Unexpected stormy course after uneventful device closure of atrial septal defect – Possibly due to post-COVID-19 inflammatory state

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ABSTRACT

COVID-19 infection has myriad manifestations from self-limiting illness to stormy multi-organ failure. A 28-year-old woman negative for COVID reverse transcription–polymerase chain reaction underwent an uneventful elective device closure of atrial septal defect on intubation anesthesia. While a brief postprocedural endotracheal bleed was noted, significant hypoxia and respiratory distress ensued after extubation with biventricular dysfunction, pleural effusion, and radiographic evidence of acute respiratory distress syndrome. COVID antibodies were positive, and inflammatory markers were elevated. After a conservative multipronged medical management including anticoagulation, antibiotics, aspirin, beta-blocker, diuretics, and sildenafil, she improved in 1 week. The clinical course during this pandemic era gives a possibility of a post-COVID inflammatory syndrome as a potential etiology.

Keywords: Acute respiratory distress syndrome, COVID antibody, multisystem inflammation, transcatheter intervention

INTRODUCTION

COVID-19 infection clinically presents with varied manifestations from minor illness to the fatal inflammatory storm with multi-organ failure. We report an unusual clinical course following device closure of atrial septal defect (ASD), possibly due to COVID-19 infection.

CASE REPORT

An asymptomatic 28-year-old woman with large left-to-right shunt through a secundum ASD measuring 25 mm, normal pulmonary venous drainage to the left atrium, and normal ventricular function on echocardiogram [Figure 1a and b] was admitted for transcatheter closure after negative reverse transcription–polymerase chain reaction (RT-PCR) for COVID-19 infection and normal preprocedural blood investigations. The right atrial pressure was elevated to 9 mmHg and the left ventricular end-diastolic pressure was 12 mmHg, but the pulmonary artery pressure was normal. After a routine uneventful placement of stiff guidewire and delivery sheath in the left upper pulmonary vein, the defect was closed on intubation anesthesia using 34 mm Cera septal occluder (Lifetech Scientific, Shenzhen, PRC) under transesophageal echocardiographic guidance. The left ventricular diastolic function (LVEDP) was not rechecked after the device closure as the baseline LVEDP was 12 mmHg. Brief postprocedural endotracheal bleeding delayed extubation by 48 h when she was managed with protamine to reverse the effect of heparin and packed red cell transfusion for a hemoglobin drop

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of 2 g/dl from baseline. Chest X-ray in the baseline had cardiomegaly with increased pulmonary flow [Figure 2a] and showed the change in the form of left upper zone infiltrates suggestive of lung bleed [Figure 2b]. After extubation, she developed progressive respiratory distress, hypoxia, and radiological evidence of acute respiratory distress syndrome [Figure 2c]. Pre discharge chest x ray [Figure 2d] documented resolution of the radiological findings Echocardiogram showed dilated right heart chambers, significant biventricular systolic dysfunction (eyeballing) mild pleural and pericardial effusions, and elevated right ventricular systolic pressures as seen by septal position [Figure 3a-c]. Computed tomography with contrast excluded pulmonary thromboembolism. It showed evidence of pleural effusion (yellow arrow), lung collapse, and features suggestive of pulmonary edema [Figure 4a-d], the inflammatory biomarkers were elevated. C-reactive protein was 24 mg/L, d-Dimer 2335 ng/mL, and the troponin I levels (0.075 ng/mL) were also elevated. Even though COVID RT-PCR was repeatedly negative, COVID total antibodies were significantly elevated to 209 units/ml) [Table 1 with reference range]. Due to logistic constraints, other biomarkers such as N-Terminal Pro–B-Type Natriuretic Peptide (NT-proBNP), interleukin-6, and COVID antibody immunoglobulin M (IgM) fraction test were unavailable. The differential diagnosis considered included infection, pulmonary thromboembolism, and post-COVID inflammatory syndrome, in view of the prevailing pandemic. She was treated with supplemental oxygen, enoxaparin 40 units twice daily, and transitioned to warfarin, a broad-spectrum antibiotic, aspirin, beta-blocker, sildenafil, and diuretics. She responded well with the reduction of biomarkers. The plan of starting methylprednisolone was abandoned in view of her clinical recovery. She was discharged on the 7th day postprocedure in a hemodynamically stable condition on aspirin, warfarin, and a weaning schedule of sildenafil. Echocardiogram before discharge showed a reduction of right ventricular dimensions, pleural effusion, and recovery of ventricular systolic function [Figure 3d-f]. On a 15-month follow-up, she is asymptomatic with normal effort tolerance.

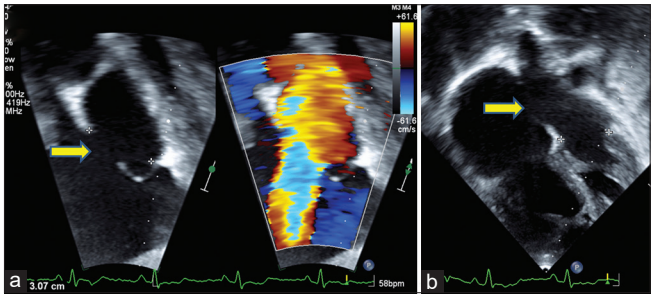

Figure 1: Echocardiogram in subcostal (a) and apical four-chamber view (b) showing secundum atrial septal defect (yellow arrow) with a thin aneurysmal inferior margin

DISCUSSION

COVID-19 infection is known to have cardiovascular complications such as myocarditis, acute myocardial infarction, cardiogenic shock, heart failure, and pulmonary arterial hypertension in patients during

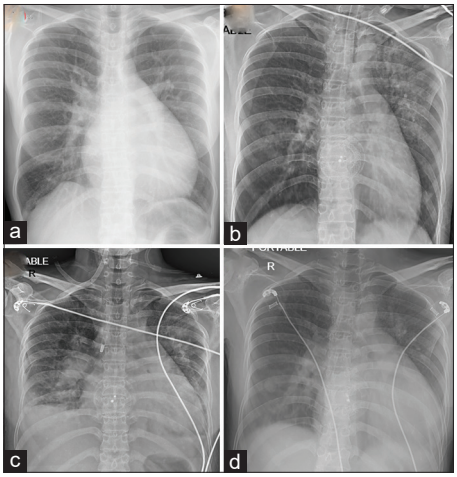

Figure 2: Chest X-ray in posterior–anterior view during (a) Preprocedure showing cardiomegaly and increased pulmonary blood flow. (b) Postprocedure after endotracheal bleeding showing haziness in the left upper zone. (c) CXR on day 3 during acute deterioration, showing increased bilateral hilar congestion with perihilar consolidation and bilateral pleural effusion. (d) Predischarge CXR in the resolution phase. CXR: Chest X-ray

Table 1: Laboratory parameters

Parameters	Basal	Day 1	Day 3	Day 4	Day 14	Reference
Hb (g %)	9.4	7.4	9.1	12.4	11.4	12.5-16
TLC (cells/μL)	5820		3730	5770	4260	4000-15,000
NLR	1.5		2.56	1.72	1.77	
Platelet (cells/μL)	189,000		125,000	150,000	165,000	150,000-450,000
CRP (mg/l)	<5		32.51	25.59	2.88 (<5)	0.00-5.00
ESR (mm/h)	14		28		13	0-20/mm 1st h
d-Dimer (ng/mL)			2335		3747	0-500
High-sensitive troponin-I (ng/mL)			0.075		0.011	0-0.02
RT-PCR for COVID	Negative		Negative			
Anti-SAR-CoV-2 (units/mL)				209		<0.80
Lactic acidosis (mmol/L)	1.4	5.2	3.1	2		0.5-2.2

CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, Hb: Hemoglobin, NLR: Neutrophil-to-lymphocyte ratio, TLC: Total leukocyte count, RT-PCR: Reverse transcription-polymerase chain reaction

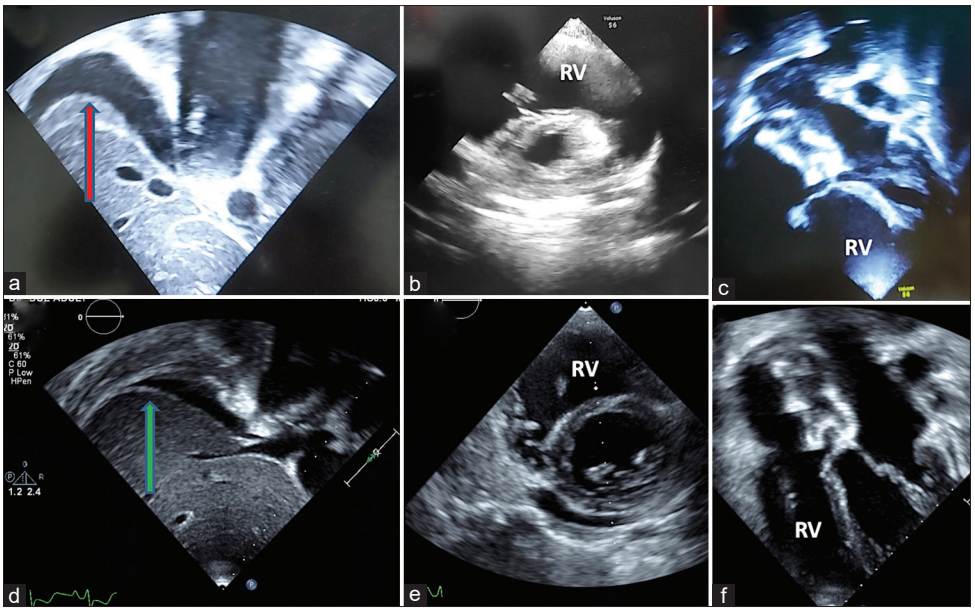

Figure 3: Echocardiogram in (a) subcostal view showing right pleural effusion (red arrow). On the third postprocedure day after the deterioration (b) parasternal short axis view and (c) and apical four-chamber view showing dilated right ventricle. Predischarge echocardiogram showing (d) reduced right pleural effusion (green arrow). Predischarge echocardiogram in parasternal short axis view (e) and (f) apical four-chamber view showing reduction of the RV dilatation and stable device position. RV: Right ventricle

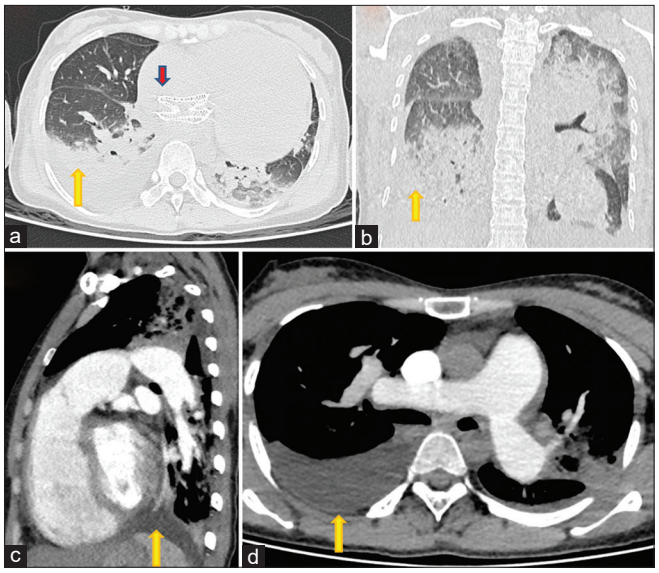

Figure 4: Computed tomographic scanning of the chest in (a) axial, (b) frontal view showing evidence of pleural effusion (yellow arrow), lung collapse and features suggestive of pulmonary edema. The atrial septal occluder is marked with red arrow (a) CT pulmonary angiogram in sagittal and axial view showing dilated right ventricle (c), dilated pulmonary artery with no evidence of thrombus (d) and significant pleural effusion in the right side (yellow arrow). CT : Computed tomography

the course and even after COVID infection.[1] Up to 50% of reported COVID-positive individuals can be asymptomatic.[2] Preprocedure screening for COVID-19 was a standard routine in the COVID pandemic. The standard RT-PCR test is sensitive in up to 70% of the cases, leaving the rest of the positive patients labeled as negative. The preprocedure negative patients can also be in the incubation period, going to manifest later. Wajekar *et al.* studied 25 asymptomatic COVID patients who underwent emergency coronary bypass grafting and found longer intensive care stays and higher mortality among them. They recommended deferring elective surgery in this subset of patients if possible.[3] Cardiac magnetic resonance (CMR) imaging inCOVID patients found features of subclinical myocarditis, myocardial edema, fibrosis, right ventricular dysfunction, etc., in up to 20%–50% of patients in different series.[4,5] Ongoing myocardial inflammation in the CMR is reported in a large number of asymptomatic patients.[6] In a group of convalescent less symptomatic and asymptomatic patients in a backdrop of ongoing subclinical inflammation, any stress will be like a second hit as described by Teuben *et al.*[7] Any cardiac intervention in this background can result in the activation of an inflammatory cascade from a combination of cardiac stress, mechanical ventilation, cardiopulmonary bypass, blood transfusion, etc.[7-9] This was compared with posttraumatic inflammatory reaction and postinfluenza acute inflammatory distress syndrome.[7,10] The entity possibly has some resemblance with COVID-induced multisystem inflammatory syndrome in children (MIS-C) among children. The other differential diagnoses were pulmonary thromboembolism and sepsis. The computed tomography pulmonary angiogram of the index patient had not revealed thrombus. Bacterial infection as a causative factor was not supported in our patient by the clinical course of acute deterioration of a relatively healthy young woman undergoing ASD device closure and subsequent response. The index unvaccinated

patient was in the post-COVID convalescent period after possibly an asymptomatic COVID infection which was not diagnosed. The manipulation of wire, sheath, and large device possibly triggered the inflammatory cascade in the backdrop of subclinical inflammatory state. Fortunately, the effects of the second hit were controlled and reversed within 1 week. The provisional diagnosis of the post-COVID inflammatory syndrome was made in view of a clinical picture similar to MIS-C in children with elevated COVID antibody title, an elevated inflammatory biomarker, the absence of any other obvious reason for the same, and complete clinical and laboratory resolution with conservative treatment in the line of MIS-C. The diagnosis was based on the overall clinical course and resemblance to the post-COVID inflammatory state though it had not completely satisfied the center for disease control criteria for the post-COVID inflammatory disorder. With the waning of the epidemic, mandatory COVID-19 screening is discontinued, thereby making the detection of asymptomatic active COVID patients more difficult. COVID-specific IgM antibody tests in suspected active COVID-19 patients who are RT-PCR negative can help the detection of the vulnerable subset.

CONCLUSIONS

Unexpected complications after transcatheter cardiac interventions that show features of nonspecific inflammation with elevated acute phase reactants, multi-organ dysfunction such as lung injury, serosal effusions, and myocardial dysfunction may indicate a possibility of the post-COVID inflammatory syndrome. Appropriate investigations should be directed toward this cause. A vigilant clinical team can screen, early diagnose, and appropriately treat such post-COVID inflammatory cascade

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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