Subacute Cardiac Tamponade in a COVID-19 Patient Despite Negative Testing

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Abstract
COVID-19 infection has been documented to cause a wide range of symptoms including cardiac complications. We present a case of subacute cardiac tamponade in a patient infected with COVID-19 in the absence of respiratory symptoms; we also review the current literature on this rare sequela. Our patient is a 67-year-old man who presented to the hospital due to intermittent chest pain for three weeks. COVID-19 polymerase chain reaction (PCR) testing was negative two times. He had an outpatient echocardiogram that showed a moderate pericardial effusion about a week prior to the hospital presentation. On admission, a repeat echocardiogram showed a large pericardial effusion with tamponade physiology. Pericardiocentesis did not reveal a clear etiology of the hemorrhagic effusion but four days later, the patient was found to be positive for COVID-19 infection without any clear respiratory illness. Given the absence of other etiology and negative workup, cardiac tamponade was attributed to pericardial inflammation from this virus and our patient improved with colchicine and steroids. We, therefore, advise providers to consider COVID-19 as a cause of hemorrhagic, cryptogenic cardiac tamponade despite negative COVID-19 testing. We also review 42 additional reported cases of cardiac tamponade in patients infected with COVID-19. COVID-19 can cause cardiac tamponade even in the absence of pulmonary disease. This case and literature review highlight tamponade as a rare complication of COVID-19 and should be considered in the differential of any acute deterioration in this patient population.

Categories: Cardiology, Internal Medicine, Infectious Disease
Keywords: hemorrhagic, effusion, respiratory, tamponade, covid-19

Introduction
COVID-19, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a respiratory illness that has been associated with a wide range of symptoms with varying severity. It has been well documented that this virus can cause cardiac complications independent of a patient’s baseline comorbidities including acute coronary syndrome, pericarditis, myocarditis, and arrhythmia [1]. Cardiac tamponade, a life-threatening condition, has been documented as a rare sequela of COVID-19 infection. We report a case of an elderly man who presented with subacute cardiac tamponade attributed to COVID-19 infection without significant concurrent respiratory symptoms. We also review the current literature on this rare complication of COVID-19 infection.

Case Presentation
Our patient is a 67-year-old man who initially presented to the emergency department with chest discomfort and intermittent dyspnea. This patient had a medical history significant for melanoma treated with radiation therapy, Barrett’s esophagus, and hyperlipidemia. These symptoms originally started about three weeks prior to presentation during which time SARS-CoV-2 polymerase chain reaction (PCR) testing was negative two times. The following week he had a stress test negative for ischemia but underwent an echocardiogram that showed a moderate pericardial effusion. He was sent home from the clinic with a course of non-steroidal anti-inflammatory drugs (NSAIDs) at that time. His symptoms persisted which prompted him to return to the emergency department.

In the emergency department, presenting vitals and physical examination was remarkable aside from tachycardia and distant heart sounds. Laboratory studies were significant for leukocytosis of 18.83 10^3/ul, C reactive protein of 31.25 mg/dl, normal electrolytes, and negative troponins. EKG was consistent with new atrial fibrillation with rapid ventricular response as well as low voltage in precordial leads (Figure 1). bedside point of care ultrasound (POCUS) showed large circumferential pericardial effusion causing diastolic collapse of the right ventricle (Figure 2). Given the concern for early cardiac tamponade, the patient was taken for emergent pericardiocentesis with the removal of 750 cc of serosanguinous fluid. The patient was then started on colchicine as well as steroids and transferred to the intensive care unit for further monitoring.
The patient reported improvement in symptoms and reverted to sinus rhythm without need for cardioversion. The pericardial drain was removed the following day without complication. Repeat echocardiogram at time of discharge showed no re-accumulation of pericardial fluid and normal left ventricular (LV) systolic function of 55% (Figure 3).
The etiology for pericardial effusion remained unclear at this time with viral pericarditis being the leading diagnosis even though viral panel, as well as SARS-CoV-2 PCR, was negative. Fluid from the pericardiocentesis was largely bloody with analysis showing 28,000 red blood cells/mm$^3$ and 1,233 white blood cells/mm$^3$ with 79% neutrophilic predominance. Fluid bacterial cultures, acid-fast stain, and autoimmune testing were all negative. Cytology and flow cytometry of pericardial fluid was also negative for malignancy. Pericardial fluid was not sent for SARS-CoV-2 testing. Due to clinical improvement, the patient was discharged home after a two-day hospital course with a regimen of colchicine and steroids for presumptive viral pericarditis.

Four days later, the patient re-presented to the emergency department due to recurrent chest pain and persistent cough. Initial vitals and examination were unremarkable with oxygen saturation of 95% on room air. The patient tested positive for SARS-CoV-2 at this time by nasal PCR. Inflammatory markers were mildly elevated with lactate dehydrogenase of 287 units/L, C reactive protein of 3.67 mg/dL, and D-dimer of 5.05 ug/ml. Repeat echocardiogram showed a small pericardial effusion, as well as a left lower lobe, infiltrate (Figure 4).
FIGURE 4: CT chest showing a small pericardial effusion as well as a left lower lobe infiltrate

Red arrow refers to pericardial effusion; yellow arrow refers to left lower lobe infiltrate.

The patient was treated with colchicine as well as dexamethasone. He remained without any significant respiratory symptoms and was discharged home after a four-day hospital course with a negative PCR test result. The patient was followed up in the cardiology clinic a week post discharge where repeat echocardiogram showed minimal pericardial fluid.

Discussion

Cardiac tamponade is a life-threatening condition that has a rare association with COVID-19 infection. The exact mechanism of cardiac injury by this virus is not well understood but is proposed to be due to the robust “cytokine storm” induced by the virus and the direct downregulation of myocardial ACE-2 receptors [1]. However, this pathogenesis is less likely in our case given the clinical picture and lack of elevated inflammatory markers especially C-reactive protein but could result from direct inflammation as usually in viral pericarditis. A meta-analysis of CT findings in patients infected with COVID-19 found that 4.55% of patients had evidence of pericardial effusion [2]. The clinical significance of this is unclear but may be related to myopericarditis induced by the virus. There have been several established cases including our patient that have documented the accumulation of pericardial fluid leading to tamponade physiology in patients infected with COVID-19.

Our case adds to a growing body of evidence that COVID-19 can lead to pericardial inflammation and cardiac tamponade independent of the patient’s cardiac risk factors. After careful literature review, we identified 44 other documented cases of cardiac tamponade in the context of COVID-19 infection (Table 1).

| Patient | Age/Sex | Comorbidities | Presenting symptoms | Presenting exam | Inflammatory markers | Cardiac markers | Radiographic findings | EKG | Pulmonary Vents | Management | Pericardial fluid | Outcome |
|---------|---------|---------------|---------------------|----------------|---------------------|----------------|----------------------|-----|----------------|------------|------------------|---------|
| 1. current case | 67 yr M | Melanoma, HLD | Chest pain, Dyspnea | Tachycardia | CRP-1.3, mg/dl | Troponin- negative | Unremarkable | Sinus tachycardia, Low voltage in precordial leads | Large, unremarkable pericardial effusion, RV diastolic collapse, LVEF- 55% | None | None | Pericardiocentesis, Colchicine, NSAID | Bloody |
| 2. Hua et al. [3] | 47 yr F | Prior myocarditis | Cough, Dyspnea, Chest pain, Fever, Hypotension | Tachycardia | Troponin T- 0.235 ng/ml | Mild pulmonary congestion | Sinus tachycardia, Canine | Global pericardial effusion, LVSF- None | None | None | Pericardiocentesis, Vasopressor | Serousanguinous |

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| No. | Authors et al. | Age | Gender | Presentation | Notable Symptoms | Cardiac | Other | Prognosis | Therapies | Imaging | Autopsy | Comments |
|-----|----------------|-----|--------|-------------|-----------------|--------|-------|-----------|----------|---------|---------|----------|
| 3   | Dal svg et al. [9] | 67 yo F | HF(70%) | Cough, dyspnea, shoulder pain | Tachycardia | CRP 15.8 mg/dl, Troponin I 0.018 mg/dl, D-dimers 1.22 mg/dl | Unremarkable | Normal | Infero-lateral ST elevation | Circular hemopericardial effusion, Early right ventricular collapse, LVSD 46% | None | Yes | Percardiacentesis, HCO, Colchicine, Steroids, Blood | \( R \) |
| 4   | Aghi et al. [3] | 70 yo F | CAD, OA, HTN | Chest pain, Dyspnea | Fever, hypoxia | Troponin I 0.037 mg/dl | - | - | Enlarged cardiac silhouette, Bilateral pulmonary edema, Infiltrates, Retro-cardiac silhouette, Diffuse T wave inversions | Large circular hemopericardial effusion, RV diastolic collapse, Septal bowing, LVSD 51% | Yes | Yes | Percardiacentesis, Vasopressor, Colchicine | Senssegreguous, Exudative | \( R \) |
| 5   | Pront et al. [9] | 65 yo F | Paracutal AF, PMH, HTN | Cough, Fever, Chills | Unremarkable | Troponin I 0.012 mg/dl | - | - | Biventricular cardiomegaly, Bilateral lung opacities, Retro-cardiac silhouette, Diffuse T wave inversions | Circular hemopericardial effusion, Early right ventricular collapse, LVSD 51% | None | None | Percardiacentesis, Sive colored, Exudative | \( R \) |
| 6   | Han et al. [7] | 49 yo M | Obeslty, OA | Dyspnea, Fatigue | Unremarkable | CRP 18.7 mg/dl, Troponin I negative | - | - | Enlarged cardiac silhouette | Large pericardial effusion, Tamperandie physiology | None | None | Percardiacentesis, Yellow | \( R \) |
| 7   | Han et al. [7] | 55 yo M | None | Cough, Chest pain, Fever, Chills | Hyperdysasia | CRP 24.8 mg/dl, Troponin I 0.012 mg/dl | - | - | Bilateral lung opacities, Middy enlarged cardiac silhouette | Large pericardial effusion, Tamperandie physiology, LVSD 29% | None | None | Percardiacentesis, Serious | \( \bullet \) |
| 8   | Huo-Rodriguez et al. [9] | 65 yo M | Obeslty, HTN | Cough, Fever, Chills | Hyperdysasia | CRP 26.2 mg/dl, Troponin I 0.044 mg/dl | - | - | Biventricular cardiomegaly, Bilateral lung opacities, Middy enlarged cardiac silhouette | Large pericardial effusion, Tamperandie physiology, Biventricular failure | Yes | Yes | Percardiacentesis, Vasopressor, ECMO | Senssegreguous | \( \bullet \) |
| 9   | Han et al. [7] | 55 yo M | Obeslty, HTN | Cough, Fever, Chills | Hyperdysasia | Troponin I 0.162 mg/dl | - | - | AF with rapid ventricular response | Low-R voltage in the pericardial leads | Yes | Yes | Percardiacentesis, Vasopressor, ECMO | Senssegreguous | \( \bullet \) |
| 10  | Pansuro et al. [9] | 69 yo F | HTN | Dyspnea, Bilateral lower extremity edema, Tachycardia, Hypoxia, Lung crackles | Tachycardia, Hypoxia, Tachycardia, Lung crackles | Troponin I 0.0007 mg/dl | - | - | AF with rapid ventricular response | Circular hemopericardial effusion, Restricted diastolic filling, LVSD 29% | None | None | Percardiacentesis, Senssegreguous, Exudative | \( R \) |
| 11  | Tanig et al. [18] | 42 yo F | CTOS, Guillain barre syndrome, AHIS, Fever | Hyperdysasia, Hypoxia, Tachycardia, Diffuse crackles | Hyperdysasia | CRP 14.7 mg/dl, Troponin I 0.20 mg/dl, D-dimers 0.43 mg/dl | Positive conduction anomalies | Low-voltage in limb leads | Moderate pericardial effusion, RA systolic collapse, LVSD 29% | Yes | Yes | Percardiacentesis, Intra-arterial balloon pumps, Vasopressor | Sensse | \( \bullet \) |
| 12  | Singh et al. [15] | 62 yo M | CAD w/ 1 stent, DMG, COPD, Obesity | AHIS, Dyspnea | Hyperdysasia | D-dimers 0.06 mg/dl | Troponin-negative | Bilateral pulmonary edema, Right pleural effusion | Low-voltage QRS | Large pericardial effusion, Tamperandie physiology | Yes | Yes | Percardiacentesis, Vasopressor, HCO, Laparosc-Renier | Biventricular, Transudative | \( R \) |
| 13  | Dah et al. [9] | 55 yo F | None | Fatigue, Fever, syncope | Unremarkable | CRP 11 mg/dl | - | - | Unremarkable | Small subcapsular, Insignificant ST elevation in inferior leads, T- wave inversions | Large pericardial effusion, None | None | Percardiacentesis, Sensse | \( R \) |
| Study | Age | Gender | Symptoms | Cause of Pericarditis | Pericardial Effusion | Troponin I | LVEF | Other Findings | Treatment | Outcomes |
|-------|-----|--------|----------|---------------------|---------------------|-----------|------|----------------|-----------|----------|
| 16. Guevarra et al. | 50 yo M | COFDD | Dyspnea | Hypothesis | - | 0.24 g/L | - | None | None | Yes |
| 15. Kibet et al. | 30 yo M | HTN, CVA | Cough, Dyspnea, Fever | Hypothesis | - | 0.58 g/L | - | None | None | Yes |
| 14. Walker et al. | 30 yo F | None | Fever, Cough, Chest pain | Tachycardia | - | Elevated | - | None | None | Yes |
| 13. Coine et al. | 50 yo M | DMG, HTN | Fever, Diaphoresis | Elevated | - | 0.58 g/L | - | None | None | Yes |
| 12. Fannis et al. | 50 yo M | CAD w/ CHAG | Dyspnea, Chest Pain | Tachycardia | - | Elevated | - | None | None | Yes |
| 11. Garcia-Cruz et al. | 64 yo M | CAD | Chest Pain, Cough, Fever | Hypothesis, Diffuse rash | - | All 3 | - | None | None | Yes |
| 10. Sauer et al. | 61 yo M | Asthma | Chest Pain, Dyspnea | Unremarkable | - | 0.22 g/L | - | None | None | Yes |
| 9. Sauer et al. | 58 yo F | HTN | Dyspnea, Fever | Decreased breath sounds, LE edema | - | Elevated | - | None | None | Yes |
| 8. Tanaya et al. | 30 yo M | DMH, CADX, HTN | Abdominal pain | Hypothesis | - | Elevated | - | None | None | Yes |
| 7. Elmore et al. | 54 yo M | None | Chest Pain | Hypothesis | - | Elevated | - | None | None | Yes |
| Study, Year | Age/Gender | Diagnosis | Anticoagulant Use | Cardiac Findings | Cardiovascular Findings | Cytokine Receptor Blocker Use | Therapeutic Intervention | Mortality |
|-------------|------------|-----------|------------------|-----------------|------------------------|----------------------------|------------------------|-----------|
| 24. Mekari et al. [34] | 28 yo M | None | Chest Pain, Dyspnea | Hypertension, Tachycardia, Hydropsy | 0.23 mg/L, D-dimer 195,321 ng/ml, D-Ferritin-1200 ug/ml, CRP-15.9 mg/dl, Interleukin-6-130 pg/ml | Enlarged cardiac silhouette, Right atrial and ventricular wall collapse, Sinus tachycardia, T-wave inversion in inferior and lateral leads, Low voltage QRS with electrical alternans | Steroids, Pericardiocentesis | Yes |
| 25. Gicca et al. [35] | 37 yo F | HTN | Dyspnea | Hypertension, Tachycardia, Hydropsy | 0.55 mg/dL, ESR-28.1 mm/hr, Ferritin-2,166 ug/ml, CRP-2.1 mg/dl, Interleukin-6-113 pg/ml | Large unremarkable pericardial effusion, RA and RV diastolic collapse, RV wall collapse | Steroids, Colchicine, NSAIDs, Steroids, Antibiotics | Recovered |
| 26. Raymond et al. [24] | 7 yo F | None | Chest Pain, Cough, Orthopnea | Tachycardia | 0.149 ng/ml, D-dimer-2.0 mg/dl, CRP-5.11 mg/dl, Troponin I-5.2 ng/ml, Interleukin-6-0.043 ng/ml | Diffuse low voltage QRS voltage collapse | Steroids, Remdesivir, Steroids | Yes |
| 27. Johny et al. [36] | 30 yo M | None | Dyspnea, Orthopnea, Palpitations | Tachycardia, Tachycardia, Muffled heart sounds | 0.01 ng/ml, D-dimer-3.95 ng/ml, CRP-130 pg/ml | Little left pericardial effusion | Steroids, NSAID, Pericardiocentesis | None |
| 28. Gill et al. [37] | 34 yo F | None | Dyspnea, Chest Pain, Weakness, | Tachycardia, Tachycardia, Unremarkable cardiomyopathy | 0.01 ng/ml, D-dimer-2.55 ng/ml, CRP-1.19 mg/dl, Troponin I-0.149 ng/ml | Large unremarkable pericardial effusion, RA and RV diastolic collapse, Sinus tachycardia, T-wave inversion in inferior and lateral leads, Low voltage QRS with electrical alternans | Steroids, Colchicine, NSAIDs, Steroids, Antibiotics | Recovered |
| 29. Ahlaf et al. [38] | 31 yo M | Down Syndrome | Dyspnea, Nodal conduction, Cough, Vomiting, Poor oral intake | Tachycardia, Hypertenstion, Hypertension, | 0.23 mg/L, D-dimer 195,321 ng/ml, D-Ferritin-158 mg/dl, Ferritin-1200 ug/ml, Interleukin-6-130 pg/ml | Enlarged cardiac silhouette, Right atrial and ventricular wall collapse, Sinus tachycardia, T-wave inversion in inferior and lateral leads, Low voltage QRS with electrical alternans | Steroids, Remdesivir, Steroids, NSAIDs, Steroids, Antibiotics | Yes |
| 30. Silvada et al. [39] | 50 yo F | HTN, DKA | Fever, Cough | Tachycardia, Tachycardia, Tachycardia | 0.23 mg/L, D-dimer 195,321 ng/ml, D-Ferritin-158 mg/dl, Ferritin-1200 ug/ml, Interleukin-6-130 pg/ml | Large unremarkable pericardial effusion, RA and RV diastolic collapse, Dilated inferior vena cava | Steroids, Colchicine, Remdesivir, Steroids | Yes |
| 31. Gopali et al. [40] | 40 yo M | CAD | None | Fever | 0.23 mg/L, D-dimer 195,321 ng/ml, D-Ferritin-158 mg/dl, Ferritin-1200 ug/ml | Bilateral ground-glass appearance, Right atrial and ventricular wall collapse, Sinus tachycardia, Diffuse low voltage QRS voltage collapse | Tocilizumab, Steroids, Colchicine | None |
| 32. Gopali et al. [41] | 45 yo M | CAD | None | Fever, Hypertension | 0.23 mg/L, D-dimer 195,321 ng/ml, D-Ferritin-158 mg/dl, Ferritin-1200 ug/ml | Bilateral pulmonary infiltrates, Pleural and | Pericardial effusion, Palindrome physiological | Remdesivir, Steroids, Inotrope | Yes |
| 33. Sampia et al. [42] | 45 yo F | None | Dyspnea, Fever, Myalgia | Tachycardia, Tachycardia, Hypertension | 0.23 mg/L, D-dimer 195,321 ng/ml, D-Ferritin-158 mg/dl, Ferritin-1200 ug/ml | Moderate pericardial effusion, RV | Colchicine, NSAID, Steroids, Antibiotics | Yes |
| Reference | Patient Age | Gender | Diagnosis | Chest Pain/Cough | Arrhythmia | Troponin | BNP | D-dimer | CRP | Ferritin | Creatinine | Hypothyroidism | Antibiotics | Vasoressin | Other Treatments | Outcome |
|-----------|--------------|--------|-----------|------------------|------------|----------|-----|---------|-----|----------|------------|---------------|-------------|------------|-----------------|---------|
| 34. Flores | 51 yo F      | None   | Syncope, Dyspnea, Hypersensitivity | -     | -     | Bilateral pericardial effusions | Bilateral patchy ground glass opacities | Low voltage, Cardiomegaly | None | None | None | Moderate pericardial effusion, RV compression, tachycardia, pulmonary hypertension, RV septal function | Yes | Yes | Fluids, IosNAAD, Colchicine, Steroids, Pericardiocentesis | E |}
| 35. Koger et al. | 71 yo F | HTN | Chest Pain, Dyspnea | Tachycardia, JVD, Decreased breath sounds | Troponin T-3.14 ng/ml | Bilateral effusion | Low voltage, Cardiomegaly | None | None | None | Moderate pericardial effusion, Late RV diastolic collapse, RV compression, LVEF-20% | Yes | None | Fluids, Pericardiocentesis | Inflammatory, Executive | E |}
| 36. Koger et al. | 57 yo F | HTN, Obesity | Chest Pain, Dyspnea, Costal extremitites | Tachycardia, Hypertension, Costal extremitites | Troponin T-3.59 ng/ml | Bilateral patchy ground glass opacities | Low voltage, Cardiomegaly | None | None | Yes | None | None | Moderate pericardial effusion, RV compression, Respiratory failure, to LV follow | None | None | Pericardiocentesis, Colchicine, NSABD | Sensengueirous | E |}
| 37. Foster et al. | 46 yo F | Factor V Leiden deficiency, Polysomy emboli | Chest Pain | Tachycardia, Hypertension, Tachycardia, JVD, Pseudo aneurism, Friction rub | Troponin T-8.4 ng/ml | Unremarkable | None | None | None | Moderate pericardial effusion, RV diastolic collapse, RV compression, LVEF-20% | None | None | None | Pericardiocentesis, Colchicine, NSABD | Sensengueirous | E |}
| 38. Fox et al. | 63 yo F | None | Orthopnea, Dyspnea, Chest pain, Cough, Fever | Tachycardia, Hypertension, Tachycardia, JVD, Pseudo aneurism, Friction rub | Troponin T-0.90 ng/ml | Cardiomegaly | None | None | None | Moderate pericardial effusion, RV diastolic collapse, LV diastolic collapse | None | None | None | Anti-biotics, NSABD, Colchicine, Pericardiocentesis | Sensengueirous, Executive | E |}
| 39. Reddy et al. | 63 yo F | Myotonia, Stem Cell, Transplant, Graft versus host disease | Chest Pain | Tachycardia, Hypertension, Tachycardia, JVD, Pseudo aneurism, Friction rub | Troponin T-0.17 ng/ml | Cardiomegaly | None | None | None | Moderate pericardial effusion, RV diastolic collapse, LV diastolic collapse | None | None | None | Anti-biotics, NSABD, Colchicine, Pericardiocentesis | Sensengueirous, Executive | E |}
| 40. Nadeen et al. | 81 yo F | HTN, DM2, ESRD, Pericarditis | Dyspnea, Orthopnea, Weightless | Hypertension, Hypersensitivity | Troponin T-0.3 ng/ml | Elevated right heart catheterogram | None | None | None | Massive pericardial effusion | Yes | Yes | Yes | Vasopressin, Lopinavir/Ritonavir, Ivermectin, Pericardiocentesis | Executive | E |}
| 41. Beckerman et al. | 55 yo M | HTN, Gout, Obesity | - | - | - | CRP-14 mg/ml, ESR-100 mm/hr | - | - | - | Low voltage, Cardiomegaly, T wave changes in inferior leads | Yes | Yes | Yes | Anti-biotics, NSABD, Tobululosamid, Remdesivir, Convalescent plasma, Colchicine, Pericardiocentesis | Sensengueirous | E |}
| 42. Skare et al. | 77 yo M | Chronic HF, HTN, DM2, COPD, O2H | - | Hypersensitivity, Tachycardia | - | - | - | 1.3 cm pericardial effusion | None | None | None | Vasopressin, Pericardiocentesis, Steroids, Colchicine | Executive, Inflammatory | E |}
| 43. Schussel et al. | 72 yo M | DM2, Persistent AF, Obstructive sleep | Fatigue | Bilateral crackles, Irregular heart rhythm, Elevated | Troponin T-0.08 mg/ml | Bilateral consolidations | - | - | - | 3-3.5 cm pericardial effusion, LVEF-20% | Yes | Yes | Yes | Pericardiocentesis, Vasopressin | Executive | E |}

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For a more comprehensive understanding, it's important to consult the full reference or a medical professional for detailed analysis and treatment.
The first case of cardiac tamponade caused by COVID-19 was documented in early 2020 by Hua et al. in a 47-year-old female without any significant medical history. Of the total 45 cases examined, only 11 (24%) had any prior cardiac comorbidities with one patient having a prior history of myocarditis. There was no troponin elevation described in seven of the cases as well which suggests that this virus can mediate inflammation of the pericardium and accumulation of fluid without direct myocardial injury. Furthermore, 20 of the 45 patients did not have a concomitant pneumonia; in fact, 18 patients were not noted to have significant respiratory symptoms from COVID-19 infection and had primarily cardiac manifestations of this illness. Such observational data reinforces the premise that COVID-19 can cause significant pericarditis without respiratory involvement.[42]

Our patient proved to be a challenging diagnosis as on first presentation there was no clear etiology for the pericardial effusion. The only reported symptoms were intermittent chest pain and shortness of breath for three weeks without any other respiratory involvement or signs of infection. The differential included infectious process, malignancy given prior history of cancer, or autoimmune etiology; initial workup, however, was negative for any clear cause. We unfortunately were unable to send pericardial fluid for SARS-CoV-2 PCR testing. Our patient had a hemorrhagic pericardial effusion which has been demonstrated in some viral pericarditis, most prominently coxsackie virus [42]. However, hemorrhagic effusions have also been documented in the current literature on tamponade in COVID-19 patients and this patient had no other risk factors for a hemorrhagic effusion aside from remote history of cancer for which cytology was negative. Our patient later tested positive for COVID-19 and we acknowledge the possibility that he could have been subsequently infected after the initial diagnosis of pericardial effusion. However, in absence of any other cause, direct COVID-induced pericarditis leading to pericardial effusion and tamponade was the most likely diagnosis.

Amongst the 36 patients with tamponade whose pericardial fluid was reported, 19 patients identified in this literature review were noted to have hemorrhagic or serosanguinous effusions on analysis after pericardiocentesis. Most commonly, hemorrhagic effusions are associated with malignancy, inflammatory states, or post infarction [43]. As mentioned above, viral pericarditis is typically noted to have a benign course, but there have been reports of hemorrhagic effusion most described in coxsackie virus infection where it is believed that the virus causes direct damage to myocardial cells or an immune-mediated injury [42]. Given the robust inflammatory response elicited by the COVID-19 infection and its cytokine storm, it may mediate hemorrhagic effusions through a similar mechanism. We urge providers to keep COVID-19 high on the differential when cryptogenic, hemorrhagic effusions of tamponade physiology are identified, even if repeat COVID-19 testing is negative.

Our patient presented with subacute cardiac tamponade as he had been experiencing symptoms intermittently for weeks prior to presentation. This case draws parallels to the patient described by Eijkeme et al. who presented with indolent symptoms and no hemodynamic compromise [21]. In fact, of the cases reviewed, only 16 (56%) presented with hemodynamic changes of hypotension and suspicion was only raised in other cases after echocardiogram showed a large pericardial effusion. This suggests that cardiac tamponade should be on the differential if a patient infected with COVID-19 experiences acute deterioration and hemodynamic compromise.

Management of cardiac tamponade is focused on prompt removal of the effusion and monitoring of hemodynamics post pericardiocentesis as well as volume resuscitation. One of the mainstays is to avoid positive pressure ventilation as increased intrathoracic pressure can impair cardiac filling [44]. This poses a problem in patients infected with COVID-19 as many require mechanical ventilation. Of the cases reported, 21 were on mechanical ventilatory support and 13 of those patients expired during hospitalization. Prompt evaluation using bedside US and drainage of pericardial fluid is of utmost importance in these patients.

TABLE 1: Covid-19 Cardiac Tamponade

| Case        | Age  | Gender | Race | Comorbidities | Presenting Symptoms | Signs & Symptoms | Treatment |
|-------------|------|--------|------|---------------|---------------------|------------------|-----------|
| Darvishi et al. [9] | 42 yrs M | Male | White | None | Chest pain, Diaphoresis, Dyspnea | Elevated blood pressure, JVD, Diastolic collapse | Pericardiocentesis, Steroids, Fluids |
| Saile et al. [9] | 28 yrs F | Female | African | None | Chest Pain, Diaphoresis | Pulsus paradoxus, Pericardial effusion | Steroids, Fluids |
| Hua et al. [9] | 47 yrs F | Male | Hispanic | None | Chest pain | Pulsus paradoxus, Pericardial effusion | Pericardiocentesis |

AF - atrial fibrillation, AMS - altered mental status, BNP - brain natriuretic peptide, CAD - coronary artery disease, CABG - coronary artery bypass graft, CK - creatinine kinase, CKD - chronic kidney disease, COPD - chronic obstructive pulmonary disease, CRP - C reactive protein, CRRT - continuous renal replacement therapy, CVA - cerebrovascular accident, DM - diabetes mellitus, ECMO - extracorporeal membrane oxygenation, ESRD - end stage renal disease, HF - heart failure, HFrEF - heart failure with reduced ejection fraction, HCQ - hydroxychloroquine, HLD - hyperlipidemia, HTN - hypertension, IVC - inferior vena cava, IVF - mechanical ventilation, NSAID - non-steroidal anti-inflammatory drug, PPM - permanent pacemaker, RA - right atrium, RV - right ventricle, "*" refers to data that was not available.
presenting with cardiac tamponade.

Ultimately, our patient was diagnosed with cardiac tamponade due to viral pericarditis mediated by COVID-19 infection. The fact that he displayed little to no respiratory symptoms, no signs of myocardial damage, and initially tested negative for COVID-19 several times contributes to the uniqueness of this as a subacute presentation of tamponade. This case along with the others highlighted in this review document cardiac tamponade as a rare complication of COVID-19 infection.

Conclusions
COVID-19 infection presents in many different ways and has been shown to affect a multitude of organ systems including the heart. We present a case of an elderly man with no cardiac comorbidities and minimal respiratory symptoms who presented with a very subacute cardiac tamponade caused by viral pericarditis secondary to COVID-19 infection. This case along with other well-documented reports included in this review highlight cardiac tamponade as a rare sequela of this viral infection. We furthermore hope to inform providers to recognize COVID-19 as a considerable differential when encountering cryptogenic, hemorrhagic pericardial effusions of tamponade physiology, even without respiratory disease.

Additional Information
Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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