

Pericardial effusion in patients with COVID-19: case series

François Sauer (), Charlotte Dagrenat, Philippe Couppie, Gaelle Jochum, and Pierre Leddet () *

Division of Cardiovascular Medicine, Centre Hospitalier de Haguenau, 64 Avenue du Professeur Leriche, Haguenau, Alsace 67500, France

Received 12 May 2020; first decision 26 May 2020; accepted 29 July 2020; online publish-ahead-of-print 9 September 2020

Background	SARS-coronavirus-2 [coronavirus disease 2019 (COVID-19)] infection is a public health issue affecting millions of people. It started in Wuhan in China in December 2019 spreading rapidly worldwide.				
Case summary	Three patients aged 51–84 developed a pericarditis related to COVID-19, associated for two of them with a myo- carditis. Case 1 was a COVID-19 cardiac tamponade without myocarditis, confirmed by a positive chest computed tomography (CT) scan. Case 2 showed a COVID-19 myopericarditis, confirmed by a positive chest CT scan and a SARS-coronavirus-2 positive swab. Case 3 was a cardiac tamponade due to COVID-19 pericarditis, with a positive polymerase chain reaction on pericardial fluid. They were all treated by colchicine and their condition improved rapidly.				
Discussion	Presumably rare, we reported three cases of pericardial effusions (PEs) occurring in a single cardiology centre. There is a higher incidence of COVID-19-related cardiac diseases such as pericarditis that can manifest as a minimal PE to a cardiac tamponade, which should result in a higher awareness of cardiologists. A systematic measure of the high-sensitivity troponin kinetic in patients affected by COVID-19 could be interesting in order to screen for po- tential myocarditis. Any unexplained haemodynamic failure or increased cardiac biomarkers should make the med- ical team search for myopericarditis by a transthoracic echocardiography.				
Keywords	COVID-19 • Pericardial effusion • Cardiac tamponade • Myopericarditis • Case series				

Learning points

- Three cases of pericardial effusions (PEs) comprising two tamponades occurred in a single cardiology centre, suggesting a higher cardiac risk than expected during the coronavirus disease 2019 (COVID-19) pandemic.
- A systematic screening for PE should be performed in COVID-19 patients either via a chest computed tomography scan in case of respiratory symptoms, or via transthoracic echocardiography in case of chest pain, haemodynamic instability, or respiratory worsening.

Introduction

Since the outbreak of clusters of viral pneumonia due to the novel coronavirus (severe acute respiratory syndrome coronavirus 2 or SARS-CoV-2) in Wuhan, China in December 2019,¹ coronavirus disease 2019 (COVID-19) has spread worldwide infecting more than 5.4 million people and causing more than 349 095 deaths as of 27 May 2020.² Coronavirus disease 2019 primarily infects the lungs, has demonstrated a wide spectrum of clinical manifestations and may even extend to other organs such as the cardiovascular system.

^{*} Corresponding author. Tel: +0388063557, Email: pierre.leddet@ch-haguenau.fr

Handling Editor: D'Amario Domenico

Peer-reviewers: Asher Elad; Rudzínski Piotr Nikodem

Compliance Editor: Camm Christian Fielder

Supplementary Material Editor: Thomson Ross

[©] The Author(s) 2020. Published by Oxford University Press on behalf of the European Society of Cardiology.

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0/), which permits non-commercial re-use, distribution, and reproduction in any medium, provided the original work is properly cited. For commercial re-use, please contact journals.permissions@oup.com

Mounting evidence is now supporting that COVID-19 affects the cardiovascular system with acute cardiac injury, high risk of thrombosis including stroke, pulmonary embolism, and acute coronary syndrome. Conversely, very few attention has been paid to pericardial effusion (PE). Only very few case reports described PE, revealed by chest pain or a deterioration of general condition.^{3–7} We hereby report a case series of three patients with cardiac and pericardial manifestations of COVID-19 at our institution. Haguenau Hospital is the secondary care centre for the North-East of France, with 482 COVID-19 patients admitted to our institution to date.

Timeline

(RR 140–400 G/L)]. Other laboratory data showed an acute kidney injury [urea at 10.1 mmol/L, Glomerular Filtration Rate (GFR) (CKD-EPI) 39 mL/min/m²)], cholestasis characterized by levels of alkaline phosphatase gamma glutamyltransferase twice the upper limit of normal and arterial blood gas measurements on room air showed an isolated hypoxaemia (Po2 of 62 kPa). The high-sensitivity cardiac troponin I (cTnI) peak was 919 ng/L (RR < 54 ng/L). The baseline electrocardiogram (ECG) showed a diffuse and discrete elevation of the ST segment with a low QRS voltage (*Figure 1*). Chest computed tomography (CT) revealed typical findings of COVID-19 with moderate peripheral ground-glass opacification and a voluminous PE (*Figure 2*). Transthoracic echocardiography (TTE) confirmed the presence of a significant and circumferential PE (22 mm) with compression of the right heart chambers.

Age	Symptoms	Previously treated with anti-coagulants	Diagnosis	Coronavirus dis- ease 2019 diag- nostic method	Specific treatment	Hospital discharge Outcome M1
Case 1 51	Day 1: Chest pain Day 21: Deterioration of the general condition + dyspnoea Day 30: Hospitalization	No	Pericarditis, compli- cated by a tamponade	 Chest computed tomography (CT) scan: + Nasopharyngeal polymerase chain reaction (PCR): - 	 Pericardiocentesis Colchicine 	Day 7Total recovery
Case 2 60	Day 1: Deterioration of the general condition Day 28: Shivers Day 30: Diffuse erythema and hospitalization	: No	Myopericarditis, with non-compressive pericardial effusion	 Nasopharyngeal PCR: + Chest CT scan: + 	Colchicine	Day 8Total recovery
Case 3 84	Day 1: Deterioration of the general condition Day 21: Dyspnoea Day 30: Hospitalization	e No	Poly-seritis, compli- cated by a cardiac tamponade	 Pericardial liquid PCR: + Chest CT scan: - Nasopharyngeal PCR: - 	Thoracentesis and pericardiocentesisColchicine	

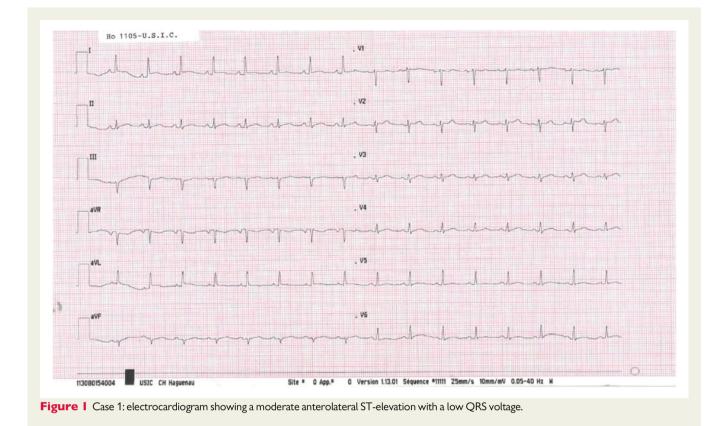
Cases presentation

Case 1

A 51-year-old man presented to our emergency department with chest pain suggestive of pericarditis (retrosternal, intensified when coughing and laying down, eased by sitting up position), dyspnoea on exertion, and deterioration of general condition. He had history of asthma and active smoking.

Haemodynamic parameters (heart rate and blood pressure) were normal without fever and there was no need for oxygen therapy at the time of admission. The physical examination was normal. C-reactive protein (CRP) was markedly increased [peak value 223 mg/L reference range (RR) < 4 mg/L] with leucocytosis [neutrophils: 11.8 G/L (RR < 7 G/L)] and thrombocytosis [platelet count: 402 G/L Following chest CT, the patient presented with acute respiratory failure, requiring oxygen therapy with a high concentration mask (flow rate: 10 L/min). An emergency pericardiocentesis allowed the extraction of 800 mL of a sero-hematic liquid. Serologies (Human Immunodeficiency Virus, Heptitis B Virus, Hepatitis C Virus, Epstein Barr Virus, CytomegaloVirus, Adenovirus, Picornavirus, Parvovirus B19) and reverse transcription polymerase chain reaction (RT-PCR) testing on nasopharyngeal swab for SARS-CoV-2 were all negative. Despite an inconclusive testing for COVID-19, the PE was considered as COVID-19 related due to (i) typical COVID-19 findings at chest CT, (ii) clinical symptoms, and (iii) epidemiological criteria.

The histological analysis showed an inflammatory exudate with few lymphocytes and no malignant cells. Treatment with colchicine 0.5 mg twice a day was initiated on Day 3. On Day 7, cardiac magnetic



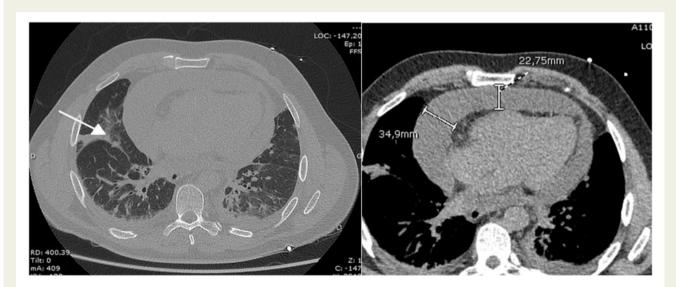


Figure 2 Case 1: chest computed tomography scan showing circumferential pericardial effusion, bilateral pleural effusion, and peripheral groundglass opacification (white arrow) consistent with coronavirus disease 2019 infection.

resonance imaging (MRI) showed signs of pericarditis without myocarditis (*Figure 3*). Clinical improvement was rapidly observed, and the patient was discharged home on Day 7 with maintenance dose of colchicine 1 mg daily for 3 months. At 45-day follow-up, the patient remained asymptomatic.

Case 2

A 60-year-old man, with no medical history except active smoking, had severe ongoing asthenia for a week and acute anosmia. One month later, he had shivers for which an antibiotic therapy by

Figure 3 Case 1: cardiac magnetic resonance imaging, four-chamber view showing circumferential pericardial late gadolinium enhancement.

amoxicillin-clavulanic acid was initiated by his general practitioner. Two days later, a diffuse erythema appeared.

On arrival at the emergency room (ER), haemodynamic parameters were stable, the temperature was measured at 39°C and there was no need for oxygen therapy. The physical examination was normal. Arterial blood gas measurements showed a moderate hypoxaemia at 75 kPa. cTnl peak was 639 ng/L. A nasopharyngeal swab was positive for SARS-CoV-2 by RT-PCR. Baseline ECG registered a normal sinus rhythm and flattened T waves in lateral leads (Supplementary material online, Figure S1). Chest CT scan revealed common patterns and distribution of patients affected by COVID-19 (Figure 4) and a moderate PE localized beside the left ventricle (LV) (<10 mm), later confirmed by TTE. Treatment with colchicine 0.5 mg twice a day was initiated on Day 1. During hospitalization, termination of a new-onset atrial fibrillation was achieved with flecainide. No curative anticoagulation (CHADS-VASC 0/9) was introduced. The patient's condition rapidly improved with laboratory tests returning to normal. The patient was discharged home on Day 5 with maintenance dose of colchicine 1 mg daily for 3 months.

Control TTE on Day 8 showed a PE growth with a 15 mm effusion measured around the LV, but no signs of cardiac tamponade and normal left ventricular ejection fraction. The same day, a cardiac MRI confirmed a predominant effusion over the lateral wall of the LV (Figure 5 and Video 1) and an inferolateral sub-epicardial delayed gadolinium-enhancement, consistent with myocarditis. The treatment remained unchanged as the patient's state was stable.

Control TTE on Day 15 showed a decrease in PE (6 mm). At 45day follow-up, the patient remained asymptomatic with no signs of recurrent pericarditis.

Figure 5 Case 2: cardiac magnetic resonance imaging, four-chamber view showing lateral wall pericardial effusion.

Case 3

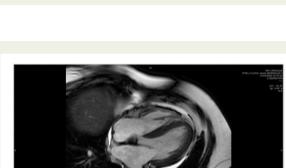
An 84-year-old woman was referred to our institution for dyspnoea, fever, and severe asthenia. She had history of hypertension and dyslipidaemia. At the ER, there was no fever on admission. There was leg swelling and attenuated basal breath sounds. Laboratory testing demonstrated an inflammatory response with peak CRP value 66 mg/L, leucocytosis (neutrophils: 11.1. G/L), lymphopenia (0.92 G/L), and thrombocytopenia (platelet count: 129 G/L). Arterial blood gas measurements on room air showed an isolated hypoxaemia (PaO2 62 kPa). Chest CT revealed a large and bilateral pleural effusion, no lung findings for COVID-19 but a PE (Figure 6). On TTE, PE was circumferential and initially measured at 7mm. A thoracentesis was achieved on Day 2 and yielded 400 mL of a serous fluid. The histological analysis showed an inflammatory exudate with lymphocytes and a nasopharyngeal swab was negative for SARS-CoV-2 by RT-PCR. Of note, COVID-19 testing was not performed in pleural fluid. Treatment with colchicine 0.5 mg once a day was initiated on Day 1 and patient was discharged home on Day 8.

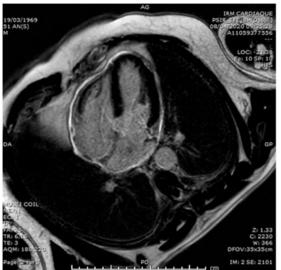
On Day 15, control TTE showed a large PE measured at 25 mm with right ventricular diastolic collapse (Figure 7 and Videos 2 and 3).

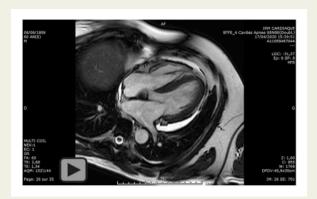


imal peripheral ground-glass opacification (white arrow).

Figure 4 Case 2: chest computed tomography scan showing min-







Video I Case 2: cardiac magnetic resonance imaging, four-chamber view showing non-compressive pericardial effusion.



Figure 7 Case 3: transthoracic echocardiography, parasternal long-axis view showing circumferential pericardial effusion.



Figure 6 Case 3: chest computed tomography scan showing bilateral pleural effusion (white arrows) and pericardial effusion (black arrow).

Thrombocytopenia (123 G/L) and lymphopenia (0.82 G/L) persisted without inflammatory syndrome. N-terminal prohormone of brain natriuretic peptide and cTnI remained within normal laboratory range. A pericardiocentesis extracted 500 mL of serous fluid. RT-PCR testing on pericardial fluid for SARS-CoV-2 was positive. Likewise, the anatomopathological technique revealed an inflammatory exudate.

A chest-abdomen-pelvis scan was carried out on Day 17 and showed no lung affection by COVID-19 and no tumoural lesion. On Day 37, a cardiac MRI showed a mild PE without right heart chambers compression nor myocarditis (*Figure 8*). At Day 45, the patient's condition subsequently improved.

Discussion

We report three cases of COVID-19-related PE of which two of them were complicated by cardiac tamponade. Differential diagnosis



Video 2 Case 3: transthoracic echocardiography, parasternal short-axis view showing circumferential pericardial effusion, leading to right heart chambers compression.

cannot be formally excluded (other viral infections, malignant disease, etc.). Each case involved either a positive COVID-19 RT-PCR and/or typical CT findings of COVID-19.

After careful literature review, we found five cases of cardiac tamponade requiring emergency pericardial drainage in Italy,³ in the USA,^{4–6} and in the UK⁷. One of them was associated with a positive RT-PCR for COVID-19 in the pericardial fluid. Four cases of myopericarditis have been described. Especially in Italy,⁸ a case of myopericarditis required dobutamine support for 2 days, antivirals and corticosteroids, but no pericardial drainage. Pericardial involvement in COVID-19 seems to be rare but remains unquantified to date. Publications on radiological data highlight infrequent PEs.⁹

The pathogenesis of COVID-19 myopericarditis is yet unresolved. Two predominant mechanisms could be relevant.¹⁰ First, the heart affinity of the virus could be explained by SARS-CoV-2 S protein direct binding to human angiotensin-converting enzyme 2¹¹ present in the human heart, which allows for a cellular infection. Indirectly, myopericarditis could follow a viral replication and dissemination in the blood, from Day 7 up to 1 month after symptoms beginning. This

Video 3 Case 3: transthoracic echocardiography, apical fourchamber view showing circumferential pericardial effusion, leading to right heart chambers compression.



Figure 8 Case 3: cardiac magnetic resonance imaging showing mild pericardial effusion (white arrow) without right heart chambers compression.

could lead to a cytokine storm syndrome and a direct myopericardial lesion by inflammatory cell infiltration, similarly to COVID-19 direct pulmonary lesions.¹²

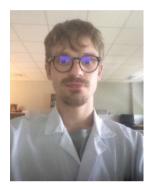
So far, physicians treating patients with COVID-19 are facing a lack of solid evidence and guidelines regarding the management of COVID-19-related pericardial disease. Non-steroidal anti-inflammatory drugs should not be introduced considering the risk of the respiratory worsening. Various studies¹³ have proposed a potential beneficial effect of corticosteroids as a treatment during cytokine storm syndrome. Colchicine is a well-known and safe therapy for pericarditis¹⁴ and seems to be an interesting treatment option in COVID-19 affections, as suggested in ongoing prospective studies¹⁵ (COLCORONA NCT04322682), due to its action on NLRP3 inflammasomes and cytokine's release.

No coronary circulation assessment was done in each case, because of the low probability of acute coronary syndrome. Moreover, each patient had a cardiac MRI showing no ischaemic injury.

Conclusion

Presumably rare, we reported three cases of PE occurring at our institution. There is a higher incidence of COVID-19-related cardiac diseases such as pericarditis that can manifest from minimal PE to cardiac tamponade. Cardiologists and emergency physicians should be aware and extensively look for PE at the time of the COVID-19 outbreak.

Lead author biography



François Sauer is a third-year resident in cardiology, who aims to specialize himself in cardiac imaging and sports cardiology. He lives in Strasbourg (France).

Supplementary material

Supplementary material is available at European Heart Journal - Case Reports online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

References

- World Heart Organization. Coronavirus Disease (COVID-2019) Situation Reports 27/05/2020. who.int/docs/default-source/coronaviruse/situation-reports/ 20200527-covid-19-sitrep-128.pdf?sfvrsn=11720c0a_2.
- Zhu N, Zhang D, Wang W, Li X, Yang B, Song J et al.; China Novel Coronavirus Investigating and Research Team. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020;382:727–733.
- Farina A, Uccello G, Spreafico M, Bassanelli G, Savonitto S. SARS-CoV-2 detection in the pericardial fluid of a patient with cardiac tamponade. *Eur J Intern Med* 2020;**76**:100–101.
- Dabbagh MF, Aurora L, D'Souza P, Weinmann AJ, Bhargava P, Basir MB. Cardiac tamponade secondary to COVID-19. JACC Case Rep 2020;2: 1326–1330.
- Purohit R, Kanwal A, Pandit A. Acute myopericarditis with pericardial effusion and cardiac tamponade in a patient with COVID-19. *Am J Case Rep* 2020;21: e925554.
- Asif T, Kassab K, Iskander F, Alyousef T. Acute pericarditis and cardiac tamponade in a patient with COVID-19: a therapeutic challenge. Eur J Case Rep Intern Med 2020;7:001701.
- Hua A, O'Gallagher K, Sado D, Byrne J. Life-threatening cardiac tamponade complicating myo-pericarditis in COVID-19. Eur Heart J 2020;41:2130.
- Inciardi RM, Lupi L, Zaccone G, Italia L, Raffo M, Tomasoni D et al. Cardiac involvement in a patient with coronavirus disease 2019 (COVID-19). JAMA Cardiol 2020;5:1–6.

- Salehi S, Abedi A, Balakrishnan S, Gholamrezanezhad A. Coronavirus disease 2019 (COVID-19): a systematic review of imaging findings in 919 patients. *Am J Roentgenol* 2020;215:87–93.
- Dong N, Cai J, Zhou Y, Liu J, Li F. End-stage heart failure with COVID-19: strong evidence of myocardial injury by 2019-nCoV. JACC Heart Fail 2020;8: 515–517.
- 11. Jin Y, Yang H, Ji W, Wu W, Chen S, Zhang W et al. Virology, epidemiology, pathogenesis, and control of COVID-19. Viruses 2020;**12**:372.
- Xu Z, Shi L, Wang Y. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. *Lancet Respir Med* 2020;8:420–422.
- Atri D, Siddiqi HK, Lang J, Nauffal V, Morrow DA, Bohula EA. COVID-19 for the cardiologist: a current review of the virology, clinical epidemiology, cardiac and other clinical manifestations and potential therapeutic strategies. *JACC Basic Transl* Sci 2020;5:518–536.
- Imazio M, Brucato A, Cemin R, Ferrua S, Maggiolini S, Beqaraj F et al.; ICAP Investigators. A randomized trial of colchicine for acute pericarditis. N Engl J Med 2013;369:1522–1528.
- Deftereos SG, Siasos G, Giannopoulos G. The Greek study in the effects of colchicine in COVID-19 complications prevention (GRECCO-19 study): rationale and study design. *Hellenic J Cardiol* 2020;61:42–45.