


Two cases of acute endocarditis misdiagnosed as COVID-19 infection

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The COVID-19 pandemic has presented countless new challenges for healthcare providers including the challenge of differentiating COVID-19 infection from other diseases. COVID-19 infection and acute endocarditis may present similarly, both with shortness of breath and vital sign abnormalities, yet they require very different treatments. Here, we present two cases in which life-threatening acute endocarditis was initially misdiagnosed as COVID-19 infection during the height of the pandemic in New York City. The first was a case of *Klebsiella pneumoniae* mitral valve endocarditis leading to papillary muscle rupture and severe mitral regurgitation, and the second a case of *Streptococcus mitis* aortic valve endocarditis with heart failure due to severe aortic regurgitation. These cases highlight the importance of careful clinical reasoning and demonstrate how cognitive errors may impact clinical reasoning. They also underscore the limitations of real-time reverse transcription-polymerase chain reaction (RT-PCR) for SARS-CoV-2 testing and illustrate the ways in which difficulty interpreting results may also influence clinical reasoning. Accurate diagnosis of acute endocarditis is critical given that surgical intervention can be lifesaving in unstable patients.

KEYWORDS

bioprosthesis, COVID-19, endocarditis, misdiagnosis, valve replacement

1 | INTRODUCTION

The COVID-19 pandemic caused by the SARS-CoV-2 virus presents new diagnostic challenges including differentiating COVID-19 infection from other diagnostic entities. Both COVID-19 infection and acute endocarditis may present with hypoxic respiratory failure, fever, and elevated inflammatory biomarkers. The task of distinguishing the two is complicated by the complexities of interpreting SARS-CoV-2 RT-PCR test results. The RT-PCR test may be negative early in the disease course¹⁻³ and may remain positive long after the initial infection due to viral clearance delay.^{4,5} Here, we present two cases of left-sided endocarditis, which were both initially attributed

to COVID-19 infection, and only correctly diagnosed after echocardiography was performed.

2 | CASE VIGNETTE 1

During the height of the COVID-19 pandemic, a 43-year-old man with unknown past medical history presented to a New York City hospital after experiencing a 1-day history of shortness of breath. On initial presentation, the patient's vital signs were as follows: oxygen saturation 81% on a nonrebreather mask, respiratory rate 22 breaths per minute, heart rate 122 beats per minute, blood pressure

101/57 mm Hg, and temperature of 36.5°C. On physical examination, the patient was diaphoretic with cool extremities. Cardiac examination was significant for tachycardia. No cardiac murmur or skin

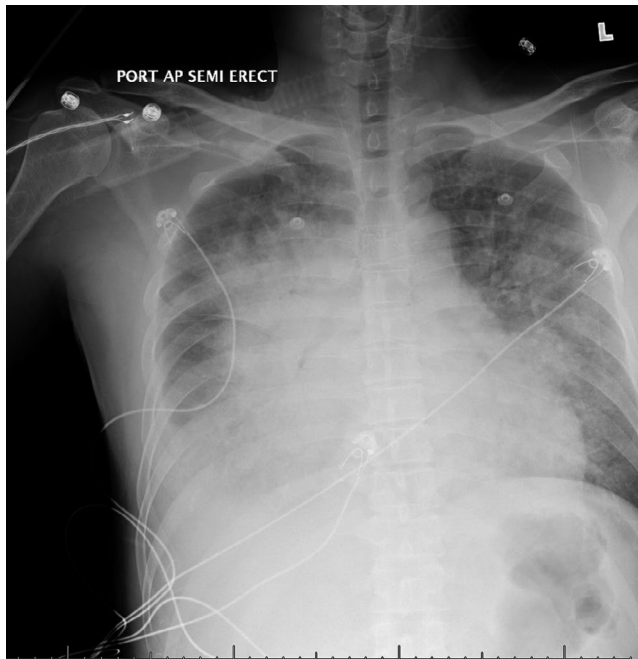
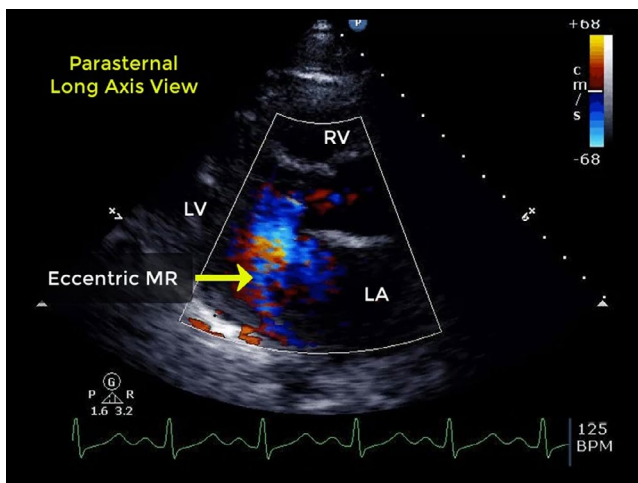


FIGURE 1 Case 1—CXR. Chest X-ray on admission demonstrates large consolidations and opacities with air bronchograms in the right lung and patchy ill-defined opacities in the left lung. They were originally interpreted as most likely representing extensive multifocal bilateral pneumonia but later proved to be pulmonary edema in the setting of endocarditis and severe acute mitral regurgitation



VIDEO 1 Case 1—TTE. Composite 3-clip video demonstrates severe eccentric mitral regurgitation (MR) due to endocarditis-related ruptured papillary muscle in the transthoracic parasternal long-axis, apical 4-chamber, and apical 3-chamber views. AML, anterior mitral leaflet; LA, left atrium; LV, left ventricle; RV, right ventricle. The full-text HTML version of this article includes video content. To view this version please visit <https://onlinelibrary.wiley.com/doi/10.1111/echo.15021>

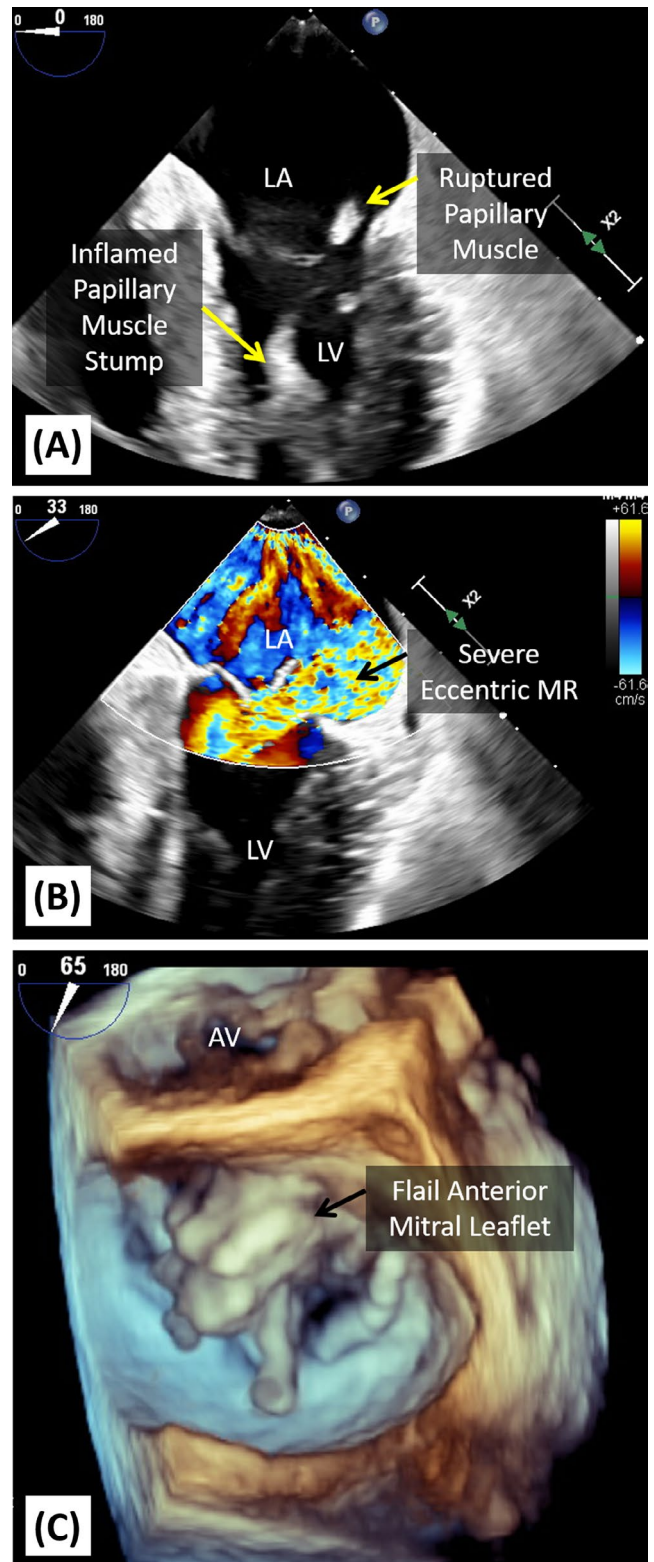
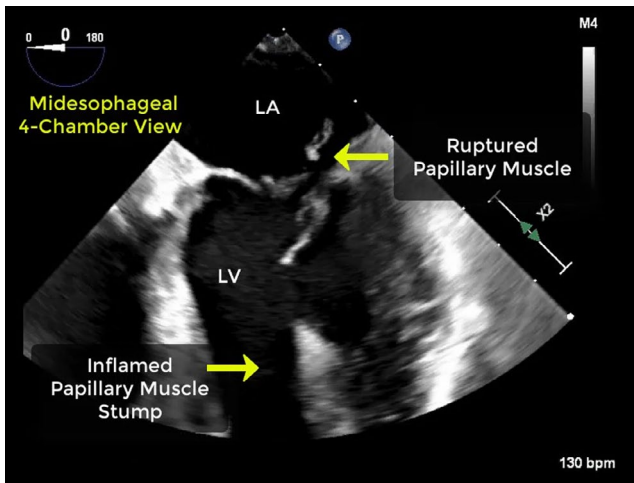
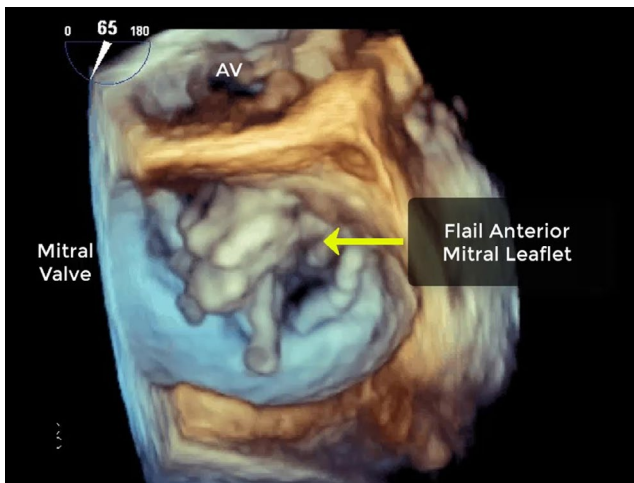


FIGURE 2 Case 1—TEE. 2D imaging demonstrates ruptured papillary muscle of the mitral valve due to endocarditis (Panel A) resulting in severe eccentric mitral regurgitation (Panel B). 3D TEE imaging shows a completely flail anterior mitral leaflet seen from the left atrial perspective during systole (Panel C). AV, aortic valve; LA, left atrium; LV, left ventricle; MR, mitral regurgitation

findings suggestive of endocarditis were appreciated. Chest X-ray demonstrated large consolidations and opacities with air bronchograms in the right lung and patchy ill-defined opacities in the left



VIDEO 2 Case 1—2D TEE. Composite 3-clip video demonstrates ruptured papillary muscle prolapsing into the left atrium during systole resulting in severe eccentric mitral regurgitation (MR) on 2D TEE. LA, left atrium; LV, left ventricle. The full-text HTML version of this article includes video content. To view this version please visit <https://onlinelibrary.wiley.com/doi/10.1111/echo.15021>



VIDEO 3 Case 1—3D TEE. Completely flail anterior mitral leaflet seen from the left atrial perspective in the so-called surgical view of the mitral valve. The full-text HTML version of this article includes video content. To view this version please visit <https://onlinelibrary.wiley.com/doi/10.1111/echo.15021>

lung (Figure 1). This was interpreted as most likely representing extensive multifocal bilateral pneumonia suggestive of COVID-19 infection. Laboratory results were significant for a troponin I of 0.18 ng/mL (normal < 0.04 ng/mL) and markedly elevated inflammatory markers including d-dimer, C-reactive protein, ferritin, and lactate dehydrogenase. The RT-PCR nasal swab for SARS-CoV-2 on admission was negative.

Shortly after arrival, the patient's oxygen requirements increased, and he required endotracheal intubation and mechanical ventilation. He was diagnosed with acute respiratory distress syndrome secondary to COVID-19 infection, with the assumption that the SARS-CoV-2 RT-PCR test was falsely negative. The patient was placed on isolation, and dexamethasone and other COVID-19 supportive therapies were initiated. SARS-CoV-2 IgM and IgG antibody tests were sent. Despite the maximum ventilatory support including an FiO_2 of 100% and a positive end-expiratory pressure of 20 mm H_2O , the patient's respiratory status continued to deteriorate, and he remained profoundly hypoxemic. He was then

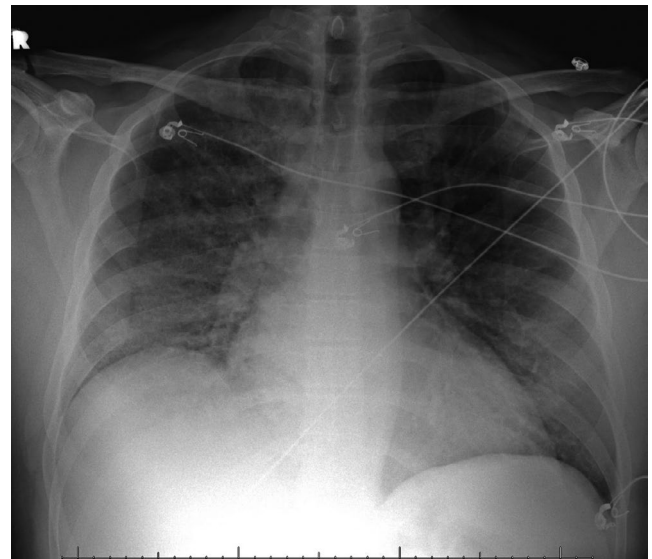


FIGURE 4 Case 2—CXR. Chest X-ray on admission demonstrates new hazy airspace opacity in the lungs bilaterally, right greater than left. These findings were originally interpreted as probably being related to pneumonia/pneumonitis including atypical organisms. They were later proved to be pulmonary edema in the setting of endocarditis and severe acute aortic regurgitation. There is also chronic elevation of the right hemidiaphragm

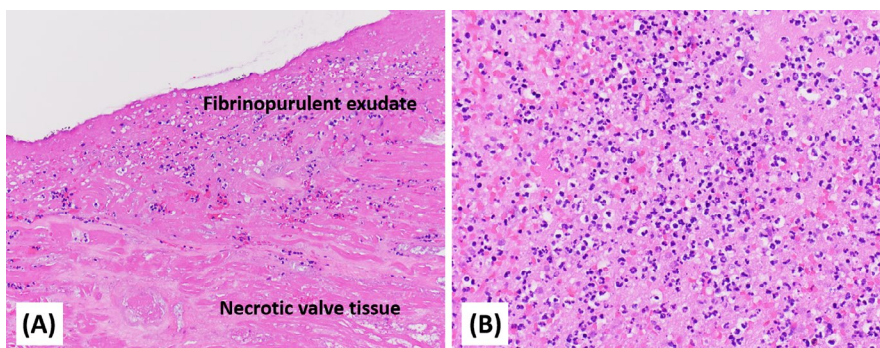


FIGURE 3 Case 1—Histopathology. Hematoxylin and eosin (H&E) stain of the mitral valve specimen shows (Panel A) fibrinopurulent exudate adherent to necrotic valve tissue; (Panel B) the fibrinopurulent exudate consists of fragmented neutrophils admixed with fibrin and red blood cells. This finding is suggestive of bacterial infection

referred for veno-venous extracorporeal membrane oxygenation (ECMO) therapy.

While undergoing evaluation for ECMO therapy, a transthoracic echocardiogram (TTE) was obtained. It revealed preserved right and left ventricular systolic function. Unexpectedly, severe eccentric, posteriorly directed mitral regurgitation was visualized (Video 1). A transesophageal echocardiogram (TEE) demonstrated a ruptured anterolateral papillary muscle resulting in flail anterior mitral leaflet and severe mitral regurgitation (Figure 2; Videos 2 and 3). The patient

was taken emergently to the operating room where inspection of the mitral valve revealed not only a ruptured anterior papillary muscle, but also a ruptured head of the posterior papillary muscle, both due to infective endocarditis. The mitral valve was replaced with a bio-prosthetic valve, with partial preservation of the native mitral valve apparatus. Histopathology confirmed the diagnosis of mitral valve endocarditis (Figure 3). A culture of mitral valve specimens grew *Klebsiella pneumoniae*, and the same organism was isolated from liver abscesses. The patient has since completed long-term intravenous

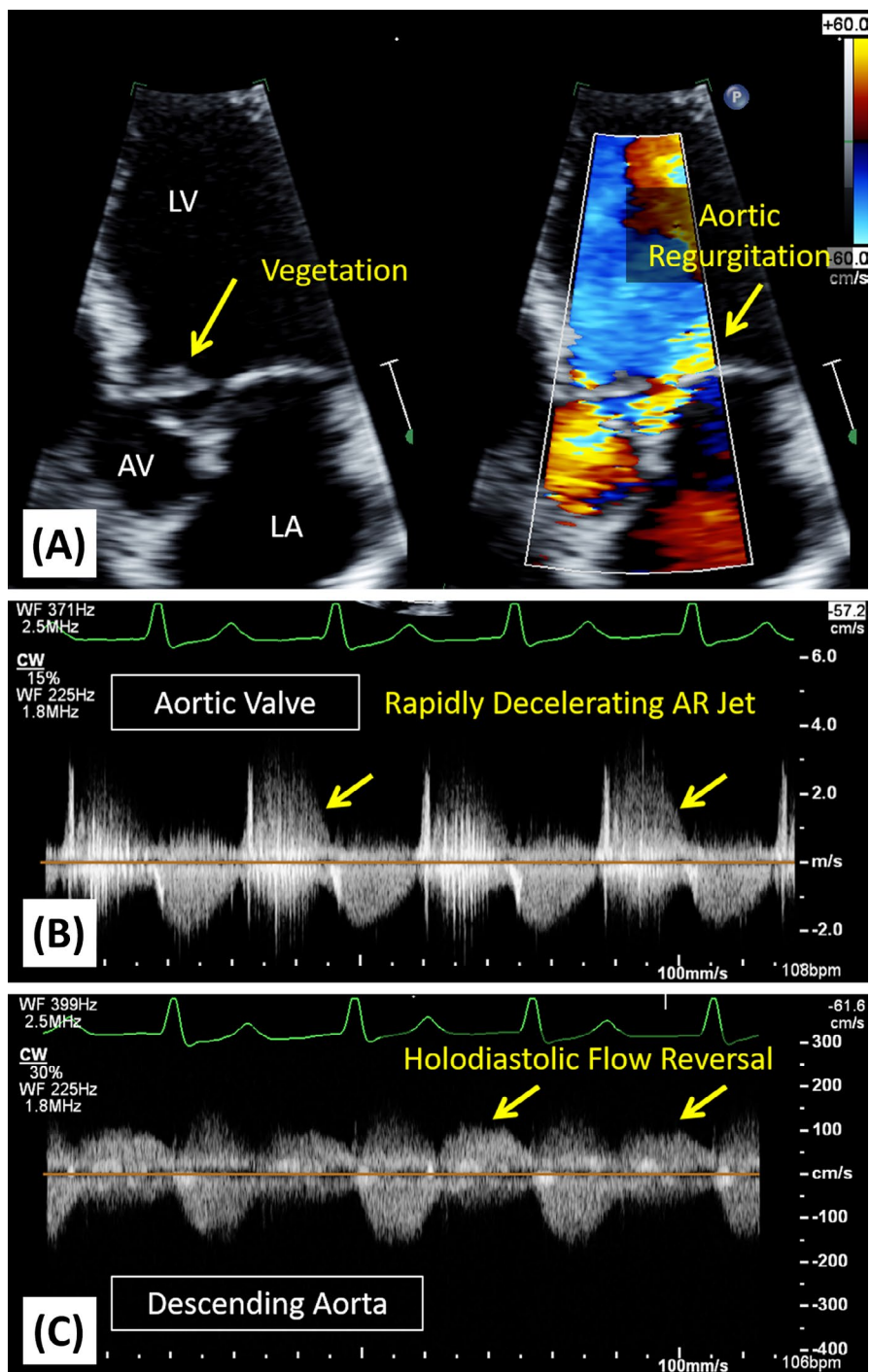
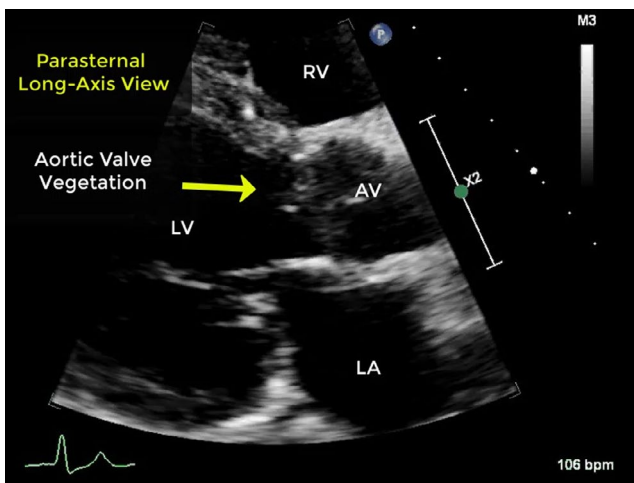


FIGURE 5 Case 2—TTE. TTE imaging demonstrates aortic valve endocarditis resulting in acute severe aortic regurgitation on color Doppler (Panel A) and spectral Doppler (Panel B). Holodiastolic flow reversal in the descending thoracic aorta (Panel C) is indicative of severe aortic regurgitation. AV, aortic valve; LA, left atrium; LV, left ventricle

antibiotic therapy and is doing well. The patient's SARS-CoV-2 IgM and IgG resulted negative.

3 | CASE VIGNETTE 2

A 38-year-old man with a history of human immunodeficiency virus infection presented to a New York City hospital during the COVID-19 pandemic with a five-day history of fatigue and cough. Two days prior to admission, the patient experienced a fever of 38.5°C at home. On arrival, the patient's vital signs included oxygen saturation 91% on room air, heart rate 136 beats per minute, blood pressure 140/41 mm Hg, and temperature 37.3°C. On physical examination, the patient was tachypneic with accessory muscle use and coarse breath sounds bilaterally. Cardiac examination was significant for tachycardia. No cardiac murmur or skin findings suggestive of endocarditis were appreciated. The chest X-ray revealed new hazy airspace opacities in the lungs bilaterally, right greater than left (Figure 4). This was interpreted as most likely being related to pneumonia or pneumonitis, possibly secondary to atypical organisms.



VIDEO 4 Case 2—TTE. Composite 3-clip video demonstrates aortic valve endocarditis resulting in severe aortic regurgitation in parasternal long-axis and apical 5-chamber views, as well as, holodiastolic flow reversal on color Doppler on suprasternal view. AV, aortic valve; LA, left atrium; LV, left ventricle; RV, right ventricle. The full-text HTML version of this article includes video content. To view this version please visit <https://onlinelibrary.wiley.com/doi/10.1111/echo.15021>

Laboratory results were notable for elevated inflammatory markers and a troponin I of 0.8 ng/mL (normal < 0.04 ng/mL). The patient's SARS-CoV-2 RT-PCR test result was positive, and he was diagnosed with COVID-19 pneumonia. He was admitted to the medical intensive care unit and started on dexamethasone and remdesivir.

Because of the elevated troponin on admission, a TTE was obtained. Unexpectedly, TTE showed severe aortic regurgitation with a pressure half time of less than 200 milliseconds and holodiastolic flow reversal in the descending thoracic aorta (Figure 5 and Video 4). There was a 1.0 × 1.0 cm mobile echodensity involving the right and noncoronary cusps on the ventricular side of the aortic valve, consistent with aortic valve endocarditis. The left ventricular systolic function was decreased with a left ventricular ejection fraction of 45%, and the LV was dilated with an end-diastolic diameter of 6.3 cm (normal ≤ 6.0 cm in men).

Initially, it was unclear if the patient's acute decompensation was due to COVID-19 pneumonia (with incidental severe aortic insufficiency) or if it was actually due to acute aortic insufficiency (with an incidentally positive SARS-CoV-2 test). After blood cultures grew *Streptococcus mitis* several days later, the diagnosis of aortic valve endocarditis, acute severe aortic regurgitation, and congestive heart failure was established.

The patient was taken emergently to the operating room where TEE confirmed the diagnosis of aortic valve endocarditis with severe aortic regurgitation (Figure 6 and Video 5). Gross inspection of the native aortic valve revealed complete destruction of the leaflets and a perivalvular abscess. The abscess was debrided, and the aortic valve was replaced with a bioprosthetic valve. Histopathology revealed necrotic valve tissue with bacterial coccal forms (Figure 7) consistent with a diagnosis of aortic valve bacterial endocarditis. The patient has since completed a course of long-term antibiotics and has been doing well.

4 | DISCUSSION

In the midst of the COVID-19 pandemic, physicians are faced with the challenge of determining if and how a COVID-19 infection may be playing a role in a patient's clinical presentation. This may be particularly challenging in patients with acute endocarditis for a number of reasons. Firstly, both acute endocarditis and COVID-19 infection may present with similar symptoms such as shortness of breath,

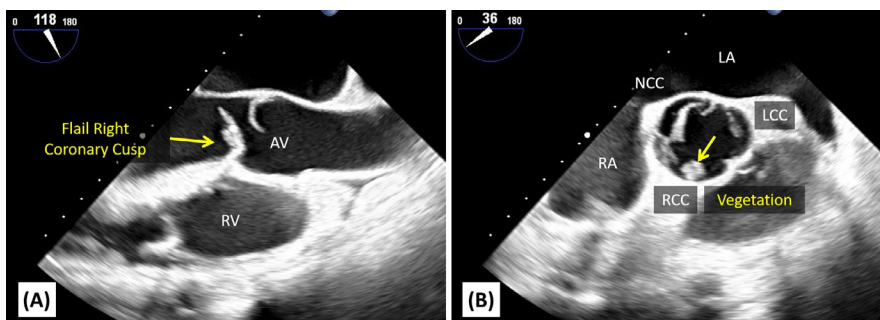


FIGURE 6 Case 2—TEE. Intraoperative 2D TEE imaging demonstrates flail right coronary cusp in long (Panel A) due to aortic valve endocarditis (Panel B)

VIDEO 5 Case 2—TEE. Composite 2-clip video demonstrates aortic valve endocarditis resulting in flail right coronary cusp and severe aortic regurgitation in the long and short-axis views of the native aortic valve. AV, aortic valve; LA, left atrium; LCC, left coronary cusp; NCC, noncoronary cusp; RA, right atrium; RCC, right coronary cusp; RV, right ventricle. The full-text HTML version of this article includes video content. To view this version please visit <https://onlinelibrary.wiley.com/doi/10.1111/echo.15021>

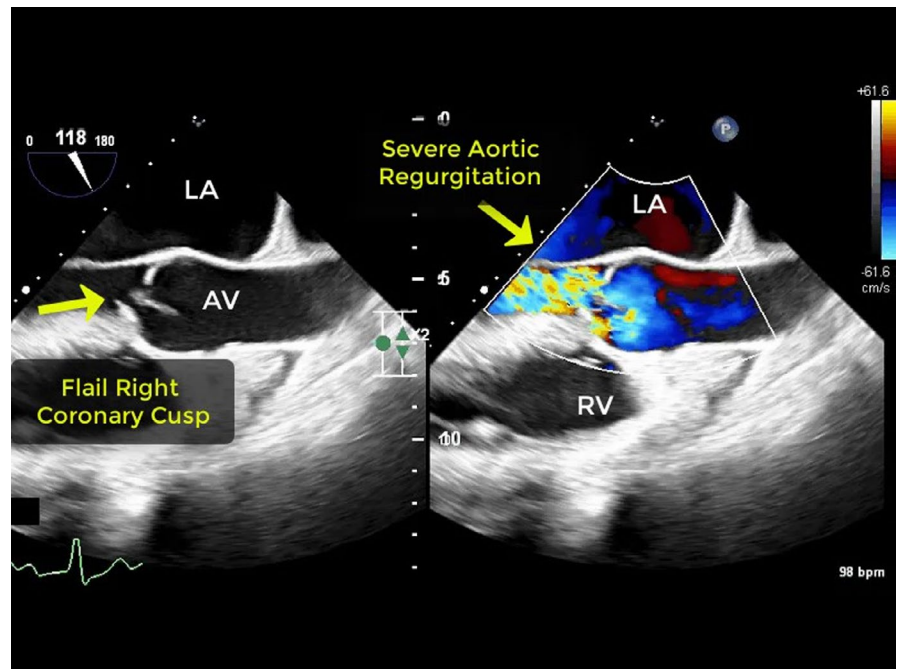
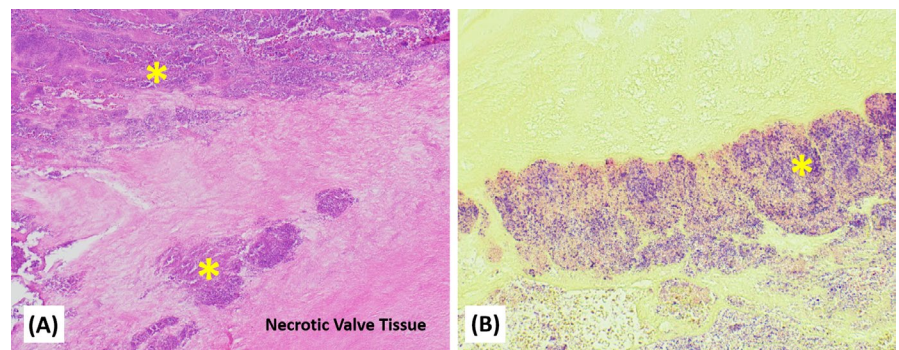


FIGURE 7 Case 2—Histopathology. H&E stain (Panel A) of aortic valve specimen shows necrotic valve tissue with coccal forms suspicious for bacteria (yellow asterisks). Brown-Hopps stain (Panel B) confirms the presence of bacteria, showing gram-positive cocci in chains (yellow asterisk)



fatigue, and fever, as well as nonspecific laboratory values and similar chest X-ray findings. Additionally, both diseases may present with a relatively rapid decompensation and may affect seemingly healthy individuals.

Another challenge in differentiating endocarditis from COVID-19 is the ambiguity of the SARS-CoV-2 RT-PCR test. Given the high rate of false negatives,¹⁻³ providers may conclude that COVID-19 infection is the diagnosis despite a negative SARS-CoV-2 test (as in Case Vignette 1). Furthermore, a false-positive result, a continued positive result long after the initial infection,^{4,5} or a true-positive result without symptoms are all scenarios that may confound the clinical picture. In Case Vignette 2, although the patient tested positive for SARS-CoV-2 RT-PCR, it was not the primary reason for the patient's acute decompensation. When interpreting SARS-CoV-2 RT-PCR results, one must understand the limitations and consider the full clinical picture.

Cognitive errors may also lead to misdiagnosis, and our clinical reasoning during the pandemic may be at increased risk of cognitive errors like confirmation bias and premature closure. Moreover, availability bias may be common during the pandemic, especially in

hospitals where COVID-19 infection is most prevalent. The cases described here highlight the importance of taking a diagnostic pause, especially if new data arise that is inconsistent with our typical illness script for COVID-19 infection.

In summary, endocarditis and COVID-19 infection may initially be difficult to distinguish due to similar presentations, ambiguous SARS-CoV-2 RT-PCR test results, and cognitive errors at play. Nonetheless, swift and accurate identification of acute endocarditis is paramount as urgent surgical intervention is often indicated and failure to intervene may have fatal consequences. As demonstrated by each of these two cases, echocardiography plays an instrumental role in differentiating COVID-19 infection and valvular disease.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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REFERENCES

1. Zhou Y, Pei F, Ji M, et al. Sensitivity evaluation of 2019 novel coronavirus (SARS-CoV-2) RT-PCR detection kits and strategy to reduce false negative. *PLoS One*. 2020;15(11):e0241469.
2. Syal K. Newly identified limitations of diagnostic tools for COVID-19 and consequences. *J Med Virol*. 2020;93:1837-1842.
3. Guo W, Zhou Q, Xu J. Negative results in nucleic acid test of COVID-19 patients: assessment from the perspective of clinical laboratories. *Ann Palliat Med*. 2020;9:4246-4251.
4. Wang X, Huang K, Jiang H, et al. Long-term existence of SARS-CoV-2 in COVID-19 patients: host immunity, viral virulence, and transmissibility. *Viral Sin*. 2020;35:793-802.
5. Li Q, Zheng XS, Shen XR, et al. Prolonged shedding of severe acute respiratory syndrome coronavirus 2 in patients with COVID-19. *Emerg Microbes Infect*. 2020;9:2571-2577.

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