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CASE REPORT

CLINICAL CASE

The "Lightbulb" Sign

A Novel Echocardiographic Finding Using Ultrasound Enhancing Agent in Fulminant COVID-19–Related Myocarditis

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ABSTRACT

We report a case of fulminant COVID-19–related myocarditis requiring venoarterial extracorporeal membrane oxygenation where the use of an ultrasound-enhancing agent demonstrated a previously undescribed echocardiographic finding, the "lightbulb" sign. This sign potentially represents a new area for the use of an ultrasound enhancing agent in the echocardiographic diagnosis of myocarditis. (J Am Coll Cardiol Case Rep 2023;28:102120) © 2023 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

A 32-year-old woman presented to her local emergency department with a 4-day history of myalgias, malaise, dry cough, and headaches. She subsequently experienced diarrhea, vomiting, anosmia, dysgeusia, and dyspnea. She did not describe having sore throat, chest pain, syncope, peripheral edema, palpitations, or contact with a case of COVID-19.

LEARNING OBJECTIVES

- To describe a novel echocardiographic sign seen with an UEA and recognize its potential role in assessing myocarditis.
- To recognize the safety and issues surrounding the use of UEA with venoarterial extracorporeal membrane oxygenation.
- To recognize the value of UEA in improving echocardiographic visualization in ill patients.

On presentation, her blood pressure was 97/76 mm Hg, her heart rate was 140 beats/min, and her respiratory rate was 22/min. Her O_2 saturation was 97% on room air, and her temperature was 38.4 °C. Her initial electrocardiogram (ECG) showed low voltages, poor R-wave progression, and nonspecific ST-T changes (**Figure 1**). A bedside echocardiogram reported biventricular global dysfunction (left ventricular ejection fraction 30%-35%). Her lactate level was 7 mmol/L. Because of her deteriorating hemodynamic status, she was transferred to our institution for mechanical circulatory support.

MEDICAL HISTORY

She did not smoke and had minimal alcohol intake. She also did not report any recreational or regular prescription drug use.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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ABBREVIATIONS AND ACRONYMS

CMR = cardiac magnetic resonance

ECG = electrocardiogram

LV = left ventricular

PW = posterior wall

UEA = ultrasound enhancing agent

VA-ECMO = venoarterial-extracorporeal membrane oxygenation

DIFFERENTIAL DIAGNOSIS

The differential diagnosis included viral myocarditis and nonischemic cardiomyopathy.

INVESTIGATIONS

Bloodwork demonstrated cardiac injury (troponin I: 8202 ng/L) and hypoperfusion (lactate increased to 10 mmol/L) with shocked liver (aspartate aminotransferase 1126 U/L, alanine aminotransferase 1,184 U/L). The result of her nasopharyngeal COVID-19 polymerase chain reaction test was positive. Multifocal patchy subpleural ground-glass opacities were evident bilaterally but were more prominent on the left side, suggesting pneumonia. Investigations are summarized in **Table 1**.

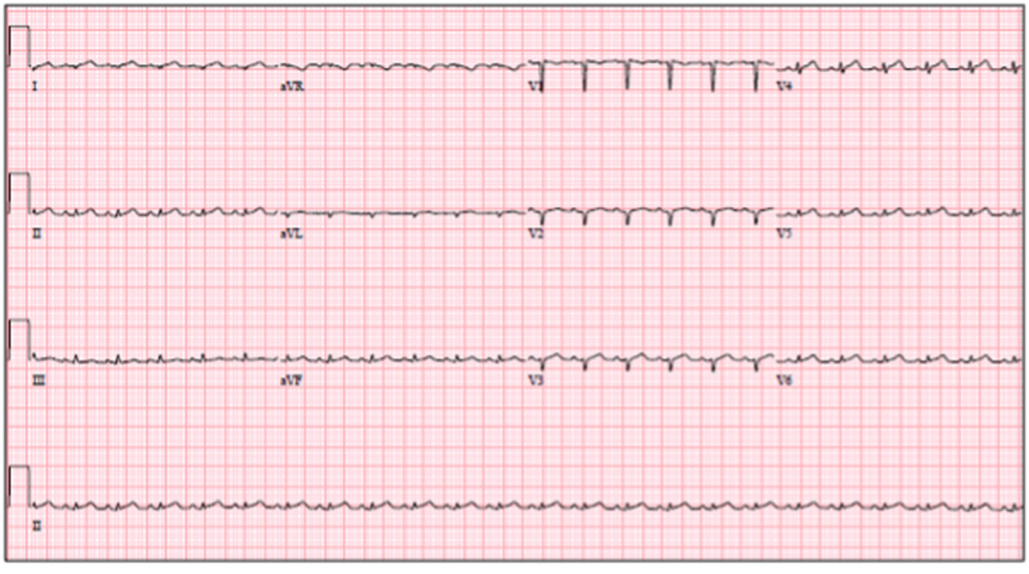
MANAGEMENT

The patient was resuscitated with 2 L Ringer's lactate and intravenous bicarbonate infusion during transport. On arrival (day 0), her cardiogenic shock worsened, despite the administration of milrinone, epinephrine, norepinephrine, and an intravenous furosemide infusion. Owing to her deteriorating left ventricular (LV) function and ongoing hemodynamic instability with associated multiorgan dysfunction, she was underwent cannulation onto femoral venoarterial-extracorporeal membrane oxygenation (VA-ECMO). On day 1, given her poor pulse pressures and LV contractility, an atrial septostomy was performed to insert an LA venting cannula. She also received intravenous heparin, dexamethasone 6 mg daily for 7 days, and tocilizumab 400 mg 1 dose on day 3. With improving LV function, pulse pressures, and biomarkers, her need for inotropic agents and pressor agents decreased, so she underwent decannulation on day 5. Her maximum O_2 requirement was 2 to 4 L by nasal prongs. She did not require mechanical ventilation or renal replacement therapy.

ECHOCARDIOGRAM. Noncontrast transthoracic echocardiography on VA-ECMO after atrial septostomy. On day 1, technically difficult imaging windows (Videos 1 to 3) demonstrated normal biventricular sizes with severe biventricular global dysfunction, and concentric increase in LV wall thickness (**Figure 2**) (interventricular septum 13 mm, left ventricular end-diastolic diameter 31 mm, posterior wall [PW] 15 mm, LV mass 100 g/m^2).

Contrast transthoracic echocardiography on VA-ECMO. On day 1, injection of an ultrasound enhancing agent (UEA) (Definity, Lantheus Medical Imaging, 2 mL of 1.5 mL Definity in 8.5 mL saline over 30 seconds) into the left internal jugular vein resulted in the rapid appearance of microbubbles within the

FIGURE 1 Patient Electrocardiogram on Initial Presentation



Minimal voltage, poor R-wave progression, nonspecific ST-T changes; Q waves in anteroseptal leads.

myocardium and papillary muscles before opacification of the LV cavity resulting from retrograde coronary perfusion (Video 4) (Philips EPIQ machine, X5-1 probe, MI 0.3) (**Figure 3**). We term this previously undescribed funding the "lightbulb sign," given the instantaneous appearance of microbubbles within the myocardium, causing it to "light up." There was a function/perfusion "mismatch" because microbubbles were visualized as a robust and homogenous signal within the myocardium, consistent with normal myocardial perfusion.

Subsequent echocardiograms on days 3 and 5 demonstrated progressive LV recovery with an echoramp study guiding the timing of ECMO decannulation. Contrast images showed improvement in LV function with a normal pattern of myocardial perfusion using the same UEA dose and echocardiographic machine, probe, and settings (Videos 5 and 6).

Postdecannulation transthoracic echocardiography. An echocardiogram after decannulation on day 16 (Video 7) demonstrated normal LV function and decreasing LV wall thickness (**Figure 4**) (interventricular septum 0.9 cm, left ventricular end-diastolic diameter 3.7cm, PW 1.2 cm, LV mass 121 g (86 g/m^2). Her left ventricular ejection fraction had improved to 67%. The pericardial effusion had resolved.

1 month after hospitalization. Cardiac magnetic resonance 3 weeks after discharge showed normal biventricular size and systolic function. Faint midmyocardial LGE was identified within the mid to apical inferoseptum, consistent with postmyocarditis findings. An echocardiogram showed normal LV dimensions (interventricular septum 0.8 cm, left ventricular end-diastolic diameter 3.9 cm, PW 0.8 cm, LV mass 92 g (60.7 g/m^2) and valves.

TABLE 1 Measurements Taken During Initial Investigations

CBC	Hgb 144 g/L, WBC 14.6 × 10^9/L, Lym 2.8 × 10^9/L, ANC 10.7 × 10^9/L, Plt 154 × 10^9/L.
Electrolytes & renal function	Na 139 mmol/L, K 4.4 mmol/L, Cl 109 mmol/L, HCO_3 18 mmol/L, Cr 79 μmol/L.
Miscellaneous	Blood glucose 7.9 mmol/L, TSH 2.8 mIU/mL, Alb 28 g/L, ALP 41 U/L, AST 1126 U/L, ALT 1184 U/L, Bili 7 μmol/L, CK 1129 U/L, CRP <4 mg/L. D-dimer 213 μg/L, LDH 297 U/L, VBG 7.26/42 mm Hg/18 mmol/L, troponin I 8,202 ng/L, lactate 10 mmol/L
Cultures	COVID-19 NP PCR positive Blood × 2 negative, urine negative Influenza A, B, and RSV PCR negative
Toxicology screen	Urine: None detected

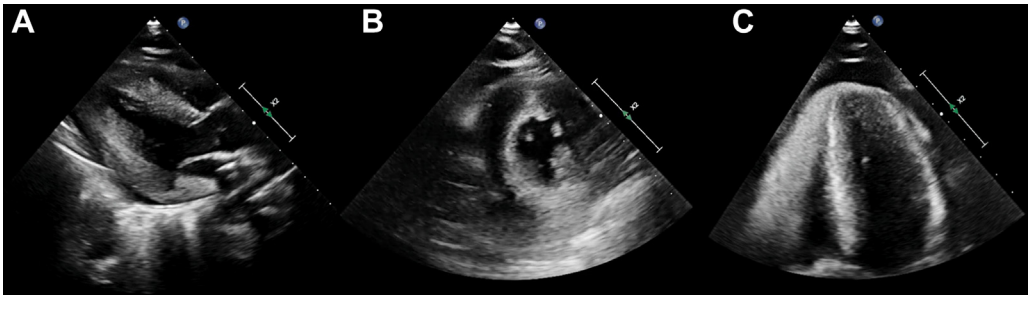
Alb = albumin; ALP = alkaline phosphatase; ALT = alanine aminotransferase; ANC = absolute neutrophil count; AST = aspartate aminotransferase; Bili = bilirubin; CK = creatinine kinase; Cl = chloride; Cr = creatinine; CRP = c-reactive protein; HCO_3 = bicarbonate; Hgb = hemoglobin; K = potassium; LDH = lactate dehydrogenase; Lym = lymphocyte count; Na = sodium; NP = nasopharyngeal; Plt = platelet count; PCR = polymerase chain reaction; RSV = respiratory syncytial virus; TSH = thyroid stimulating hormone; VBG = venous blood gas; WBC = white blood cell count.

DISCUSSION

Myocarditis is a known complication of COVID-19.[1,2] Cardiac magnetic resonance (CMR) is the primary imaging modality used to diagnose myocarditis[3,4] because of its ability to characterize myocardium from T2-weighted images demonstrating myocardial edema and abnormal T1 extracellular volume, and late gadolinium enhancement images demonstrating hyperemia and tissue fibrosis.[3,4] Whereas CMR is widely used for assessing suspected myocarditis, we believe that UEA use during echocardiography can additionally aid in rapidly identifying these patients, and it has additional value in resource-poor environments where CMR may not be readily available.

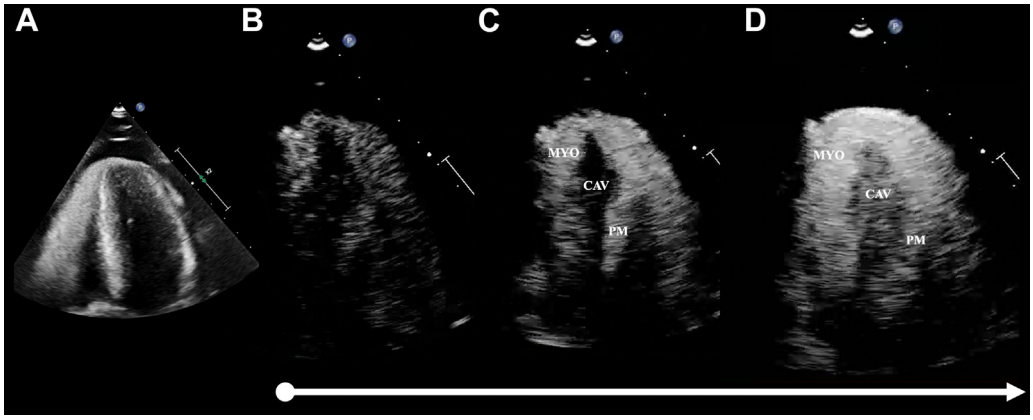
The rapid uptake of UEA by our patient's myocardium is indicative of an intact hyperemic microvasculature, which is consistent with the known

FIGURE 2 Noncontrast Echocardiogram of Patient on Day 1 During VA-ECMO



Parasternal long-axis view (A), parasternal short-axis view (B), and apical 4-chamber view (C) show a significant concentric increase in left ventricular wall thickness and small pericardial effusion.

FIGURE 3 Comparison of Echocardiograms Without Versus With Contrast Material

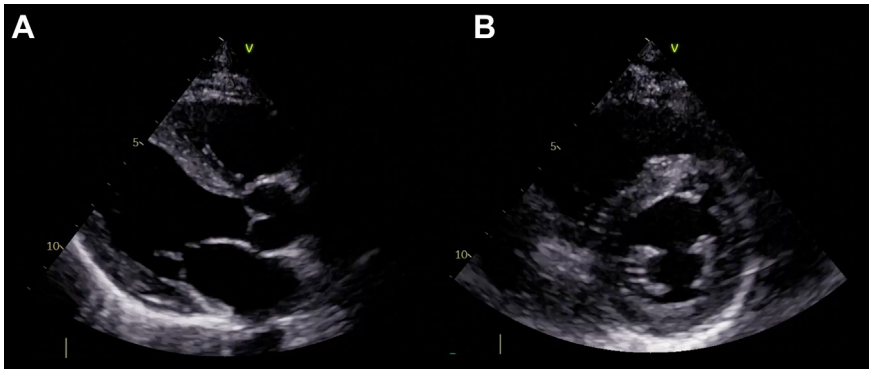


(A) Apical 4-chamber view without contrast material. (B) Immediately after injection, microbubbles are visualized in the myocardium but not the left ventricular (LV) cavity. (C) With time, the myocardium and papillary muscles become clearly delineated. (D) Microbubbles in the LV cavity occur after uptake in the myocardium and papillary muscles.

pathophysiology in patients with severe inflammation.[3] Although this finding can be partly explained by the VA-ECMO circuit, which allows for immediate retrograde filling of the coronaries with UEA (Figure 5), we have not observed this appearance in patients without myocarditis patients who have a similar VA-ECMO configuration. This suggests that the "lightbulb sign" is unique to an inflammatory process and has a potential role in the rapid identification of myocarditis at the bedside. This identification is crucial, inasmuch as patients recognized to have myocarditis have excellent long-term survival and lower need for cardiac transplantation compared with those who present with a more insidious course.[5] The profound uptake of UEA microbubbles may also be a prognostic sign associated with increased likelihood of LV recovery, as seen in our patient, who presented in cardiogenic shock but with appropriate supportive therapy had full recovery of LV function within a week.

Although there are limited reports on UEA safety in ECMO patients, available publications support their use but advise caution when dealing with circuit interference alerts.[6] In our patient, we used UEA contrast material on 3 separate occasions (days 1, 3, and 5) while she was using VA-ECMO. The alarm for bubble detection in the line was expected and silenced with no clinically appreciable impact. It is imperative that the ECMO perfusionist be available to adjust settings and enable proper functioning of the device.

FIGURE 4 Noncontrast Echocardiograms of Patient After Recovery on Day 16



(A) Parasternal long-axis view and (B) parasternal short-axis view demonstrate recovery and reduced left ventricular wall thickness.

FOLLOW-UP

The patient was transferred to the ward on day 8 and discharged home on day 10. One month after discharge, she was seen in the heart function clinic with no clinical complaints. The results of her cardiac and respiratory examinations were normal. Her pulmonary function tests showed normal lung volumes, spirometry, and diffusion capacity. Her transthoracic echocardiogram showed normal biventricular function with no wall motion abnormalities.

CONCLUSIONS

This case describes a novel "lightbulbsign" seen on the transthoracic echocardiogram of a patient receiving ECMO, who had fulminant COVID-19-related myocarditis. This finding with the administration of UEA highlights its potential utility in assessing acute myocarditis.

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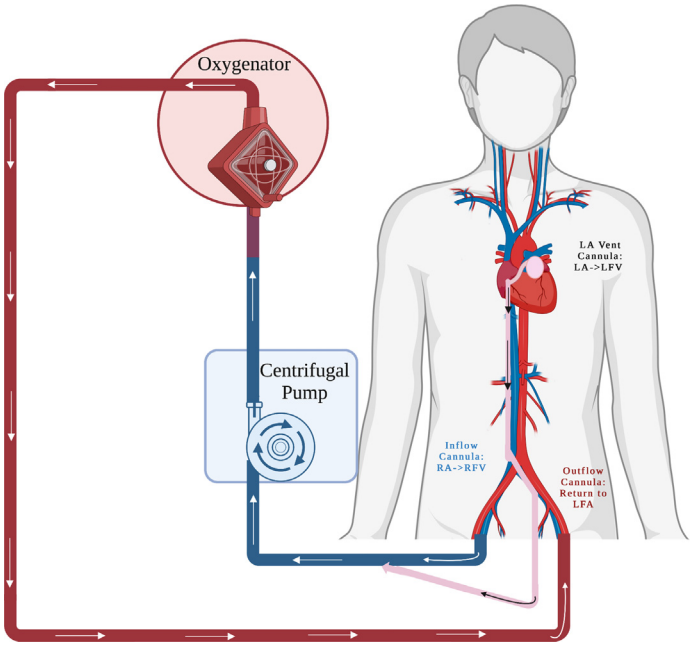
FIGURE 5 Configuration of Venoarterial Extracorporeal Membrane Oxygenation Using Femoral Cannulation and Left Atrial Vent



The venous cannula via the right femoral vein is at the level of the superior cavoatrial junction. The arterial cannula via the left femoral artery is at the tip of the common iliac artery. The venting cannula via the left femoral vein is in the left atrium via a septostomy. Injection of ultrasound enhancing agent via the left internal jugular vein would travel to the right atrium and be sucked into the venous cannula. This would be ejected via the extracorporeal membrane oxygenation circuit into the femoral artery, which would retrogradely fill the aorta and coronaries. Created with BioRender.com.

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KEY WORDS COVID-19, echocardiogram, myocarditis, ultrasound enhancing agent

APPENDIX For supplemental videos, please see the online version of this paper.