



Transient left ventricular clot in COVID-19-related myocarditis is associated with hypereosinophilic syndrome: a case report

Naghmeh Ziaie^{1,2} · Parviz Amri Maleh³ · Mohammad Mostafa Ansari Ramandi⁴ · Roghayeh Pourkia^{1,2} · Kayvan Latifi⁵ · Davood Mansouri^{6,7,8,9}

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Abstract

Frequent clinical presentations have been reported in patients with Coronavirus disease 2019 (COVID-19). It may be associated with multi-organ and cardiovascular involvements such as myocarditis and clot formation. Hypereosinophilic syndrome (HES) is a rare disease diagnosed with idiopathic eosinophilia and organ involvement. Here, we report a patient with COVID-19 who presented with clot formation and myocarditis. One month after discharge, regarding persistent peripheral/bone marrow hypereosinophilia and clot in echocardiography, fluorescent in situ hybridization (FISH) analysis was done that showed FIP1L1-CHIC2 fusion (PDGFR α rearrangement) in 18% of scored cells and PDGFR β rearrangement in 12% of scored cells, which confirmed HES diagnosis. Clot formation may be a late manifestation of COVID-19 or myocarditis due to COVID-19, or the first manifestation of HES that COVID-19 might provoke in this rare syndrome.

Keywords Hypereosinophilic syndrome · Coronavirus · COVID-19 · Case report · Left ventricular clot

Abbreviations

ACE	Angiotensin-converting enzyme
COVID-19	Coronavirus disease 2019
CT	Computed tomography
HES	Hypereosinophilic syndrome
LVEF	Left ventricular ejection fraction
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2

Naghmeh Ziaie and Davood Mansouri have contributed equally to this work.

✉ Naghmeh Ziaie
ziaiexn@yahoo.com

✉ Davood Mansouri
dmansouree@gmail.com

¹ Department of Cardiology, Babol University of Medical Sciences, Babol, Iran

² Clinical Research Development unit of Rouhani Hospital, Babol University of Medical Sciences, Babol, Iran

³ Department of Anesthesiology, Faculty of Medicine, Babol University of Medical Sciences, Babol, Iran

⁴ Cardiovascular Diseases Research Center, Birjand University of Medical Sciences, Birjand, Iran

⁵ Department of Adult Intensive Care Unit, Ayatollah Rouhani Hospital, Babol University of Medical Sciences, Babol, Iran

Background

Coronavirus disease 2019 (COVID-19) was first appeared in December 2019, in Wuhan, China [1]. Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an enveloped positive-sense single-stranded RNA (+ ssRNA) virus that causes COVID-19 [2]. Although a number of antiviral and biologic therapies have been provided so far, none of them was approved as the definitive treatment for this disease [3, 4]. A wide spectrum of clinical presentations has been reported in patients with COVID-19. The incidence of

⁶ Department of Clinical Immunology and Infectious Diseases, National Research Institute of Tuberculosis and Lung Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran

⁷ The Clinical Tuberculosis and Epidemiology Research Center, National Research Institute of Tuberculosis and Lung Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran

⁸ Pediatric Respiratory Diseases Research Center, National Research Institute of Tuberculosis and Lung Diseases, Shahid Beheshti University of Medical Sciences, Tehran, Iran

⁹ Masih Daneshvari Hospital, Darabad Avenue, Shahid Bahonar Roundabout, PO Box: 19575154, Tehran, Iran

cardiovascular manifestations, including thromboembolic events, heart failure, cardiogenic shock, and acute coronary syndrome may increase following COVID-19 in both general population and patients with pre-existing cardiac problems [5]. On the other hand, hypereosinophilic syndrome (HES) is a rare disease diagnosed with idiopathic eosinophilia and organ involvement. It most often occurs in males typically in the third to sixth decades of life [6]. Cardiac problems may cause apical thrombus formation easily visualized on two-dimensional echocardiography [7]. Cardiac involvement is seen in approximately 60% of patients with HES, which is the main reason for morbidity and mortality in these patients. Considering the complexity of cardiac thrombus formation in COVID-19 and HES, thromboembolic and myocardial events should be urgently taken into consideration. Here, we report a patient with COVID-19 who presented with thrombus formation and myocarditis.

Case presentation

A 39-year-old female with COVID-19 was admitted to Babol University hospital because of chest pain, orthopnea, cough, and evidence of ground glass opacity in both lungs and hypoxia considering the primary chest computed tomography (CT) scan (Fig. 1). Her husband was also infected with SARS-CoV-2. Her primary infection with COVID-19 was accompanied by coughs and exacerbated asthma, which was treated outpatient with hydroxychloroquine and ofloxacin. She was a known case of reactive airway disease and

had a recent history of weight loss in the past two months because of diet and exercise and she was admitted to hospital due to progressive symptoms and hypoxia for 5 days. On admission, she had bibasilar crackles, bronchial asthma and elevated jugular venous pressure. Her vital signs were blood pressure of 100/60 mmHg, heart rate of 125 beats/minute, temperature of 37.2 °C, and respiratory rate of 26/min, oxygen (O₂) saturation of 90% in ambient air, and 95% with O₂ supplementation. Considering her signs and symptoms, the first diagnosis was acute decompensated heart failure possibly due to COVID-19 myocarditis.

The patient was treated with furosemide infusion, spironolactone and piperactam. Intermittent bilevel positive airway pressure ventilation was also used for the patient. Subcutaneous heparin was also administered with a dose of 5000 U every 8 h. Because of her poor response to the treatment, dexamethasone 4 mg every 8 h was administered for 3 days. Subsequently, her vital signs stabilized and she had an O₂ saturation of 98% in ambient air. Serial echocardiography showed improvement of left ventricular ejection fraction (LVEF) to 45% and interestingly, the apical LV clot (hypermobile 1.5 × 1.5) (Fig. 2). After multidisciplinary team discussion and the patient's refusal for surgery it was concluded to put the patient on anticoagulation (heparin 2400u/ 24 h) and avoid surgery. On repeated echocardiography, the clot had disappeared after 3 days and there was no sign of peripheral embolism. She was discharged on

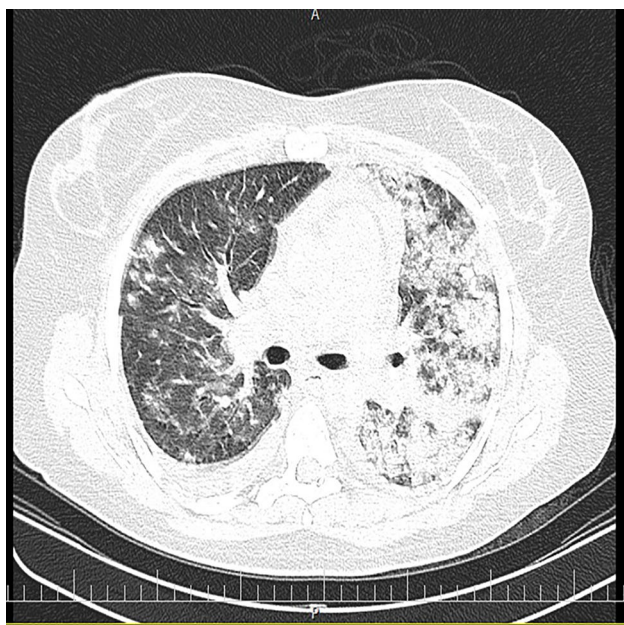


Fig. 1 Ground glass opacification and patchy infiltration are shown

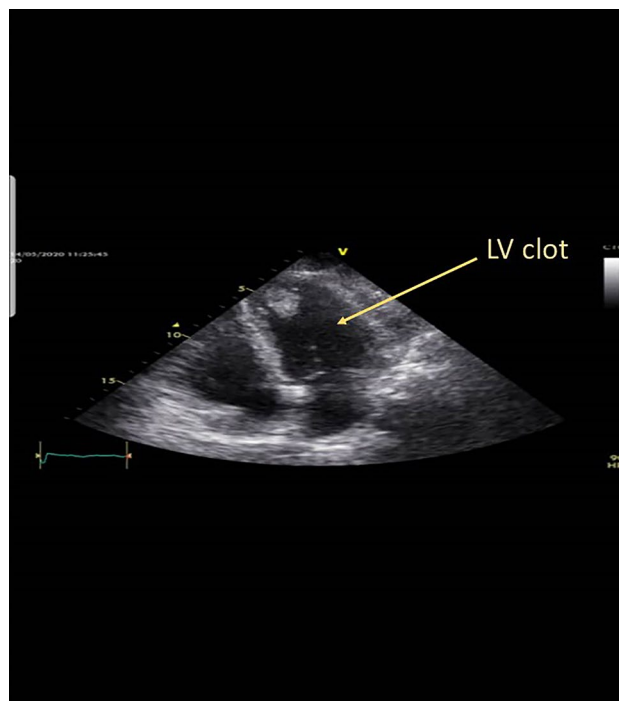


Fig. 2 Left ventricular apical clot is illustrated

β -blocker, angiotensin-converting enzyme (ACE) inhibitor, spironolactone, and warfarin.

Laboratory data of the patient are summarized in Table 1. Because of hypereosinophilia detected one month after discharge, all causes of eosinophilia were ruled out, including parasites, autoimmune disease, malignancy, etc., which were all normal. Bone marrow aspiration and biopsy showed a marked increase in the number of eosinophils (30%). On echocardiography, she had moderate LV systolic dysfunction, with an ejection fraction (EF) of 30–35%. The right ventricle had mild enlargement and dysfunction and restrictive diastolic pattern was observed. There was moderate

mitral and tricuspid regurgitation and mild pericardial effusion. Coronary CT angiography was done for the patient which was normal. Cardiac magnetic resonance (CMR) imaging was also done for the patient, which revealed myocardial edema and hyperemia in favor of active myocarditis (Fig. 3a) subendocardial to transmural fibrosis (Fig. 3b) in mid to apical part of the inferoseptal wall and mid-lateral subepicardial fibrosis was also present. Given persistent peripheral/bone marrow hypereosinophilia, fluorescent in situ hybridization (FISH) analysis was done that revealed FIP1L1-CHIC2 fusion (PDGFR α rearrangement) in 18% of the scored cells and PDGFR β rearrangement in 12% of the scored cells in favor of HES (Supplementary material). Considering persistent peripheral/bone marrow hypereosinophilia and LV clot formation during hospital admission, HES was finally confirmed and the patient was referred to a hematologist. She uses tyrosine kinase inhibitors (imatinib) and improved dramatically. The last eosinophil count was 1000 (cells/ml) while LV-EF in controlled echocardiography was 45% and cardiac medication was continued. According to the FISH results and clinical response of the patient to corticosteroids and clot formation during admission, HES was finally confirmed.

Table 1 Laboratory data of the patient

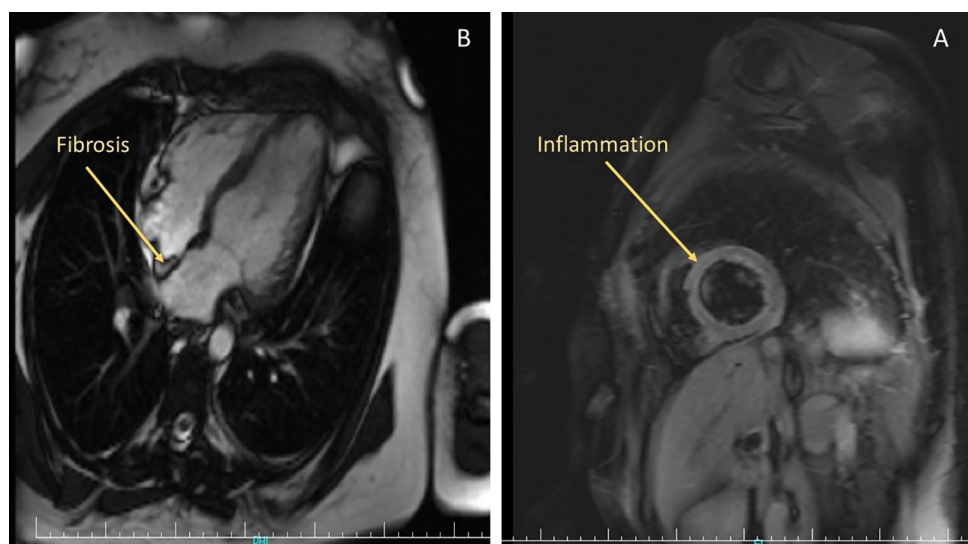
	On admission	During admission
Hg, mg/dl	12	10
WBC, count/ml	9000	4000
Lymphocyte, count/ml	2160	1500
ESR, mm/h	85	40
Hs-CRP, mg/L	103	10
Creatinine, mg/dL	1.2	1.2
NT-proBNP, ng/L	23,000	2000
ALT, U/L	340	100
AST, U/L	220	46
IL-6, IU/ml	8	–
PCT, ng/ml	<0.1	–
D-dimer, mcg/mL	1350	–

Hg Hemoglobin, WBC White Blood Cells, ESR Erythrocyte Sedimentation Rate, Hs-CRP High-Sensitivity C-Reactive Protein, NT-proBNP N-terminal pro B type natriuretic peptide, ALT Alanine aminotransferase, AST Aspartate aminotransferase, L-6 Interleukin-6, PCT Procalcitonin

Discussion

To date, COVID-19 has indicated several multi-organ involvements and presentations, including cardiovascular involvement [8]. Apart from cardiac injury and myocarditis, several reports have shown increased thrombotic events in such patients [9, 10]. While little is known about the possible late presentations and consequences of COVID-19, we describe a patient with myocarditis and acute heart failure one month after SARS-CoV-2 infection who develops a large

Fig. 3 Myocardial inflammation **a** in SRIR scene and fibrosis **b** in late GAD scene are shown



transient LV clot during admission, which resolves shortly after intravenous anticoagulation. However, HES is associated with poor prognosis usually. One of the reasons for blood stasis and thrombus may be damage to the endocardial tissue, providing a hypercoagulable state, and the loss of regional contractile function [10]. According to recent studies, coagulopathy and massive intravascular clot formation are enormously observed in most severely ill patients [11].

HES is a group of rare disorders with persistent increase in eosinophil counts in peripheral blood, which results in organ damage. The diagnostic criteria for HES are the presence of a persistent eosinophilia (1500/mm³) for more than 6 months accompanied by organ involvement, the paucity of evidence for allergic, parasitic, or other known reasons for eosinophilia, and organ damage [12]. Although cardiac involvement is best approved using an endomyocardial biopsy, this method may be difficult to obtain sufficient samples in the area of fibrosis. Therefore, several noninvasive modalities have been introduced instead, including echocardiography and CMR. The benefits of these techniques are that they are noninvasive and can be also utilized for following up the patients and their response to the treatment. In addition, they obviate the risks of biopsy preparation [13].

Echocardiography is essential for HES diagnosis and provides sufficient detection of thickened endocardium and intraventricular thrombus. Furthermore, it can detect intracardiac thrombi and valvular involvement as well as an increment in endomyocardial echodensity at the fibrotic stage of the disease [13]. The prominent finding in echocardiography for HES is obliteration of the LV or right ventricle apex with laminar thrombus, with the fibrotic stage and restrictive pattern, occurring in later stages [14]. Although LV clot could be counted as a late presentation of COVID-19 infection during myocarditis, the eosinophilia and fibrosis in CMR and the good response to corticosteroids were in favor of HES in this patient. Actually, we did not know whether HES has been the result of direct effect of COVID-19 in this patient or SARS-CoV2 played a triggering role in the emergence of underlining HES.

In conclusion, in this case report, we demonstrate thrombus formation and myocarditis due to COVID-19 and hyper-eosinophilia after discharge in a patient with COVID-19 using echocardiography and Cardiac MRI, demonstrating HES. Although COVID-19 can cause many cardiovascular presentations such as myocarditis and thrombosis, it seems that it has provoked the sign and symptoms of HES, thereby resulting in cardiovascular involvement. In addition, clot formation may be a late manifestation of COVID-19 or myocarditis due to COVID-19, or the first manifestation of HES that COVID-19 might provoke in this rare syndrome. Regarding COVID-19 clinical manifestations and related comorbidities, it is suggested to consider that COVID-19 may trigger other rare diseases such as HES.

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Authors' contributions NZ coordinated the study, PAM, MMAR, RP, KL, DM were responsible for the patient care and data collection. NZ interpreted the data from cardiac MRI and FISH. All authors provided comments on the report at various stages of development. All authors read and approved the final manuscript.

Data availability Please contact the corresponding author for data requests.

Declarations

Conflict of interest The authors declare that they have no competing interests.

Informed consent Written informed consent was obtained from the patient for publication of this case report. We assure that a copy of the consent form is available for review by the journal upon request.

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