Journal of Acute Disease

Case Report

doi: 10.4103/2221-6189.347781 jadweb.org

Sudden cardiac death in a case of Crohn´s disease with COVID−19: A case report

Neeraj Kumar[1]✉, Subhajit Ghosh[2], Abhyuday Kumar[2], Sanjeev Kumar[3], Prem Kumar[4]

Departments of [1]Trauma & Emergency, [2]Anaesthesiology, [3]CTVS, and [4]Radiology, All India Institute of Medical Sciences, Patna, India

ABSTRACT

Rationale: The mechanism of sudden cardiac death in COVID-19 can be multifactorial. Cardiac hypersensitivity to 5-ASA therapy leading to myocarditis has been reported in some cases. Cytokine storm syndrome and idiosyncratic reaction with mesalazine use may lead to sudden cardiac death in COVID-19. Use of immunosuppressants in hospitalized COVID-19 patients should be continued with caution, especially in patients with inflammatory bowel disease.

Patient's concern: A 75-year-old man who was tested positive for SARS-CoV-2 was admitted with a history of shortness of breath for the last two days. He was a known case of Crohn's disease treated with mesalazine.

Diagnosis: COVID-19 pneumonia with underlying Crohn's disease leading to sudden cardiac death.

Intervention: Remdesivir, antibiotics, steroids, low molecular weight heparin, tablet zinc, tab vitamin C, and other supportive treatment were started. Because of increased inflammatory markers, itolizumab was given to the patient on the 2nd day.

Outcome: On the 5th day of the intensive care unit, the patient complained of sudden chest pain with respiratory distress leading to bradycardia and asystole and could not be resuscitated.

Lessons: Causes for sudden cardiac death in COVID-19 pneumonia patients with Crohn's disease is multifactorial. Although mesalazine may be a safe and effective drug in the management of inflammatory bowel disease, it can induce sytokine strom syndrome and idiosyncratic reactions that could be one of the reasons of sudden cardic death. Therefore, we should be aware of its serious and potentially life-threatening complications, especially in COVID-19 infected patients.

KEYWORDS: COVID-19; Sudden cardiac death; Chron's disease

1. Introduction

Inflammatory bowel diseases (IBD) like Crohn's disease (CD) and ulcerative colitis (UC) are chronic inflammatory diseases of the intestines that may present with many venous vascular comorbidities such as deep venous thrombosis or portal vein thrombosis. These chronic systemic inflammations may lead to endothelial dysfunction and platelet aggregation and serve as a precursor to the development of atherosclerosis and coronary artery disease (CAD)[1]. As per the literature, SARS-CoV-2 can lead to unfavorable outcomes in elderly patients with comorbidities, for example, cardiovascular dysfunction[2]. Sudden cardiac death (SCD) has emerged as one of the most challenging concerns amid the COVID-19 pandemic[3]. Although the direct causal association between SCD and COVID-19 remains unproven, but some published data may suggest a plausible association.

Significance

We should be aware of serious and potentially life-threatening complications like sudden cardiac death, especially in COVID-19 patients with underlying inflammatory bowel disease. Cardiovascular complications caused by cytokine storm syndrome (raised inflammatory markers) and idiosyncratic reactions with mesalazine use may precipitate sudden cardiac death. So, immunosuppressants in hospitalized COVID-19 patients should be continued with caution. Besides, every patient deserves risk stratification based on a clinical background of the disease.

✉To whom correspondence may be addressed. E-mail: neeraj.jlnmc@gmail.com

How to cite this article: Kumar N, Ghosh S, Kumar A, Kumar S, Kumar P. Sudden cardiac death in a case of Crohn's disease with COVID-19: A case report. J Acute Dis 2022; 11(3): 123-126.

Article history: Received 14 February 2021; Revision 29 March 2021; Accepted 10 June 2021; Available online 27 June 2022

2. Case report

Departmental Ethics Committee, All India Institute of Medical Sciences Patna, Bihar, India, approved the reporting of this case, and the informed consent was obtained from the patient's relatives.

A 75-year COVID-19 patient was admitted to our intensive care unit because of the shortness of breath for the last 2 days. He was a known case of Crohn's disease and hypothyroidism and was on tablet mesalamine 1 g and tablet levothyroxine 25 μg daily. He had stable vitals and maintained saturation on the non-rebreathing mask with a reservoir bag. As per our institutional COVID-19 management protocol, remdesivir, antibiotics, steroids, low molecular weight heparin, tablet zinc, tablet vitamin C, and other supportive treatment were started. Because of increased inflammatory markers, itolizumab was given to the patient on the 2nd day. Artery blood gas was within acceptable limits with a PaO_2/FiO_2 ratio of 121. The normal arterial blood gases were PH of 7.36, PaO_2 of 78 mmHg, $PaCO_2$ of 33 mmHg, HCO_3 of 21 mmol/L. The chest X-Ray finding was typically suggestive of COVID-19 with patchy areas of ground-glass opacity in the middle and lower zones in the right and middle zone in the left, with normal costophrenic angle (Figure 1). On the 3rd day, oxygen requirement was further increased, and oxygen saturation dropped below 90% with a respiratory rate of 38-40 rates per minute. He was put on a high-flow nasal oxygenation machine with a FiO_2 of 0.8 and with a flow rate of 5 L/ min. On the 4th day, the patient's condition was improved, and oxygen saturation was maintained between 95%-97% on transnasal high flow oxygen therapy with FiO_2 of 0.6 and at a flow rate of 5 L/min. Routine investigations on days three and four were almost normal except for the inflammatory markers which were raised (Table 1). A day-by-day clinical progression is shown in Table 2.

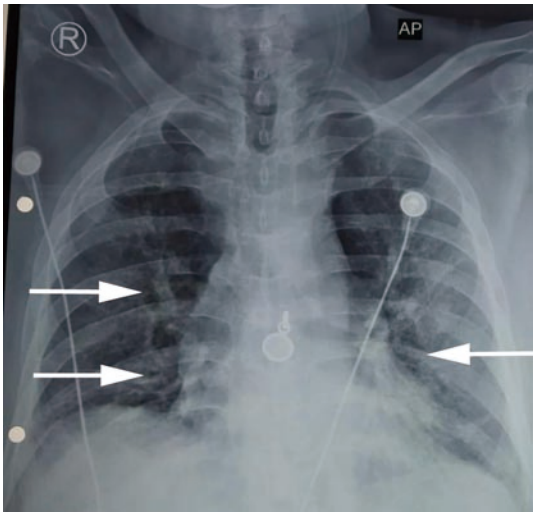

Figure 1. The chest X-ray (AP-view) of a 75-year-old man with COVID-19. White arrows show extensive opacities in bilateral lungs.

Table 1. Day wise laboratory and inflammatory markers values.

Variables	Day 1	Day 2	Day 3	Day 4	Day 5
Haemoglobin, g/dL	9.8	9.7	10.0	8.2	9.0
White blood cells, $\times10^3$/dL	10.59	8.82	10.31	9.21	8.98
Neutrophil, %	95.9	94.6	97.4	97.0	96.1
Lymphocyte, %	2.8	4.1	1.7	1.6	2.2
Neutrophil/lymphocyte	34	24	57	61	44
Serum creatinine, mg/dL	1.11	0.80	1.18	0.85	0.84
Serum urea, mg/dL	25.3	22.2	46.5	53.1	48.6
Serum sodium, meq/L	126.99	131.00	131.82	133.7	135.67
Serum potassium, meq/L	4.14	4.29	4.21	4.39	4.81
Total bilirubin, mg/dL	0.74	0.62	0.62	0.58	0.84
Serum glutamic-oxaloacetic transaminase, U/L	29.5	42.4	51.4	43.8	67.7
Serum glutamic pyruvic transaminase, U/L	24.0	23.4	34.4	38.9	74.9
Albumin, g/dL	3.39	3.09	3.18	2.80	2.79
Total protein, g/dL	5.44	5.05	5.40	4.09	4.27
pH	7.422	7.477	7.404	7.420	7.48
$PaCO_2$, mmHg	32	20.4	29.2	28.1	26.5
PaO_2, mmHg	84.4	96.8	82.9	126.9	80
HCO_3, mmol/L	21.0	15.2	18.4	18.8	20.1
Lactate, mmol/L	1.1	1.2	0.9	1.3	1.2
PaO_2/FiO_2 ratio	84.4/70	96.8/80	82.9/60	126.9/45	80/60
Activated partial thromboplastin time, seconds	29.84	27.38	31.10	30.42	28.23
International normalized ratio	0.97	0.84	0.89	0.93	0.90
Ferritin, ng/mL	218.9	329	383	407	455
Interleukin-6, pg/mL	459.9	489	364.5	339.3	209
Lactate dehydrogenase, U/L	989.59	845.43	878.12	909.32	911.65
Procalcitonin, ng/mL	0.143	0.234	0.121	0.164	0.131
Random-glucose, mg/dL	196	187	168	173	182
Plasma d-dimer, mcg/mL	0.35	0.25	0.21	0.19	0.23
C-reactive protein, mg/dL	191	208	185	168	154
Platelet, $\times10^3$/dL	131	120	167	166	150
Trop T test	-	-	-	-	Negative

Table 2. Clinical course of the patient during ICU stay.

Day of ICU stay	Oxygen therapy	PO_2/FiO_2	Inflammatory markers	Vitals
Day 1	NRMRB	121	Increased	RR: 30-34; others within normal range
Day 2	NRMRB	121	Increased	RR: 32-34; others within normal range
Day 3	HFNO	138	Increased	RR: 38-40; others within normal range
Day 4	HFNO	282	Increased	RR: 30-32; others within normal range
Day 5	HFNO	133	Increased	RR: 30-40 rate/min; On the 5th day, the patient complained of sudden chest pain with respiratory distress followed by bradycardia and asystole

NRMRB: Non rebreathing mask with reservoir bag; HFNO: High flow nasal oxygenation; RR: Respiratory rate (rate/min).

On the 5th day, the patient complained of sudden chest pain with respiratory distress. A 12-lead electrocardiograph was taken which showed no significant ST-segment change, and trop T was negative. 2-D bedside echocardiography did not show any evidence of pulmonary embolism with normal chamber size and normal left ventricular ejection fraction. But the patient immediately went into bradycardia and followed by asystole. Cardiopulmonary resuscitation was initiated promptly per Advanced Cardiac Life Support protocol; all reversible causes, including tension pneumothorax, cardiac tamponade, and electrolyte/metabolic disturbances were ruled out. However, the patient was not revived and was declared dead.

3. Discussion

The mechanism of SCD in COVID-19 can be multifactorial. However, it remains difficult to ascertain the most common mechanism involved due to a lack of data. Both tachyarrhythmia and bradyarrhythmia have been reported in COVID-19. Fatal arrhythmias in COVID-19 may also result from hypoxia, cardiac dysfunction, severe systemic inflammatory state, electrolyte derangements, intravascular volume imbalances, and drug side effects[4]. Guo *et al.*[5] suggested life-threatening arrhythmias have been variably reported from 10% to 16% of patients hospitalized for severe COVID-19, more commonly in the setting of elevated troponin indicating myocardial injury. Some of the proposed causes of sudden cardiac death in COVID-19 are acute myocarditis (stress-induced cardiomyopathy), acute coronary syndrome, hypoxia, pulmonary thromboembolism, coronary thrombosis, stroke, cardiac tamponade, electrolyte imbalance, underlying channelopathies, and drug-induced arrhythmias. Direct arrhythmogenesis by COVID-19 cytokines has a direct electrophysiological effect on the myocardium, IL-6, tumor necrosis factor-α, and IL-1 can prolong ventricular action potential duration. These cytokines may induce cardiac sympathetic system hyperactivation, which can trigger life-threatening arrhythmic events in patients with long QT[6]. In our case, QT/QTc was 348/452 ms, so the possibility of any QTc prolongation was ruled out. The deep vein thrombosis and pulmonary embolism was also ruled out because of normal echocardiography findings with normal d-dimer and prothrombin time.

Studies have found that IBDs are associated with an increased risk of CAD, cerebrovascular diseases, and peripheral arterial diseases[7]. High levels of circulating cytokines and C-reactive protein are characteristic of IBD, and it is therefore expected to contribute to endothelial dysfunction and atherogenesis. The possible causes of increased cardiovascular events in patients with IBD can be raised inflammatory markers, endothelial dysfunction, hypercoagulability, and release of endotoxins and lipoproteins[7].

The drug mesalazine (5-ASA) is efficacious in active Crohn's and ulcerative colitis and are generally regarded as a safe and well-tolerated medication[8]. Cardiac hypersensitivity to 5-ASA therapy leading to myocarditis has been reported in some case studies, and the first reported death from myocarditis associated with mesalazine use was in 1990[9]. In documented literature, hypersensitivity appears to be an idiosyncratic reaction rather than dose-dependent due to its occurrence in patients on very low amounts of mesalazine such as 0.5 g a day[10].

In our case, sudden cardiac death was possibly due to cardiovascular complications caused by cytokine storm syndrome (raised inflammatory markers) and idiosyncratic reaction with mesalazine use. Our patient had a high-risk factor for cardiovascular complications due to COVID-19, IBD, and mesalazine. Mesalazine is very safe and efficacious in the management of inflammatory bowel disease but we should be aware of its serious and potentially life-threatening complications that may occur especially if it has to be used in COVID-19 infected patients.

To sum up, immunosuppressants in hospitalized COVID-19 patients should be continued with caution. There should be a baseline electrocardiograph to check QTc interval and look for other risk markers of tachy or bradyarrhythmias. Metabolic parameters including electrolytes, fluid volume, and acidosis should be actively sought and treated at the earliest possible, especially in the ICU. Every patient deserves risk stratification based on his/her clinical background with complete available information.

Conflict of interest statement

The authors report no conflict of interest.

Funding

This study received no extramural founding.

Authors' contributions

N.K.: Manuscript writing, proofreading, and final drafting; S.G.: Case management; manuscript writing A.K.: Final drafting; S.K.: Proofreading; P.K.: Proofreading.

References

[1] Hansson GK. Inflammation, atherosclerosis, and coronary artery disease. *N Engl J Med* 2005; **352**(16): 1685-1695.

[2] Yang X, Yu Y, Xu J. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: A single-centered, retrospective, observational study. *Lancet Respir Med* 2020; **8**(5): 475-481.

[3] Beri A, Kotak K. Cardiac injury, arrhythmia, and sudden death in a COVID-19 patient. *Heart Rhythm Case Rep* 2020; **6**(7): 367-369.

[4] Bhatla A, Mayer MM, Adusumalli S. COVID-19, and cardiac arrhythmias. *Heart Rhythm* 2020; **30**(8): 451-460.

[5] Guo T, Fan Y, Chen M. Cardiovascular implications of fatal outcomes of patients with Coronavirus disease 2019 (COVID-19). *JAMA Cardiol* 2020; **5**(7): 811-818.

[6] Enea LP, Mohamed B, Leopoldo CP. COVID-19, arrhythmic risk, and inflammation mind the gap! *Circulation* 2020; **142**(1): 7-9.

[7] Schicho R, Marsche G, Storr M. Cardiovascular complications in inflammatory bowel disease. *Curr Drug Targets* 2015; **16**(3): 181-188.

[8] Hanauer SB, Strömberg U. Oral Pentasa in the treatment of active Crohn's disease: A meta-analysis of double-blind, placebo-controlled trials. *Clin Gastroenterol Hepatol* 2004; **2**(5): 379-388.

[9] Kristensen KS, Høegholm A, Bohr L, Friis S. Fatal myocarditis associated with mesalazine. *Lancet* 1990; **335**(8689): 605.

[10]Vayre F, Vayre-Oundjian L, Monsuez JJ. Pericarditis associated with longstanding mesalazine administration in a patient. *Int J Cardiol* 1999; **68**(2): 243-245.