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Potential Cardiomyopathy in a Mortality Case with COVID-19: A Case Report

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A B S T R A C T

Background: The current report presents the clinical presentations and paraclinical findings of the second confirmed mortality case of the coronavirus disease 2019 (COVID-19) outbreak in Qom, Iran, with an emphasis on the results of the direct cardiac consequences of COVID-19 infection.

Case Report: A 63-year-old male patient was admitted to the Emergency Department of Kamkar-Arabnia hospital in Qom, with productive coughs, chills, anorexia, and fever. The patient had taken no recent trips and had no exposure to individuals with respiratory symptoms. Pulmonary auscultation and related imaging indicated serious pulmonary involvements. Laboratory findings showed evidence of anemia, uremia, hepatic dysfunction, and cardiac involvement, including electrocardiography changes, cardiac enzyme elevation, and relatively large cardiac space in the chest X-ray. Mortality occurred by cardiopulmonary arrest with a prominent feature of asystole and no little response to long durations of resuscitation which could originate from both acute respiratory distress syndrome as well as direct cardiac involvement.

Conclusion: Considering the enormous capability of coronaviruses for miscellaneous pathogenesis and outstanding mortality rate of COVID-19, it is necessary to pay more concentrated attention to the direct cardiac consequences of this disease.

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Introduction

The novel coronavirus, formerly referred to as 2019 novel coronavirus (2019-nCoV), caused an epidemic of severe acute respiratory syndrome (SARS) in Wuhan, China, and subsequently progressed globally to form a pandemic of coronavirus disease 2019 (COVID-19) in numerous countries, nearly in all continents worldwide (1-4). The pandemic of COVID-19 has been also reported with confirmed cases in all provinces of Iran (5-10). Many medical centers, clinicians, and researchers around the world are currently sharing their data and experiences of COVID-19 in order to participate in the global attempt to control the pandemic (4). The knowledge of the precise extent of coronavirus

infection caused by COVID-19 is crucial for optimal clinical and preventive practices.

Emerging evidence indicates that the direct damage of coronavirus infection is not merely confined to the pulmonary tissue or immune system lymphocytes and may well reach beyond them. There have been reports pointing to the susceptibility of various organs and systems to this infection, including the digestive tract, liver, kidneys, thyroid gland, heart, and even the brain (11). Such extensive infections could have direct effects on the dramatic mortality rates of the disease.

Direct cardiac involvements gained outstanding interest worldwide (5-10), leading to a universal experience of more efficient care; however, more information in this regard adds to the knowledge of this new field, and clinical findings are being added to previous experimental findings every day. Nevertheless, there has been limited knowledge of the clinical relevance, significance, and applicability of coronavirus pathogenesis. It is believed that the exact mechanism of injury is not confirmed, indicating that the definite clinical diagnosis in this regard is an outstanding question; therefore, up-to-date research is necessary in order to obtain further information about cardiovascular involvements and guide information toward a more efficient clinical practice and better outcomes.

With this background in mind, the aim of the current report is to investigate the clinical presentations and paraclinical findings of the second confirmed mortality case at the initiation of the COVID-19 outbreak in Iran, with an emphasis on the findings associated with direct cardiac involvement of COVID-19 infection.

Case Report

On February 10, 2020, a 63-year-old male patient was admitted to the Emergency Department of Kamkar-Arabnia hospital, a tertiary center for infectious diseases in Qom, Iran, and one of the medical centers of Qom University of Medical Sciences. The patient symptoms were productive coughs, chills, anorexia, and fever which did not abate upon outpatient treatments. The medical history of the patient included hypothyroidism and hyperlipidemia. In addition, he had taken no recent trips and had no exposure to individuals with respiratory symptoms.

The patient body temperature was 39.0°C. Moreover, he had a respiratory rate of 18 breaths per minute, normal oxygen saturation (99%), and no respiratory distress. Pulmonary auscultation revealed bilateral rales as coarse crackles. The chest X-ray (Figure 1) and later computed tomography

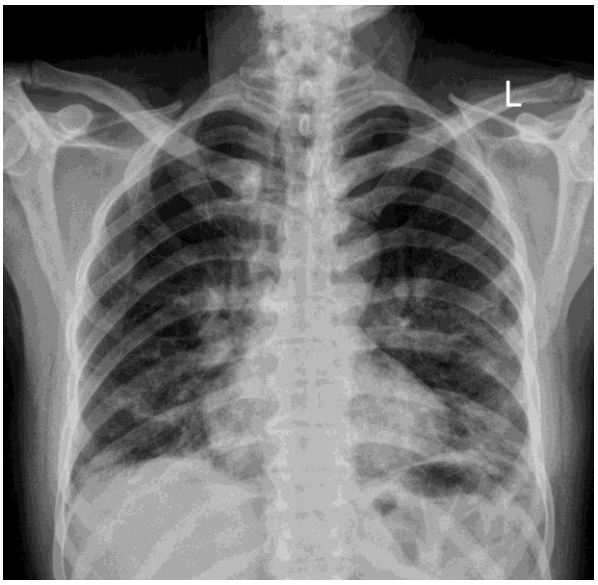

Figure 1. Chest X-ray of the patient; presence of patchy infiltrates of both lungs, particularly in the lower fields

(CT) scan (Figure 2) showed bilateral infiltrates, with a nearly diffused pattern as well as a wide mediastinum.

Laboratory findings included a complete blood count (CBC) (Table 1) obtained at the time of referral and daily after admission. Platelet count was normal on admission and after several days (130-190 thousand per mm^3), while turning into thrombocytopenia (90 thousand cells mm^3) on the subsequent days. Red blood cell count (3.53-4.0 million cells per mm^3), hemoglobin (10.9-12.4 g/L), and hematocrit (32.4-37.7%) decreased all during the admission to the patient demise. Total white blood cell (WBC) counted as a lower limit of normal (4,000-6,500 cells per mm^3) turned into leukocytosis as much as 18,000 cells per mm^3. Lymphopenia both in terms of percentage and count (14%; 560 cells per mm^3) gradually deteriorated (10-5%; 513-895 cells per mm^3); however, the neutrophil percentages and counts increased (85-91%; 3,400-16,300 cells per mm^3) in all CBCs.

Creatinine and blood urea nitrogen (Table 2) were normal on admission (1.1 and 31 mg/dL, respectively) with a rising trend afterward (1.5-2.0 and 44-87 mg/dL, respectively).

Other assessments, including the liver function enzymes of alanine transaminase, aspartate transaminase, and alkaline phosphatase, were observed to be mildly elevated (89, 63, and 162 IU/L, respectively) with a rising trend afterward (110, 103, and 346 IU/L, respectively). However, bilirubin (total and direct), prothrombin time, partial thromboplastin time, and international

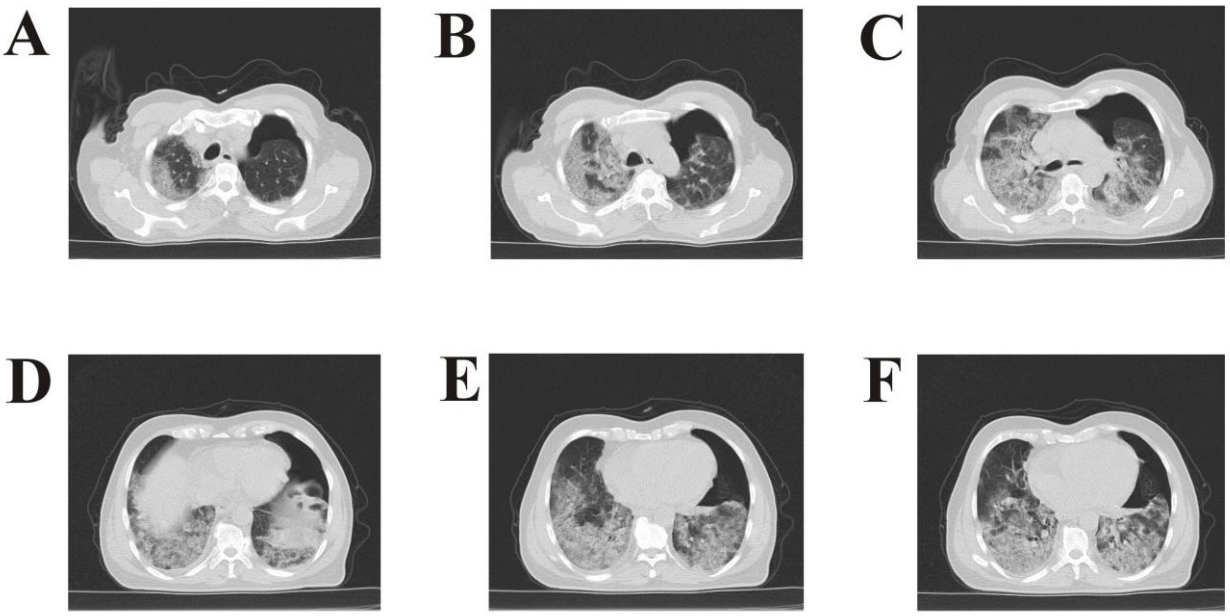

Figure 2. Chest computed tomography scan of the patient; presence of bilateral pulmonary involvement, more prominent in the lower fields of both lungs (D-F) and upper fields of the right lung (A-C)

Table 1. Complete blood count of the patient since admission to mortality

Complete blood count (cells per mm³)	1st day	3rd day	4th day	5th day	6th day	7th day (Mortality)
White blood cell count	4,000	6,500	5,700	8,100	12,000	17,900
Neutrophil count	3,400 85%	5,850 90%	5,300 88%	7,300 91%	10,200 85%	16,300 91%
Lymphocyte count	560 14%	585 9%	513 9%	567 7%	1,200 10%	895 5%
Platelet count	130,000	115,000	145,000	190,000	Missed	90,000
Red blood cell count	3.9 million	3.83 million	3.53 million	4 million	3.95 million	3.9 million
Hemoglobin (g/dL)	11.5	11.7	10.9	12.4	12.2	12.3
Hematocrit (%)	32.4	35.1	33.1	37.7	36.8	35.5

Green values within normal range; blue values considered decrease

Table 2. Kidney function and serum electrolytes of the patient since admission to mortality

Serum parameter	1st day	6th day	7th day (Mortality)
Kidney function (mg/dL)			
Blood urea nitrogen	31	44	87
Creatinine	1.1	1.5	2.0
Electrolytes (mEq/L)			
Sodium (Na)	136	139	138
Potassium (K)	4.1	3.4	3.4

normalized ratio remained normal. Electrolytes of sodium and potassium and pancreatic enzymes, including amylase and lipase, were also normal. The obvious elevation in creatine phosphokinase (CPK=777 IU/L), lactate dehydrogenase (LDH=761-930 IU/L), troponins (20.8 ng/mL), and D-dimer (mg/L) indicated sufficient cell lysis which could be hepatocytes or myocytes.

To investigate the source of the infection, blood and sputum culture and serology for hepatitis B and hepatitis were assessed all showing negative results. Throat and mid-turbinate swabs were obtained for some viral tests which were negative for influenza viruses A and B, parainfluenza, human metapneumovirus, adenovirus, and respiratory syncytial virus; however, reverse transcription-quantitative polymerase chain reaction confirmed the 2019-nCoV infection. Electrocardiography (EKG) assessments on admission and at the critical stage (Figure 3) showed sinus rhythm, right bundle branch block pattern, right axis deviation, wide QRS, ST-T changes, and inverted T-wave. Serial analysis of blood gases showed metabolic alkalosis turning into respiratory and metabolic acidosis at the patient critical stage.

Due to extreme increases in body temperature during admission, several antipyretics were

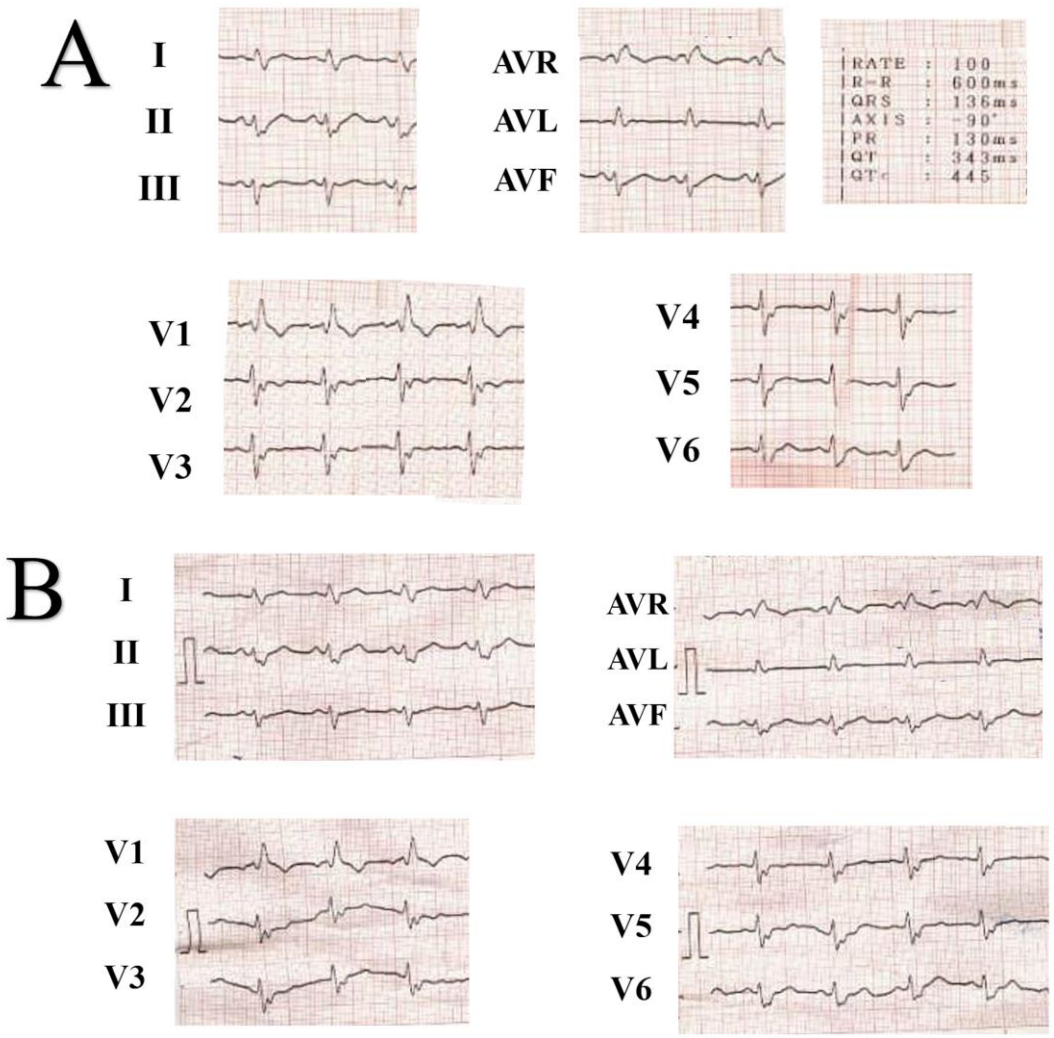

Figure 3. Electrocardiograms of the patient on the 1st day (A) and 3rd day (B) indicating changes possibly associated with cardiomyopathy

prescribed for the patient although the patient gradually showed resistance to fever treatment (body temperature: 36.5-39.5°C) and developed respiratory distress and hypoxia (oxygen saturation: 50%), indicating initial recovery (oxygen saturation: 93-89%) by respiratory supports, despite being short-lived. The chest tube was applied to the patient due to suspected pneumothorax. He was transferred to the intensive care unit (ICU) where he was conscious but quite restless and toxic. The patient became more toxic while oxygen saturation dropped to as low as 80% after 1 day of ICU admission and then to 55-69% after 2 days. On February 14, 2020, progressive hypoxia continued and apnea occurred followed by asystolic cardiac arrest. The mortality occurred and one hour of resuscitation was unsuccessful.

Discussion

The current report presents the second mortality in Iran, occurring due to SARS confirmed to be the novel coronavirus disease (i.e., COVID-19). This mortality is reported in Qom, located in the central region of Iran, known as one of the primary initiators of the outbreak in Iran. A detailed evaluation revealed the clinical and paraclinical presentations mainly in line with those reported in previous studies (12) and updated reports, despite the presence of variations in the presentations. These variations could be of importance both scientifically and clinically, particularly in terms of cardiac involvement. The presentations of this patient are discussed in detail in this part.

As pointed out in the literature, it has been already known that the coronavirus could be associated with acute viral respiratory illnesses, mainly the common cold and SARS, particularly the pandemic of 2002 and 2003 which was initiated in southern China. The current pandemic could be comparable to other coronavirus infections and

previous outbreaks of SARS in some of its details, or it might actually be the re-emergence of SARS predicted to occur and become global (13, 14). The present case was presented with the signs and symptoms typical of SARS rather than the common cold and then showed dominant representations of pneumonia rather than an upper respiratory tract infection.

The clinical presentations of COVID-19 or coronavirus infection, in general, are typically associated with fever, dyspnea, and hypoxemia. In addition, typically, dry coughs are reported most of the time accompanied by chills, malaise, and myalgia. Imaging for SARS coronavirus and COVID-19 have been reported to show various infiltrates in the chest X-ray and chest CT scan, mainly initiating from lower fields (12, 15, 16).

Similar to the above-mentioned setting, the patient was presented with coughs and fever with pulmonary involvement both observed in pulmonary auscultation and imaging, indicating pneumonia in both lungs (figures 1 and 2). The presence of productive coughs differently appearing in the present patient and case of "The Patient Zero" previously reported from Iran (5) could be considered in the clinical course of Iranian patients or elderly patients with acute respiratory symptoms.

The epidemiologic analyses previously reported demonstrated more cases and more critical cases in men and the elderly (17-20). Similarly, the current reported case was male and over 60 years. The reports have pointed to several risk factors associated with the poor prognosis of COVID-19. Most authors have mentioned age as an important risk factor. A report on the clinical course of critically ill COVID-19 patients reported the median age for non-survivors to be 64.6 years (2, 20-22). Another epidemiologic analysis reported the age distribution in COVID-19 patients to be skewed toward older age groups and a median age of 45 years for all the patients together with a median age of 70 years for mortalities. The authors suggested an age-related susceptibility to COVID-19 infection and outcomes. Therapeutic and triage strategies for COVID-19, published in February 2020, recommend special consideration for elderly patients, particularly those older than 65 years (16).

According to the literature, it has been indicated that the risk factors for acute respiratory distress syndrome (ARDS) caused by coronavirus include the age of over 50 years, pregnancy, and comorbidities, such as cardiovascular disease, diabetes, and hepatitis (12). Pregnancy, immunosuppression, cerebrovascular events, and chronic medical illnesses are also reported as outstanding risk factors for poor prognosis of COVID-19 (2, 17, 19, 23, 24). Considering the aforementioned reports, the mortality of the present case had no risk factor other than age, leading to suggest that age may also be accompanied by a risk of direct cardiac involvement.

Regarding the reported current patient, exposure history did not indicate any trips to high-risk regions or human-to-human contact with the pathogen. The exact mode of pathogen transmission is still unknown, and the known mechanisms include exposure to infected humans, infected animals, oral-fecal roots, and contaminated surfaces (12); the current case may have experienced the latter. Due to unknown exposure, the incubation period could not be estimated for the patient.

The hallmark finding of coronavirus infection in the routine laboratory assessments is lymphopenia with the cut-off point of lower than 1,100 per mm (3, 12, 16). However, total WBC might remain normal or slightly decrease. The present patient showed lymphopenia and relatively increased neutrophil counts with total WBC slightly decreased on admission. Aminotransferases were altered with increased LDH, CPK, and troponins in line with the previous findings on coronavirus infection (6).

Kidney function was impaired in the patient. Studies reported a special affinity of the coronavirus to kidney cells experimentally and clinical kidney dysfunction in many patients with COVID-19 (3, 12, 17, 20, 24). It should be considered that the patient was not presented with hypoxemia on admission; nevertheless, he showed anemia, uremia, hepatic dysfunction, and cell lyses, altogether suggesting a poor prognosis for the case.

Special consideration could be devoted to the evidence of cardiac involvement, including EKG changes, cardiac enzyme elevation, relatively large cardiac space in chest imaging, and cardiopulmonary arrest with a prominent feature of asystole and no little response to long durations of resuscitation. Theoretically, the pathogen could invade any human cell exposed to the bloodstream, possessing the angiotensin-converting enzyme II receptor, including hepatocytes and myocytes; however, the affinity to ciliated epithelial cells, pneumocytes type II, and kidney cells are well-known (12).

Similar to the present report, Long et al. reported in their review that the cardiovascular system is also affected by the novel coronavirus infection, and the consequences included a wide range of myocardial injuries, namely myocarditis, acute myocardial infarction, heart failure, dysrhythmia, and venous thromboembolic event. Moreover, currently, routine care for COVID-19 interacts with cardiac care, thereby recommending the emergency management of COVID-19 to seriously consider cardiovascular

conditions (25-27). Babapoor et al. reported in their review that myocardial injury is among the influential pathogenic features of COVID-19. The aforementioned review collected several investigations demonstrating increased cardiac enzymes, mostly cardiac troponin I and T, together with decreased cardiac function in the COVID-19 patients related to morbidities; nonetheless, the exact mechanism is unclear.

In addition, direct damage to cardiomyocytes is suggested as one of the possible mechanisms among other local and systemic mechanisms (28-30). There are several reports proposing stress cardiomyopathy or takotsubo cardiomyopathy in pregnant and non-pregnant patients with COVID-19, some of which were confirmed by cardiac angiography (31-35). All the above-mentioned cardiovascular complications could have been the core pathogenesis of the current patient. Due to the limited knowledge of COVID-19 and potential for cardiovascular complications, cardiologic assessments in this patient were confined to cardiology consultation and EKG assessments as previously described.

Viral myocarditis is proposed as a category of the causes of cardiomyopathies. It has been suggested as the etiological factor behind some idiopathic cardiomyopathies or sudden cardiac mortalities (19, 20). Based on the evidence obtained from animal studies, it is suggested that coronavirus infection may lead to viral myocarditis and progress into further consequent complications, including delighted or hypertrophic cardiomyopathy, heart failure, or cardiac mortality. This outcome has even been proposed as an experimental model for dilated cardiomyopathy (36-39).

Acute cardiac injury has been reported in the recent outbreak of COVID-19 in China to be as much as 12% in all patients, with highly significant increased rates of 31% in the ICU patients, 21% in critically ill patients, and 28% in mortalities (40). It could be hypothesized theoretically, clinically, and evidentially that cardiac injury is closely associated with the critical trend of COVID-19. Clinically, it is well-known that a small fraction of severe respiratory syndromes, especially febrile syndromes, progress rapidly into fulminant and fatal myocarditis, leading to cardiogenic shock and failure of multiple organs. For these patients, it is vital to incorporate aggressive cardiac support into intravenous inotropic and, if necessary, mechanical circulatory support. According to the literature, the survival potential is estimated to be as much as half of the cases which go on to a marked improvement of the cardiac function near to normal (25). If the case is even relatively true for COVID-19, it could help to improve the medical management and outcome of critical patients.

It should be considered that immune responses to viral antigens induce myocardial depressant effects and, in some cases, invade myocardial proteins, eventually resulting in decreased cardiac function. Moreover, deteriorating respiratory dysfunction in SARS may lead to ARDS and ultimately failure of multiple organs. Nevertheless, a clinical evaluation may reveal cardiac complications beyond these effects. The prominent symptoms of all cardiomyopathies include breathlessness exceptionally or at rest, supine dyspnea, cough, and fatigue, which might occur in the absence of peripheral edema and congestion. These presentations misleadingly overlap with the symptoms of SARS (25). Even chest pain, if present, is overlooked in the catastrophic end-stage patients and claimed to accompany the coronavirus infection (17).

The clinical course and outcome of COVID-19 in the present reported case could be attributed to all the above-mentioned fatal clinical settings, although it could be helpful to take into account more extensive probabilities in COVID-19 patients showing catastrophic trends. The updated evidence has to seriously look for such probabilities, including the potential for the neuroinvasion of COVID-19, despite the afferent neural branches of the respiratory system toward the cardiorespiratory center in the brain stem. The infection of the central nervous system (CNS) by coronavirus has been claimed to partially contribute to respiratory failure (41-43). It is also declared that some of the symptoms of coronavirus

Study Highlights

What is the current knowledge?

- Direct damage of the novel coronavirus infection is not merely confined to the pulmonary tissue or immune system lymphocytes.
- Reports are pointing to the susceptibility of various organs and systems to COVID-19 infection, including the digestive tract, liver, kidneys, thyroid gland, heart, and even the brain.

What is new in this report?

- This case report of a COVID-19 patient indicated that there is evidence of cardiac involvement, which is closely associated with critical clinical trends.
- There is a need for more serious responsiveness to the cardiac consequences of COVID-19.

COVID-19: Coronavirus disease 2019

infection, including nausea, vomiting, headache, and even parts of respiratory arrest, originate from the infection of the CNS (41). There are specific types of the coronavirus known in animal studies, namely the neurotropic types, which induced encephalitis, demyelination, and experimental multiple sclerosis (18, 20, 41-44). Considering the enormous capability of coronaviruses for miscellaneous pathogenesis and outstanding mortality rate of COVID-19, it is necessary to pay more concentrated attention toward the direct cardiac consequences of this disease.

Conclusion

The second mortality of COVID-19 in Iran was reported to be accompanied by the evidence of cardiac involvement and closely associated with critical clinical trends, pointing to the need for more serious responsiveness to the cardiac consequences of COVID-19.

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Conflict of interest

The authors declare that there is no conflict of interest.

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Ethical approval

The current report does not include any intervention with human participants.

Authors' contributions

All the authors have contributed to the writing or editing of this case report. Furthermore, all the authors have read and approved the final version of the manuscript.

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