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ARRHYTHMIAS

INTERMEDIATE

CASE REPORT: CLINICAL CASE

Electrical Storm in COVID-19

Connor O'Brien, MD,[a,*] Ning Ning, MD,[b,*] James McAvoy, MD,[c] James E. Mitchell, MD,[a] Neil Kalwani, MD,[b] Paul Wang, MD,[b] Duy Nguyen, MD,[b] Risheen Reejhsinghani, MD,[b] Angela Rogers, MD,[a] Javier Lorenzo, MD[c]

ABSTRACT

COVID-19 is a global pandemic caused by SARS-CoV-2. Infection is associated with significant morbidity and mortality. Individuals with pre-existing cardiovascular disease or evidence of myocardial injury are at risk for severe disease and death. Little is understood about the mechanisms of myocardial injury or life-threatening cardiovascular sequelae. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2020;2:1256–60) © 2020 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/).

An 82-year-old woman presented from her skilled nursing facility to our emergency department for evaluation of 2 days of cough, fever to 38.3°C, and dyspnea requiring 6L nasal cannula to maintain peripheral oxygen saturation of 92%.

PAST MEDICAL HISTORY

Her medical history included mild asthma, heart failure with preserved ejection fraction, coronary artery disease (percutaneous coronary intervention 2010), paroxysmal atrial fibrillation (AF), hypertension, obesity, and total hip arthroplasty 1-month prior.

LEARNING OBJECTIVES

- The differential for electrical storm in COVID-19 remains broad.
- Myocarditis and cytokine storm may not be universal drivers of cardiac sequelae in COVID-19.
- Management of these arrhythmias requires consultation with expert, multidisciplinary teams.

DIFFERENTIAL DIAGNOSIS

Her differential diagnosis included bacterial/viral pneumonia, acute on chronic heart failure with preserved ejection fraction, pulmonary embolism, and coronavirus disease-2019 (COVID-19).

INVESTIGATIONS

On arrival she was hemodynamically stable: heart rate 62 beats/min, blood pressure 130/84 mm Hg, respiratory rate of 18, and oxygen saturation 98% on 6L nasal canula. Physical examination noted bilateral rales. Chest x-ray showed patchy bilateral consolidations with mild interstitial edema (**Figure 1**). A computed tomography pulmonary angiogram revealed no pulmonary embolism but bilateral interlobular septal thickening and peripheral ground glass opacities most prominent in the posterior and lower zones. Laboratory tests were remarkable for a white blood cell count of 6.0 k/μl, absolute lymphocyte count of 350/μl,

From the [a]Division of Allergy, Pulmonology, and Critical Care Medicine, Stanford University, Stanford, California; [b]Division of Cardiovascular Medicine, Stanford University, Stanford, California; and the [c]Division of Anesthesiology, Perioperative, and Pain Medicine, Stanford University, Stanford, California. *Drs. O'Brien and Ning contributed equally to this paper. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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 *JACC: Case Reports* author instructions page.

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hemoglobin 8.8 mg/dl (7.7 mg/dl 1 month prior), hyponatremia to 129 mmol/l, ferritin of 1,167 ng/ml, N-terminal pro-brain natriuretic peptide of 721 pg/ml, and C-reactive protein of 4.9mg/dl (Figure 2A). Remaining laboratory tests were within normal limits. A nasopharyngeal swab was sent for severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) and respiratory viruses, blood cultures were collected, vancomycin and cefepime were started, and the patient was admitted to a negative-pressure room.

MANAGEMENT

Within hours, the patient developed increased work of breathing and hypoxia requiring intubation. She was sedated with propofol and hydromorphone infusions; suspected sedation-related hypotension was treated with norepinephrine and vasopressin infusions. An echocardiogram revealed a left ventricular ejection fraction of 68%, estimated right ventricular systolic pressure of 33 mm Hg, right atrial pressure of 8 mm Hg, and small left ventricular end-diastolic volume of 40 ml. She developed AF with rapid ventricular response with rates to 155 beats/min. The ventricular response rate was controlled with an amiodarone infusion. Serial troponins were not elevated and electrocardiogram (ECG) revealed AF but was otherwise normal (Figure 1). Propofol was transitioned to dexmedetomidine allowing vasopressor cessation. She converted to normal sinus rhythm; amiodarone infusion was converted to oral.

She was mechanically ventilated on a volume control mode with 50% FiO2 and positive end expiratory pressure of 10 cm H2O with inhaled nitric oxide for hypoxemia support. Tidal volume was set to 340 ml (6 ml/kg based on ideal body weight). Plateau pressure was 24 cmH_2O with a driving pressure of 14 cmH_2O. Proning protocol was initiated with at least 12 h prone as well as active diuresis to maintain a central venous pressure <10 mm Hg. On hospital day 1 her SARS-CoV-2 polymerase chain reaction returned positive, and she was enrolled in a remdesivir trial. Vancomycin and cefepime were stopped on days 3 and 4, respectively.

On day 10, she developed a persistent fever of 38.1°C and vasopressor requirement (Figure 2B). Chest x-ray showed worsening consolidation of her right lower and right upper lung fields. Vancomycin and cefepime were resumed. The patient's static pulmonary compliance decreased and oxygen requirements rose to 70% FiO2 and positive end expiratory pressure of 12 cmH_2O to maintain a saturation

ABBREVIATIONS AND ACRONYMS

AF = atrial fibrillation

COVID-19 = coronavirus disease-2019

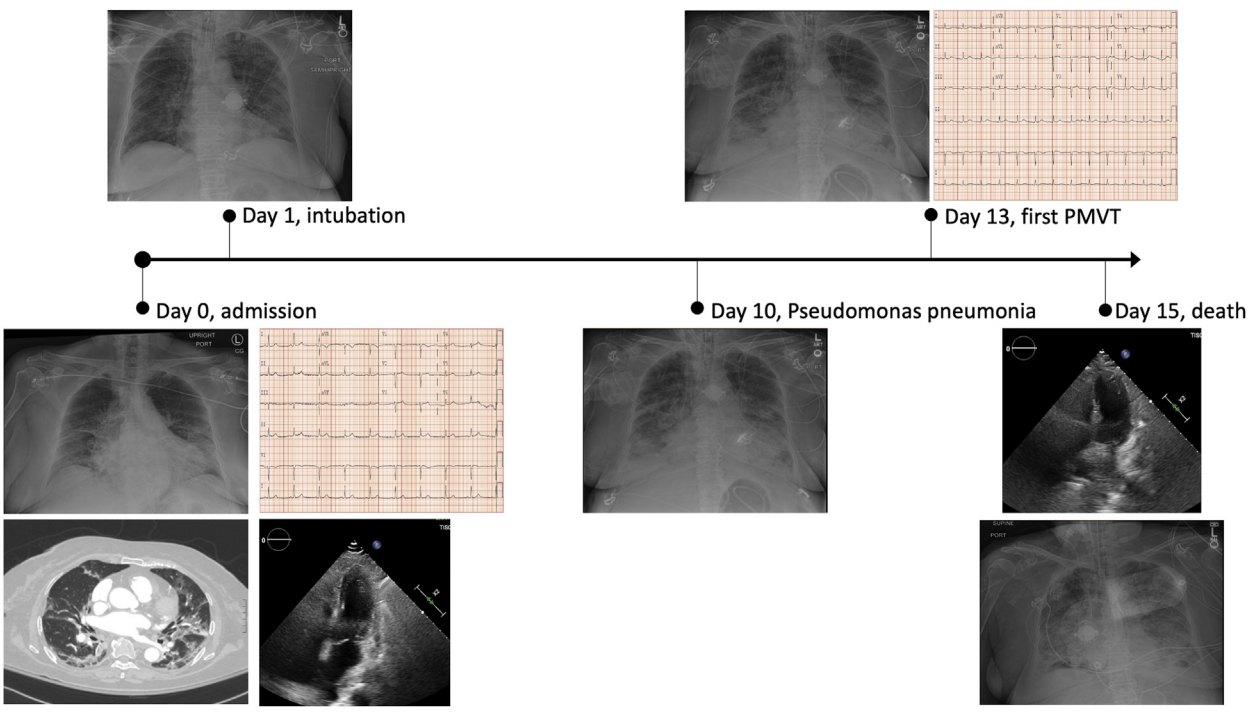
DCCV = direct current cardioversion

ECG = electrocardiogram

PMVT = polymorphic ventricular tachycardia

SARS-CoV-2 = severe acute respiratory syndrome-coronavirus-2

FIGURE 1 Timeline of Clinical Developments and Associated Studies



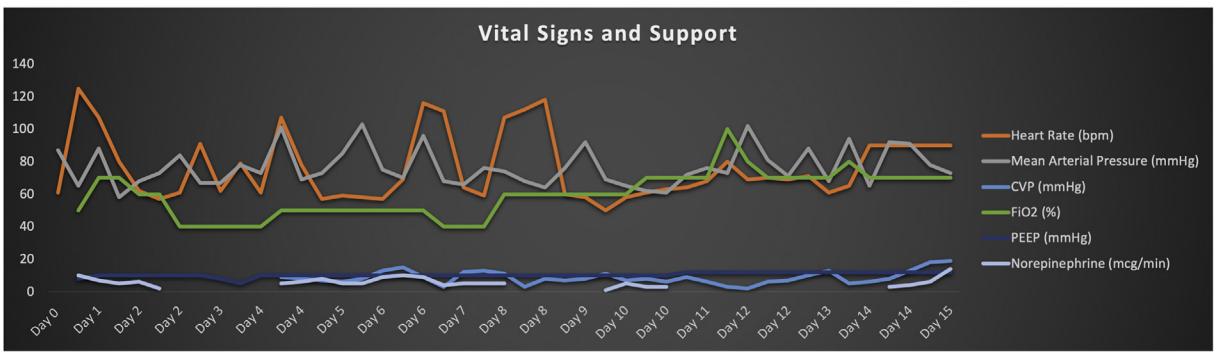
PMVT = polymorphic ventricular tachycardia.

FIGURE 2 Lab and Vital Sign Flow Sheet

A

	Day 0	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14	Day 15
Tmax (°C)	37.5	39.4	37.7	37.8	38.5	38.3	37	36.5	38.5	37.6	38.1	37.4	37.3	37.9	38.9	38.9
WBC (K/μL)	6	5	5.1	5.3	6.1	11.4	9	9.4	9.5	8.3	3.8	5.4	8.7	12.6	17.3	18.6
Absolute Neutrophil Count (K/μL)	5.30	3.86	3.69	4.31	5.53	9.30	N/A	8.06	8.57	7.25	3.27	4.33	7.82	10.66	12.11	N/A
Absolute Lymphocyte Count (K/μL)	0.35	0.82	0.90	0.79	0.39	1.70	N/A	1.01	0.47	0.60	0.29	0.67	0.50	0.78	2.25	N/A
Potassium (mmol/L)	4.1	4.6	4.2	4	4.2	4.3	4.2	3.5	3.8	4.3	3.8	3.5	3.9	3.8	6.8	5.8
Creatinine (mg/dL)	0.48	0.45	0.37	0.56	0.38	0.37	0.5	0.45	0.44	0.84	1.43	1.74	2.05	2.19	2.45	2.14
CRP (mg/dL)	4.9	N/A	17.8	N/A	N/A	17.6	N/A	30.6	N/A	28.1	N/A	N/A	N/A	21.5	N/A	N/A
Ferritin (ng/mL)	1167	N/A	N/A	N/A	N/A	N/A	N/A	833	N/A	N/A	N/A	N/A	N/A	1075	N/A	N/A
D-Dimer (μg/mL)	N/A	N/A	NA	N/A	N/A	6.68	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	9.22
Procalcitonin (ng/mL)	0.12	0.13	0.21	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	0.9	N/A	N/A	N/A	N/A
Troponin (ng/mL)	<0.017	N/A	N/A	<0.017	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	0.092	0.113	0.086
NT-proBNP (pg/mL)	721	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	12,658	N/A	N/A
CK, MB (ng/mL)	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1.6	3	4.5
Lactate (mmol/L)	1.9	2.3	1.7	1.4	2.3	1.8	2.6	2.2	2.1	1.5	1.4	1.2	1.3	1.2	5.4	4.4
pH	N/A	7.34	7.32	7.29	7.38	7.33	7.36	7.37	7.37	7.33	7.28	7.33	7.32	7.27	7.22	7.17

B



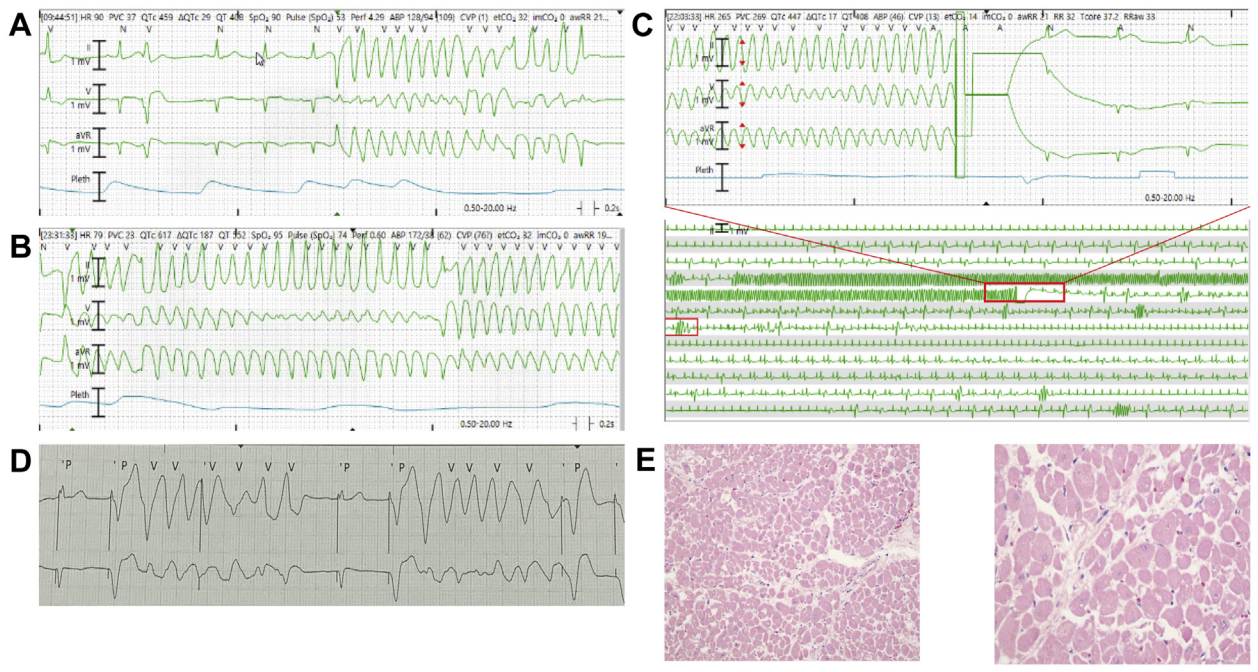
(A) Graphical trends in vital signs, oxygen supplementation, and vasopressor dose. **(B)** Laboratory tests during admission. bpm = beats per minute; CRP = C-reactive protein; CVP = central venous pressure; NT-proBNP = N-terminal-pro-brain natriuretic protein; PEEP = positive end expiratory pressure; WBC = white blood count.

of 92%. Respiratory and blood cultures grew *Pseudomonas aeruginosa*. Antibiotics were narrowed to piperacillin-tazobactam. Her creatinine increased gradually to 2.05 mg/dl on day 12.

On intensive care unit day 13 she developed multimorphic ventricular ectopy (Figure 3A) precipitating hemodynamically unstable polymorphic ventricular tachycardia (PMVT) (Figure 3B) requiring direct current cardioversion (DCCV) (Figure 3C). Laboratory tests acquired 10 h preceding and immediately after cardioversion showed no evidence of electrolyte derangement. No vasopressors were administered pre- or post-DCCV. Post-cardioversion ECG demonstrated normal sinus rhythm with QTc of 462 ms and notably no ischemic changes. Laboratory tests preceding DCCV identified an elevated troponin (0.092 ng/ml) and N-terminal-pro-brain natriuretic protein (12,658 pg/ml), implications of which were unclear in the setting of new-onset renal dysfunction. Central venous pressure remained <10 mm Hg. Given concern for borderline QTc prolongation, all QTc-prolonging medications (amiodarone and trazodone) were stopped. Lidocaine infusion was initiated, and metoprolol was added to suppress ectopy. A follow-up echocardiogram showed no evidence of ventricular dysfunction, chamber enlargement, or wall motion abnormality. Electrical instability precluded cardiac magnetic resonance imaging.

The patient continued to have early coupled premature ventricular contractions initiating episodes of sustained PMVT despite shortening of her QTc interval to 400 to 440 ms, heart rate of 60 to 70 beats/min, and no evidence of ischemia with stable ECGs and downtrending troponin levels (Figures 1 and 2A). She required 3 more DCCVs, at which point a transvenous pacer was placed and overdrive pacing initiated at 90 beats per minute effectively suppressing premature ventricular contractions temporarily. Unfortunately, she continued to have progressive kidney injury with worsening hyperkalemia (peak 7.4 mmol/l) and acidemia requiring initiation of continuous veno-venous hemofiltration. She became progressively hypotensive, requiring vasopressors. Biventricular function and mixed venous saturation were notably normal. Despite right ventricular pacing, she developed

FIGURE 3 Telemetry Strips and Histopathology



(A) Initial episode of percutaneous coronary intervention (PMVT). **(B)** Sustained PMVT on day 13. **(C)** Evidence of recurrent PMVT through right ventricular pacing. **Red box** shows the heart rhythm immediately post-direct current cardioversion. **(D) Top**, successful direct current cardioversion (DCCV) of PMVT. **Bottom**, rhythm strip pre- and post-DCCV. **(E)** Hematoxylin and eosin stain of myocardium showing no evidence of lymphocytic infiltration or microvascular thrombosis. Left image is 10x magnification and right image is 40x magnification.

recurrent nonsustained PMVT not requiring further DCCV (Figure 3D). Troponin remained persistently positive (peak 0.113 ng/ml). Repeat surveillance cultures were negative.

Despite best efforts, the patient experienced worsening multiorgan failure. After sharing her prognosis with the family, life-sustaining therapy was withdrawn and she passed.

An autopsy was requested. Gross examination of the heart demonstrated left ventricular cardiac hypertrophy and atrial dilation as well as focal, mild coronary atherosclerosis in the left anterior descending artery (estimated 30% occlusion) with an intact, patent intracoronary metal stent in the mid-left anterior descending. Histologic sections of the myocardium demonstrated mild, patchy fibrosis. There was no evidence of an inflammatory cell infiltrate or myocyte necrosis, precluding a diagnosis of myocarditis (Figure 3E). There was no evidence of background cardiomyopathic changes or microvascular thrombosis. Ultrastructural examination demonstrated similar findings, without evidence of viral particles.

DISCUSSION

This case illustrates the clinical challenges of managing cardiovascular complications of COVID-19 infection. COVID-19 is known to enter cells via the angiotensin-converting enzyme II receptor (1), which is expressed in myocardium, raising concern that the virus could directly infect the heart. Studies of SARS-CoV-1 demonstrated replication in myocardium (2), raising suspicions that viral myocarditis may explain the high degree of morbidity and mortality seen in patients with COVID-19 with evidence of myocardial injury.

Although the evidence for myocarditis is biologically plausible, acute respiratory distress syndrome is a complex biological state. Furthermore, COVID-19 myocardial injury has a diversity of presentations (3,4). Many of the patients suffering myocardial injury during COVID-19 have preexisting cardiovascular disease, predisposing them to type 2 myocardial infarction, stress-induced cardiomyopathy, and secondary cardiac injury. Although case reports have described acute cardiovascular collapse with troponin

elevation and imaging evidence of myocardial inflammation (4), many cases have a more protracted course averaging 2 weeks (3). Although direct viral injury is possible, drivers like cytokine storm, critical illness, and ischemia are plausible.

Our case illustrates the occurrence of malignant ventricular arrhythmias in a patient with COVID-19–related multiorgan dysfunction, and the association of cardiac complications with poor clinical outcome. Based on clinical and postmortem analysis, viral myocarditis, plaque rupture, microvascular thrombosis, and QT-prolongation appear to be unlikely drivers. Cytokine storm is possible, but her downtrending C-reactive protein, <2-fold increase in d-dimer, normal white count, and afebrile state at the time of arrhythmia onset do not support this theory. Postulating whether remdesivir contributed to this electrical storm remains challenging given limited experience. However, a relationship seems unlikely, as treatment ended on hospital day 5 and drug half-life is reported as 35 h (5). Our case likely describes a multifactorial epiphenomenon emerging from vulnerable patient substrate under strain from protracted critical illness.

CONCLUSIONS

Although myocarditis and cytokine storm may be significant drivers of morbidity and mortality in COVID-19, this case highlights that not all cardiovascular complications are the result of direct viral injury or systemic inflammation specific to SARS-CoV-2. Prolonged critical illness likely contributes significantly to the high incidence of cardiovascular insults. Determining specific pathophysiologic mechanisms of cardiac sequelae is essential to guiding therapy in this critically ill population.

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ADDRESS FOR CORRESPONDENCE: Dr. Connor O'Brien, Stanford Hospital and Clinics, Department of Pulmonology, Allergy, and Critical Care Medicine, 300 Pasteur Drive, Room H3143, Stanford, California 94305. E-mail: coobrien@stanford.edu. Twitter: @coobrien.

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KEY WORDS cardioversion, electrocardiogram, preserved ejection fraction, ventricular fibrillation, ventricular tachycardia