasal oxygen therapy at home . She had no surgical intervention in her history except the history of a femoral vein catheter insertion in the previous hospital admission as an intravenous access .She did not report any symptoms in favor of underlying rheumatologic disorder (arthralgia, photophobia , history of fetal loss , ... ) .

Initial evaluation revealed tachycardia (heart rate=110/ minute) and tachypnea (respiratory rate = 20 / minute ) with blood pressure 100/80 and without fever. Oxygen saturation with nasal O<sub>2</sub> was 94% . Pulmonary computed tomography angiography (CT angiography) revealed acute pulmonary embolism in the right pulmonary artery and left lower lobe branch with evidence of cystic changes in both lung fields and ground glass opacities ( Figure1A and B ) . Transthoracic echocardiography (TTE) showed normal left ventricular size and preserved systolic function (left ventricular ejection fraction (LVEF ) =50 %) with normal right ventricular (RV) size and mild dysfunction . Laboratory tests revealed normal serum creatinine level (1 mg /dl ) , aspartate transaminase (AST) =45 U/L , alanine transaminase (ALT) =66 U/L , alkaline phosphatase (ALK p) =106 U/L , ferritin= 964 ng/ml , White blood cells (WBC) = 19000 cells /mm<sup>3</sup> , neutrophil count = 80% , erythrocyte sedimentation rate (ESR) =33 , qualitative C-reactive protein (CRP)= 2+ , N-Type pro brain-natriuretic peptide (NT-Pro BNP) = 5300 pg/ml , Troponin I= 0.02 ng/ml (normal level <0.06 ) and other lab tests were unremarkable . Polymerase chain reaction (PCR) for SARS-CoV-2 was negative. Although the patient was not completely eligible for fibrinolytic therapy based on the hemodynamic status and paraclinical test results, due to her low pulmonary reserve and probable hypercoagulable state , two doses of reteplase (10 mg ) were administered based on the personalized medicine . On the second day after admission , echocardiography was repeated due to the sudden onset of hypotension, and showed a sharp drop in the LVEF from 50 to 25 % with global hypokinesia, without a significant change in RV size and function. Vasopressor (Norepinephrine ) was initiated and the serum lactate level was measured, which demonstrated elevated levels (4.5 mmol/dl ) . Emergent coronary angiography did not show significant lesions . Methylprednisolone (1 gr ) was initiated due to highly suspicious myocarditis in the acute inflammatory setting . The next day , limited bedside TTE delineated mildly improved LV systolic function (LVEF=35%) and subsequent doses of methylprednisolone (500mg ) were administered over the following days, which resulted in rapid improvement of the hemodynamic status and discontinuation of vasopressors . TTE was repeated again on the 5<sup>th</sup> day, which demonstrated normal LV size and function (LVEF=55%), but a large mobile mass was detected in the atrial side of the tricuspid valve (16 mm) .

All the blood cultures were negative and rheumatologic tests ( including complement levels , anti-cardiolipin antibody (IgM and IgG ) , antinuclear antibody (ANA ) and anti double stranded DNA (anti-dsDNA ) were unremarkable, except elevated lupus anticoagulant (105 with normal range 25-65 unit ) . ESR increased from 6 to 110 and the WBC count increased to 22000 cells /mm<sup>3</sup> after an initial drop . Based on the echocardiography findings and the presence of a rapidly enlarging mass , Libman-Sacks endocarditis (due to multi-organ inflammatory state) and fungal endocarditis were the two main differential diagnoses . Empirical treatment was initiated with caspofungin , imipenem , gentamicin and linezolid . The vegetation size did not show an increase in the following days and after 10 days of hospitalization , she underwent cardiac surgery to replace the tricuspid valve with a mechanical valve (Figure2 ) . Direct smear from the vegetation

delineated fungal hyphae (Figure 3) and the results of culture and PCR of the vegetation were in favor of a *Candida albicans* infection that was sensitive to amphotericin, voriconazole and caspofungin and resistant to itraconazole and fluconazole. Intra-operative myocardial biopsy did not show evidence of active inflammation and PCR tests to detect viruses (COVID-19, Influenza, herpes and cytomegalovirus) were negative. She was treated with liposomal amphotericin (150 mg/day) for 21 days and was discharged with oral voriconazole (300 mg BID first, then 200mg BID).

## Discussion

Late complications of COVID-19 infection have been reported with different presentations (1), but the exact mechanism and the best treatment strategy remains to be determined. A prospective study on 418 outpatients in Switzerland revealed that more than half of them suffered from prolonged symptoms after COVID-19 infection. Post-COVID syndrome has been defined as persistent symptoms of COVID-19 infection after 3 months. Fatigue, dyspnea and smell/taste or memory problems have been reported by patients (2), but persistent inflammation has also been documented by elevated levels of neutrophils, CRP, fibrinogen and neutrophil to lymphocyte ratio (1). Uveitis and other ocular complications, which indicates the inflammatory state, can manifest during the acute phase of COVID-19 (3) and even after COVID-19 vaccination (4). In our patient, visual problems were observed together with the respiratory symptoms of COVID-19 infection and relapsed after the incomplete initial treatment.

Obesity has been introduced as an underlying associated condition with chronic inflammation (5), but our patient had a normal body mass index (BMI).

Multisystem inflammatory syndrome (MIS) has been described previously in children and adults after COVID-19 infection (6) or after COVID-19 vaccination (7) but the exact pathophysiology of this syndrome has not been described comprehensively. It can lead to different pattern of myocardial involvement including delayed myocarditis (8). The role of the underlying inflammatory state and pro-coagulative effects of COVID-19 infection should be considered (9). The presence of concomitant LV systolic dysfunction and elevated troponin levels indicating myocarditis has also been reported with other presentations. Considering the common manifestations of MIS in adults, our patient did not show the typical signs and symptoms of this syndrome (mostly Kawasaki-like manifestations), which could have been due to her history of treatment with corticosteroid (9).

## Conclusion

In conclusion, the pathophysiology of the late complications of COVID-19 infection are not fully understood, but they are as important as the acute phase of the disease and can be fatal. Close periodic follow-up of the patients to evaluate the presence of persistent inflammation should be advocated.

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Authors contributions :

Mehran Lak : Data gathering , editing the text

Sepideh Jafari Naeini : Data gathering , writing the text

Alireza Omidi Farzin : Data gathering

Manoochehr Hekmat : data gathering

Atoosa Gharib : Data gathering , preparing figures

Ethical statement and acknowledgement:

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#### Data availability statement :

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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