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CASE REPORT

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# Gore Cardioform ASD device thrombus weeks after COVID-19 infection

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## Abstract

Device-related thrombosis and device-related endocarditis after atrial septal defect (ASD) transcatheter closure are extremely rare. It is known that COVID-19 infection could lead to a thrombotic microangiopathy-like phenomenon. We present the case of a 14-year-old female who developed fever and was found to have a thrombus on the right atrial side of the ASD closure device weeks after an asymptomatic COVID-19 infection and negative COVID-19 test 2 days before transcatheter ASD closure. Although there is no certainty that the thrombus was related to the prior COVID-19 infection, the possibility of an ongoing COVID-19-related hypercoagulable state should be entertained.

**KEYWORDS**

atrial septal defect, COVID-19, device-related endocarditis, device-related thrombosis, transcatheter closure

## 1 | INTRODUCTION

Device-related thrombosis after atrial septal defect (ASD) transcatheter closure is uncommon. COVID-19 infection is known to incite a hypercoagulable state, the duration of which remains unknown. There is no existing data regarding adequate workup or duration of time a procedure requiring device deployment should be delayed following COVID-19 infection.

## 2 | CASE PRESENTATION

A 14-year-old-female was diagnosed with a secundum ASD and a mildly aneurysmal atrial septum, but not an atrial septal aneurysm by the definition of >10 mm of excursion. Her right ventricle was dilated. Past medical history was unremarkable except for a prior asymptomatic COVID-19 **infection** confirmed by positive polymerase chain reaction (PCR). Despite being asymptomatic 1 month later, a COVID-19 Real Time-PCR (RT-PCR by Cepheid Inc.) continued to test positive with a cycle threshold (CT) of 34, for which the procedure was canceled and rescheduled 3 weeks later. Before the procedure a COVID-19 Point-of-care (ID now; Abbott Laboratories) was negative, and the catheterization was performed. At that time, the patient's white blood cell count (WBC) was 7.5 × 10k/μl, and platelets were 260 × 10k/μl. The procedure was performed with intracardiac echo (ICE) guidance. Immediately after obtaining access, 5000 IUs of intravenous heparin were administered. Based on the stop-flow diameter of 21 mm by both fluoroscopy and ICE, it was elected to close the ASD with a 37 mm Gore Cardioform ASD occluder. The ACT measured 24 min after the initial heparin dose was 171; therefore, 4000 IU of heparin were administered. Due to the aneurysmal nature of the atrial septum, initial deployment led to the device prolapsing across the superior portion of the septum into the right atrium. The device was re-sheathed, re-advanced into the left atrium, and redeployed. Once adequate positioning was documented by both fluoroscopy and ICE, the device was released (Figure 1, Supporting Information Video 1). A second ACT was measured 29 min after administering 4000 IU of heparin and was 210. Deployment was completed and the delivery sheath withdrawn 23 min later, and therefore no additional ACTs were measured. On postprocedure Day 1 echocardiogram showed a well-positioned device with no residual shunt (Supporting Information Video 2), and chest X-ray showed stable device position and normal lung fields. The patient was discharged the day after the procedure in good clinical condition on

  

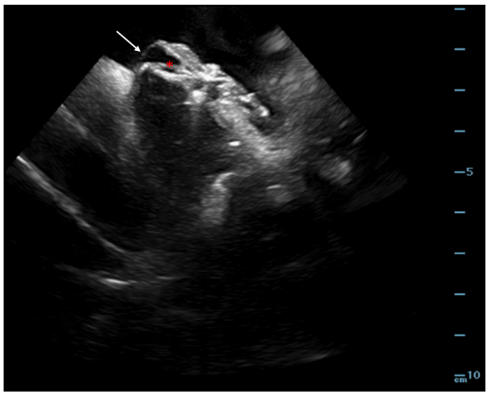

**FIGURE 1** Intracardiac echocardiogram showing device deployed across the atrial septum. Note the septum primum between the inferior portions of the left and right atrial discs (*), and residual aneurysm of the septum primum on the right atrial side of the device (arrow) [Color figure can be viewed at wileyonlinelibrary.com]

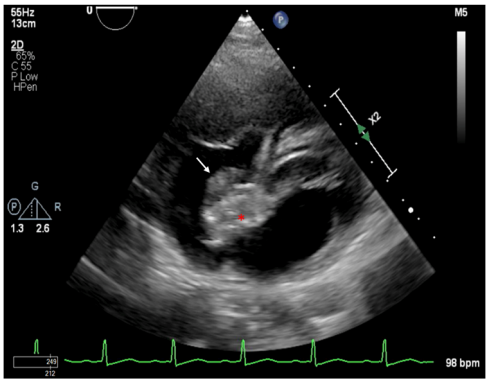


**FIGURE 2** Transthoracic echocardiogram performed on postoperative day 2 in the setting of fever. Note the dense mass (arrow) on the right atrial side of the closure device (*) [Color figure can be viewed at wileyonlinelibrary.com]

325 mg aspirin daily. One day after discharge, she presented with two febrile episodes up to 101.9 F associated with body aches and was re-admitted. Laboratory work-up was significant for: WBC 24.1 × 10k/μl (*N*: 4.8–10.6 × 10k/μl) with neutrophil count 20.5 × 10k/μl (*N*: 1.9–8.1 × 10k/μl), platelet count 127 × 10k/μl (*N*: 150–500 × 10k/μl), procalcitonin 11 ng/ml (*N* < 0.1 ng/ml), C-reactive protein 6.9 mg/dl (*N* < 1 mg/dl), LDH 678 IU/L (*N*: 390–580 IU/L), prothrombin time 15.1 s (11.6–15.4 s), partial thromboplastin time 34.9 s (22.8–38.2 s), ferritin 94 ng/ml (*N*: 9–125 ng/ml), and D-dimer 6.85 μg/ml (*N*: 0.27–0.41 μg/ml). An echocardiogram (Figure 2, Supporting Information Videos 3A and 3B) showed a small mobile mass attached to the inferior portion of the right atrial disc concerning for a vegetation or thrombus, and otherwise there were no changes. Blood cultures were negative. Karius, an extremely sensitive assay that can identify pathogens based on sequencing microbial cell-free DNA, was also negative. CXR was unchanged with stable device position and clear lungs.

Because of the finding on the echocardiogram, a thrombophilia workup was performed. It was essentially negative except for a

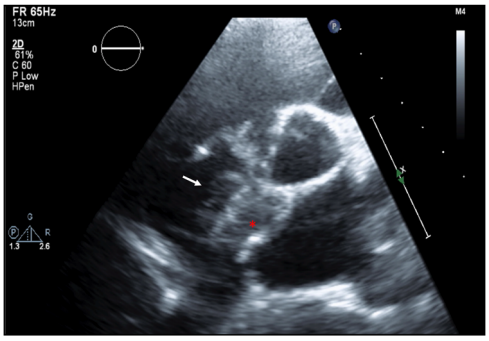


**FIGURE 3** Transthoracic echocardiogram performed on postoperative day 5. Note that the mass (arrow) on the right atrial side of the closure device (*) is now translucent, suggesting that the etiology was a thrombus-filled sac of aneurysmal septum primum on the right atrial side of the device [Color figure can be viewed at wileyonlinelibrary.com]

weakly positive cardiolipin Ab IgM of 20 (weak positive 15–39) with normal IgG and a slightly decreased protein C activity at 62% (70%–150%). The following studies were normal: Factor V Leiden, Prothrombin Gene Mutation, Antithrombin III assay, Protein S activity, homocysteine level, Factor VIII activity, lipoprotein A, β-2 glycoprotein, and lupus anticoagulant. She was started on a heparin infusion. Because of multiple elevated inflammatory markers, she was also started on intravenous vancomycin and gentamycin, and oral rifampin for the unlikely possibility of bacterial endocarditis. COVID-19 testing was repeated, and the patient was found to be positive by RT-PCR testing with a CT of 35.3. Repeat echocardiogram (Figure 3) 3 days after admission showed decreased density of the mobile mass which was now thought to represent resolution of the suspected thrombus within the remnants of the redundant atrial septum.

Since the three blood cultures remained negative, in the context of the negative Karius test and an afebrile, nontoxic appearing patient during the entire hospitalization, she was not thought to have bacterial endocarditis, and antibiotics were discontinued. The patient was discharged home on Day 3 on daily aspirin 81 mg and warfarin 5 mg to keep INR between 2 and 3. On follow-up 1 week after discharge, she was well appearing with no symptoms and the echocardiogram was unchanged. Three months later, the thrombus had entirely resolved (Figure 4, Supporting Information Video 4). She continues to be clinically stable with a well-positioned device. She will continue daily aspirin 162 mg to complete a total of 6 months of treatment.

## 3 | DISCUSSION

Device thrombosis after ASD transcatheter closure is uncommon, with an estimated rate of 1.0%.[1] The incidence appears to be similar in the different available devices, although in some studies the Amplatzer device appears to confer a lower risk.[1,2] Atrial fibrillation

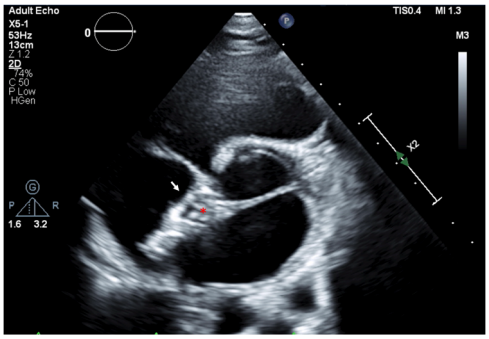


**FIGURE 4** Transthoracic echocardiogram performed on 3-months follow-up. Note the resolution of the mass (arrow) on the right atrial side of the closure device (*) [Color figure can be viewed at wileyonlinelibrary.com]

and the presence of an atrial septal aneurysm have been found to increase the risk of device-related thrombosis.[2] The FDA approved the Gore Cardioform ASD occluder in 2019. The ASSURED clinical study that led to approval reported a device-related thrombus in one patient out of 125, similar to what has been reported for other devices.[3] Occasionally an earlier iteration of this device could develop a "bloated" appearance due to rapid expansion of the right atrial (RA) disc post-deployment caused by blood collecting within the Goretex membranes, for which a fenestration was placed in the RA disc to allow exiting of the blood. This phenomenon has also been seen to a lesser extent with the Gore Cardioform ASD occluder, which also has a fenestration in the RA disc, but has not been shown to result in a higher risk of thrombus formation to date. In this case, there was no evidence of rapid expansion of the RA disc immediately after deployment, but whether some amount of blood could have been trapped within the device and served as a nidus for thrombus formation cannot be absolutely excluded. Device-related endocarditis, which this patient did not exhibit, is exceedingly rare. A meta-analysis of 28,142 patients reported three patients with device-related endocarditis, one ASD, and 2 PFO patients.[1] A review of the literature by Amedro et al. found only 21 reported cases of device-related endocarditis.[4]

Thrombus formation on an ASD device would not typically present with fever and leukocytosis. Similarly, the presence of fever and leukocytosis with a rising cycle threshold value of 35.3, confirming the patient's lower viral load and therefore raising the possibility of an inflammatory response associated with COVID-19. In the absence of any other clear explanation, it could be hypothesized that it was a transient post-inflammatory response secondary to the recent COVID infection, in essence an incomplete multi-systemic syndrome associated with COVID (MIS-C), as clearly demonstrated by increased inflammatory markers. The cumulative incidence of thrombotic complications in critically ill ICU patients with proven COVID-19 pneumonia is 31%, with 27% venous and 3.7% arterial thrombotic events.[5] The procoagulant shift caused by COVID-19 is associated with the severity of the infection.[6] Our patient was asymptomatic with documented low viral load (CT of 34) 3 weeks before the procedure and tested negative on POC-PCR (Abbott Laboratories) 2 days before the procedure. On readmission post device ASD closure her RT-PCR showed persistent but lower viral load with a CT of 35.3. In our practice patients with CT ≥ 34 are considered to have a low viral load, to be no longer infectious, and are cleared for elective surgical procedures.

COVID-19 triggers pro-inflammatory cytokines leading to hyper inflammation, which promotes endothelial dysfunction inducing a microangiopathy-like prothrombic state. Angiotensin-converting enzyme 2 (ACE2), a major component of the renin-angiotensin-aldosterone system (RAAS), is the receptor used by COVID-19 to infect endothelial cells. Decreased ACE2 leads to an angiotensin II predominant state, increasing aldosterone, which augments angiotensin-converting enzyme expression, causing an enhanced breakdown of bradykinin, preventing the normal bradykinin-mediated increase in tPA. RAAS imbalance ultimately exacerbates microthrombi development.[7] COVID-19 coagulopathy (CAC) is associated with a relatively modest decrease in platelet count, elevated lactate dehydrogenase, and most distinctively a high D-dimer level,[6,8] all of which were found in our patient. However, these derangements in the clotting cascade can be seen in any patient with non-Covid related thrombosis.[9]

Our patient's thrombophilia work-up did not reveal any abnormalities that would increase her risk of a device-related thrombus. The cardiolipin Ab IgM is nonspecific and can be positive in response to any inflammatory process. The slight decrease in Protein C activity may represent its consumption due to the thrombus formation rather than thrombophilia.

Limited information has been reported regarding patients undergoing necessary or urgent procedures in the setting of a recent COVID-19 infection. A 4-month-old baby with a cardiac teratoma was reported to undergo heart surgery 2 weeks after testing positive for COVID-19 with no complications.[10] Berkhordari et al. reported that 21 out of 25 patients with COVID-19 who underwent heart surgery, mainly coronary artery bypass grafting, had smooth respiratory outcomes.[11] However, neither of these procedures required leaving a foreign body in the blood stream as with our patient. An international, multicenter, prospective cohort study among 140,231 patients undergoing all types of surgery found that operating at <7 weeks after COVID-19 diagnosis increased the risk of mortality, while a planned delay of ≥7 weeks was associated with similar mortality when compared with patients without preoperative COVID-19 infection.[12] Although there is no proof that the complication our patient experienced was Covid-related, the duration of the hypercoagulable state due to COVID-19 and the adequate follow-up studies needed for surgical clearance remain unknown. Elective cardiac catheterization with implantation of intravascular devices should perhaps be deferred until there is no evidence of any Covid-19 viral load in the system.

## 4 | CONCLUSION

Thrombus formation on an ASD device is very uncommon. COVID-19 infection is known to confer a pro-thrombotic state. We describe a patient who developed a thrombus on an ASD device 7 weeks after an

asymptomatic Covid-19 infection, with a very low viral load by RT-PCR with a CT of 35.3 two days after the procedure. Although a direct cause and effect cannot be established, it may be advisable to delay completely elective catheterization requiring implantation of intravascular devices for a longer time, and until there is no detectable Covid-19 viral load.

## CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

## DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no data sets were generated or analyzed during the current study.

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## SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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