



Acute pericarditis after COVID 19 in a peritoneal dialysis patient

Bernardo Marques da Silva¹ · João Oliveira¹ · Marta Pereira¹ · José António Lopes¹ · Cristina Pinto Abreu¹

Received: 21 December 2021 / Accepted: 12 April 2022
© The Author(s) under exclusive licence to The Japan Society of Nephrology 2022

Abstract

COVID-19 is known to affect numerous organs which have ACE-2 receptors, lung being the most involved organ. Nevertheless, cardiac involvement is not uncommon and can occur through a variety of manifestations. The authors hereby report a case of pericarditis following SARS-CoV-2 infection. A 54-year-old man with end stage kidney disease under peritoneal dialysis presented with acute chest pain approximately 1 month after being diagnosed with COVID-19. Electrocardiogram revealed widespread ST segment elevation. The diagnosis of acute pericarditis secondary to the viral infection was made and the patient was treated accordingly. Etiology of acute pericarditis can be very varied, and, in many times, no cause is ascertained. In such circumstances, viral or immune mediated etiologies are assumed. In our case, since no cause was proven, pericarditis was assumed as secondary to the SARS-CoV-2 infection. This entity is probably underdiagnosed. In patients undergoing dialysis, uremic pericarditis is commonly the etiology. However, different causes must be taken into consideration, COVID-19 being one of them.

Keywords Acute pericarditis · COVID-19 · Peritoneal dialysis

Introduction

Syndrome of acute respiratory distress syndrome coronavirus-2 (SARS-CoV-2), which is responsible for coronavirus disease 19 (COVID-19), was initially detected in Wuhan (China) in December 2019 and declared pandemic in March 2020 by WHO. The virus enters human cells by binding its S protein to Angiotensin Converting Enzyme 2 receptor (ACE-2) in human cells. This receptor is found particularly in respiratory tract and cardiac cells which can be correlated with disease manifestations [1, 2]². Although respiratory symptoms are much more frequent, there are some reports of cardiac disease including acute coronary syndrome, myocarditis, pericarditis, dysrhythmia and heart failure. We here report a case of acute pericarditis following COVID-19 [3].

Case report/case presentation

The authors describe the case of a 54-year-old man with end stage kidney disease (ESKD) of undefined cause identified 5 years ago. The patient was born in São Tomé e Príncipe and was transferred to Portugal due to the absence of any dialysis modality available at his home country. He was in automated peritoneal dialysis (APD) program maintaining an optimal dialysis efficacy (weekly Kt/v 1.9 to 2.21).

Two months before the present episode, the patient underwent radical nephrectomy due to a complicated cyst. In the post operative period he transitioned to HD and two weeks after surgery he was admitted for acalculous pancreatitis (BISAP 1). During this hospitalization he was exposed to a high-risk contact with a confirmed COVID-19 patient. After 5 days he developed a dry cough and fever and SARS-CoV-2 infection was confirmed by qualitative nucleic acid amplification test (NAAT) in a nasopharyngeal swab. In the following days, type 1 respiratory failure was established requiring progressively greater amounts of supplemental oxygen. The maximum fraction inspired oxygen (FiO₂) required was 60% delivered through venturi mask and therapy with dexamethasone was used, while on oxygen, as per hospital protocol. A chest computed tomography showed findings compatible with COVID-19 pneumonia and bacterial overinfection. The

Bernardo Marques da Silva and João Oliveira have contributed equally to this work.

✉ Bernardo Marques da Silva
bmsilva@campus.ul.pt

¹ Department of Nephrology and Renal Transplantation, Centro Hospitalar Universitário de Lisboa Norte, Av. Prof. Egas Moniz MB, 1649-028 Lisbon, Portugal

patient had not been immunized with anti-Sars-CoV-2 vaccination. Patient was discharged 26 days after the diagnosis and resuming his PD program at home.

Ten days after discharge the patient was readmitted to hospital complaining of an acute sharp chest pain for 2 days, radiating to the dorsal region, exacerbated with decubitus and unrelated to exercise or breathing. Electrocardiogram (ECG) showed widespread ST segment elevation concave up and PR depression in precordial leads. These features pointed to the diagnosis of acute pericarditis. Laboratory test results revealed increased high sensitivity troponinT 99 ng/L, which was stable on serial measurements, elevated NT Pro-BNP 12,735 pg/mL, C-reactive protein 10.5 mg/dL and procalcitonin 0.72 ng/mL. Echocardiography excluded pericardial effusion, revealed normal heart cavities without hypertrophy, adequate global and left ventricle systolic function and no segmental motility changes. Given the typical chest pain and ECG changes, the diagnosis of acute pericarditis was made.

There was no evidence of dialysis inefficacy (weekly Kt/v 2.1). Further etiological investigation revealed negative auto-antibodies screening (antinuclear, anti-SSA, anti-SSB, anti-dsDNA, anti-MPO, anti-PR3 and anti-HLAB27) and there was no change in complement fractions (C3 and C4). There were positive IgG titers for cytomegalovirus and Epstein–Barr but viral DNA loads were negative. Viral serologies were negative for coxsackie, adenovirus and echovirus. The patient was immune to hepatitis B virus due to previous contact. Hepatitis C and HIV screening were negative. Investigation for a possible mycobacterial etiology revealed a negative interferon-gamma release assay. Serologies for *C. burnetti*, blood cultures for aerobic and anaerobic bacteria and fungi were also negative. It was not identified any drug associated with acute pericarditis, trauma or cardiac surgery. Due to timing of occurrence and exclusion of other etiologies a diagnosis of viral acute pericarditis secondary to COVID-19 was established.

Accordingly, the patient was treated with ibuprofen 400 mg 3 times per day and colchicine (maximum dose 0,5 mg bid). 2 days later, chest pain subsided and serum inflammatory marker levels decreased. Patient was discharged with ibuprofen for 2 weeks and colchicine for 3 months. In 6 months of follow-up, the patient remained asymptomatic.

Conclusions and discussion

Acute pericarditis is an inflammation of the pericardial sac. Diagnosis is made when two out of four criteria are met: pleuritic sharp chest pain that improves by sitting and leaning forward; pericardial rub; new widespread ST elevation or PR depression on ECG; pericardial effusion [4]. Our patient

was diagnosed on the basis of typical chest pain and ECG changes.

Etiology is highly variable. It can be secondary to drugs and toxins or to radiation, can have a metabolic cause and it can happen as a post cardiac injury syndrome. In most cases, however, no cause is identified. In such circumstances, etiology is assumed to be viral or immune mediated [5, 6].

In our case, etiology is not simple to ascertain. However, uremic pericarditis, the most obvious cause in a patient with chronic kidney disease under dialysis, seems unlikely. A good dialysis efficacy (with a Kt/v greater than 1.7) and the absence of pericardial effusion are arguments against this etiology. Electrocardiographic alterations derive from inflammation of the epicardium, since the parietal epicardium is electrically inert. In uremic pericarditis, these are not usually present given the absence of epicardial injury, which, furthermore, supports our hypothesis [7, 8].

Other common causes of pericarditis were also excluded. Post-cardiac injury syndromes were excluded, since the patient had no myocardial infarction, was not submitted to any surgery, and did not suffer any trauma. No drug the patient was on is commonly associated with pericarditis and the patient improved without any of them being withdrawn. Immunological study was negative, so an auto-immune cause is also unlikely. Serologies and investigation of other infectious causes were all negative. Therefore, the most plausible cause for pericarditis in this clinical scenario remains COVID-19, since no other cause was identified, and viral infection are among the most common causes of pericarditis. In addition, the temporal relationship between SARS-CoV-2 infection and pericarditis is compatible with a viral etiology.

SARS-CoV-2 affects mainly the lungs, but many organs may be involved, including the heart. Cardiac injury has been described in up to 17% of the patients and it increases the risk of mortality [9, 10]. Several cases of pericarditis due to COVID-19 have been described, although its real frequency is not known. A meta-analysis of 2676 hospitalized patients with COVID-19 revealed a prevalence of pericardial effusion of 3% on chest computed tomography [11]. These findings suggest that it is underdiagnosed. This can result in many patients not receiving appropriate treatment to a condition with a mortality which is not neglectable. *Diaz-Arocutipa* et al. reported an in-hospital mortality of 6% [12].

Despite many cases of pericarditis being attributable to COVID-19, the virus itself is not usually encountered in biopsy specimens or in the pericardial fluid, a feature similar to other viruses [13–16]. Viral studies are not routinely performed, given the low diagnostic yield and the relatively benign course that this disease encompasses with its most common causes [17].

Acute viral pericarditis is characterized by an inflammatory response to an acute injury to the pericardium. The virus itself may trigger inflammation or it may arise from

the release of cellular debris which, through the formation of the Nod Like Protein Receptor 3 (NLRP3) inflammasome, intensifies local and systemic inflammatory response [18]. Although pathophysiology is unknown, cytotoxic and immune mediated effects related to the systemic inflammatory response, with an overproduction of pro-inflammatory cytokines, and, eventually, the cytokine storm caused by SARS-CoV-2 are thought to lead to pericardial inflammation [19, 20].

Treatment of pericarditis associated with SARS-CoV-2 infection is similar to that recommended for pericarditis due to other viruses, with studies confirming the safety of anti-inflammatory therapies in the setting of COVID-19 [21]. Corticosteroids are not used as first option. However, one should notice that dexamethasone reduced mortality in COVID-19 patients that required oxygen supplementation [22]. Hence, in patients in the acute phase of SARS-CoV-2 infection requiring oxygen, corticosteroids may be used as first line therapy for pericarditis.

Many cardiovascular complications have been associated with COVID-19, and pericarditis, although rare, is one of them. A high degree of suspicion is required, especially in dialytic patients. In this case, practitioners should be alerted to the different features that allow an accurate differential diagnosis.

Declarations

Conflict of interest The authors have declared that no Conflict of interest exists.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional committee at which the studies were conducted and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

References

- Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, et al. SARS-CoV-2 cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell*. 2020;181:271–280.e8.
- Wang D, Hu B, Hu C, Zhu F, Liu X, Zhang J, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA*. 2020;323:1061.
- Azevedo RB, Botelho BG, de Hollanda JVG, Ferreira LVL, de Andrade LZJ, Oei SSML, et al. Covid-19 and the cardiovascular system: a comprehensive review. *J Hum Hypertens*. 2021;35:4–11.
- Adler Y, Charron P, Imazio M, Badano L, Barón-Esquivias G, Bogaert J, et al. 2015 ESC guidelines for the diagnosis and management of pericardial diseases. *Eur Heart J*. 2015;36:2921–64.
- Maestroni S, Di Corato PR, Cumetti D, Chiara DBLC, Ghidoni S, Priscacaru L, et al. Recurrent pericarditis: autoimmune or auto-inflammatory? *Autoimmun Rev*. 2012;12:60–5.
- Caforio ALP, Brucato A, Doria A, Brambilla G, Angelini A, Ghirardello A, et al. Anti-heart and anti-intercalated disk autoantibodies: evidence for autoimmunity in idiopathic recurrent acute pericarditis. *Heart*. 2010;96:779–84.
- Gunukula SR, Spodick DH. Pericardial disease in renal patients. *Semin Nephrol*. 2001;21:asnep0210052.
- Rostand SG, Rutsky EA. Pericarditis in end-stage renal disease. *Cardiol Clin*. 1990;8:701–7.
- Guzik TJ, Mohiddin SA, Dimarco A, Patel V, Savvatis K, Marelli-Berg FM, et al. COVID-19 and the cardiovascular system: implications for risk assessment, diagnosis, and treatment options. *Cardiovasc Res*. 2020;116:1666–87.
- Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. *JAMA Cardiol*. 2020;5:802.
- Muhammad SZ, Ahmed A, Shahid I, Khalid A, Menezes RG, Sheikh MU, et al. Chest computed tomography findings in hospitalized COVID-19 patients: a systematic review and meta-analysis. *Le Infez Med*. 2020;28:295–301.
- Diaz-Arocutipa C, Saucedo-Chinchay J, Imazio M. Pericarditis in patients with coronavirus disease. *J Cardiovasc Med* 2021. 2019. <https://doi.org/10.2459/JCM.0000000000001202>.
- Sala S, Peretto G, Gramegna M, Palmisano A, Villatore A, Vignale D, et al. Acute myocarditis presenting as a reverse Tako-Tsubo syndrome in a patient with SARS-CoV-2 respiratory infection. *Eur Heart J*. 2020;41:1861–2.
- Yao XH, Li TY, He ZC, Ping YF, Liu HW, Yu SC, et al. A pathological report of three COVID-19 cases by minimal invasive autopsies. *Zhonghua bing li xue za zhi = Chin J Pathol*. 2020;49:411–7.
- Fox K, Prokup JA, Butson K, Jordan K. acute effusive pericarditis: a late complication of COVID-19. *Cureus*. 2020. <https://doi.org/10.7759/cureus.9074>.
- Zhou P, Lou YX, Wang XG, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. *Nature*. 2020. <https://doi.org/10.1038/s41586-020-2012-7>.
- Permanyer-Miralda G, Sagristá-Sauleda J, Soler-Soler J. Primary acute pericardial disease: a prospective series of 231 consecutive patients. *Am J Cardiol*. 1985;56:623–30.
- Chiabrando JG, Bonaventura A, Vecchié A, Wohlford GF, Mauro AG, Jordan JH, et al. Management of acute and recurrent pericarditis. *J Am Coll Cardiol*. 2020;75:76–92.
- Aghagoli G, Gallo Marin B, Soliman LB, Sellke FW. Cardiac involvement in COVID-19 patients: risk factors, predictors, and complications: a review. *J Card Surg*. 2020;35:1302–5.
- Chen G, Wu D, Guo W, Cao Y, Huang D, Wang H, et al. Clinical and immunological features of severe and moderate coronavirus disease 2019. *J Clin Invest*. 2020;130:2620–9.
- Imazio M, Brucato A, Lazaros G, Andreis A, Scarsi M, Klein A, et al. Anti-inflammatory therapies for pericardial diseases in the COVID-19 pandemic: safety and potentiality. *J Cardiovasc Med*. 2020;21:625–9.
- RECOVERY Collaborative Group. Dexamethasone in hospitalized patients with Covid-19. *N Engl J Med*. 2021;384:693–704.

Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.