CASE REPORT

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COVID-19 Associated Acute Viral Myocarditis and Thyroid Gland Follicular Neoplasm in a Hemodialysis Patient

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ABSTRACT

Since the first cases were reported in Wuhan, China, COVID-19 has spread swiftly worldwide and is caused by SARS-CoV-2. The development of myocardial injury is associated with significantly worse clinical course and increased mortality. However, currently, it is unclear whether cardiac injury occurred in COVID-19 patients. Histological results obtained directly from the viral infection of the myocardium (i.e., SARS-CoV-2 viral myocarditis) or indirectly from the complications of COVID-19, showed that only a portion of patients infected with the virus developed viral myocarditis. Therefore, it is possible that with more autopsy evidence of SARS-CoV-2 and more correlation with the severity of the viral infection, viral myocarditis will emerge. Although COVID-19 manifests primarily as respiratory disease, few cases of cardiac injury without respiratory involvement or febrile illness have been reported. The pathogenesis of cancer and viral infections is due to the inability of the immune system to distinguish between self and non-self. Several oncogenic (hepatitis B virus, hepatitis C virus, human papilloma virus, Epstein-Barr virus, and HIV) and oncolytic viruses (coxsackievirus, reovirus, vaccinia virus, and adenovirus) are known to cause and regress various cancer types. We report a case of atypical manifestation of COVID-19-induced acute myocarditis and thyroid gland follicular neoplasm in a hemodialysis patient with no respiratory symptoms. This case illustrates that COVID-19 can present atypically and affect non-respiratory organ systems.

The association between infection and cardiovascular disease has long been recognized in the form of Chagas disease, diphtheria, tuberculous pericarditis, viral myocarditis, and others. Almost any infectious pathogen can cause myocarditis or heart disease.[1] Authorities from the Chinese Center for Disease Control and Prevention reported that, among more than 44 000 confirmed cases of COVID-19, about 81% were asymptomatic or presented with mild symptoms such as cough, fever, fatigue, and myalgia.[2] Although, for these cases, home management and self-isolation are the appropriate measures, 14% developed a severe form of the disease, and 5% were critical, requiring hospitalization and intensive care unit admission, respectively.[2]

COVID-19 mortality rates vary between various countries, with genetic factors and climate differences between countries postulated as the etiology for this variation.[3] Elderly individuals, patients with comorbidities, and pregnant women are particularly at risk for severe forms. COVID-19 thus represents a threat to patients on maintenance dialysis, who frequently display multiple comorbidities and are particularly vulnerable to infection.[4] In one study, for example, nearly one-third of hospitalized dialysis patients with COVID-19 died; those who died were older (75 vs. 62 years) and had more comorbidities.[3] Unlike other individuals who can observe a strict lockdown, they still need to come to the dialysis center thrice weekly.[5]

A recent study in China with 1590 COVID-19-positive patients showed cancer as one of the most serious comorbidities that increase the risk of acquiring COVID-19.[6,7] Human leukocyte antigens are a group of identification molecules located on the surface of all cells in a combination that is almost unique for each person, thereby enabling the body to distinguish self from non-self. The inability of the

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immune system to distinguish between self and non-self could be explained by the pathogenesis of cancer and viral infections. Both viruses and cancers express proteins that are recognized by host T-cells and both could prompt T-cell mediated inflammation.[8]

Similar to other severe acute respiratory outbreaks (SARS-CoV, MERS-CoV), comorbidities such as hypertension and malignancy predispose COVID-19-positive patients to adverse clinical outcomes.[6,9–11]

CASE REPORT

Our patient was a 38-year-old Omani male with known hypertension and end-stage kidney disease (ESKD) on a regular thrice weekly hemodialysis sessions since January 2011.

He was diagnosed with COVID-19 on 19 July 2020 after he presented with fever and diarrhea. He presented with mild to moderate infection, so he was not admitted to the hospital and remained at home. He was quarantined for two weeks and attended the medical center thrice weekly for dialysis in an isolated room. During that time, he presented to the cardiology outpatient clinic with exertional breathlessness associated with retrosternal chest pain. During clinical examination, his physical activity was limited as he walked with an aiding stick after right below knee amputation and left above knee amputation, so functional capacity could not be fully assessed by the attending clinician. His electrocardiogram showed a normal sinus rhythm with left ventricular hypertrophy (LVH) by voltage criteria.

His chest X-ray revealed a cardiomegaly with no abnormalities in both lungs. A new echocardiography was compared to the one done in 2019. The old one showed upper normal left ventricular (LV) size with intact function with an ejection fraction (EF) of 55%. The new one revealed deterioration of LV functions with dilated dimension, concentric LVH, dilated left atrium, regional wall motion abnormalities in the form of hypokinesia of the whole anterior wall, basal interventricular septum, basal inferior wall, basal posterior wall, grade I diastolic dysfunction, impaired systolic function, and an EF of 35%.

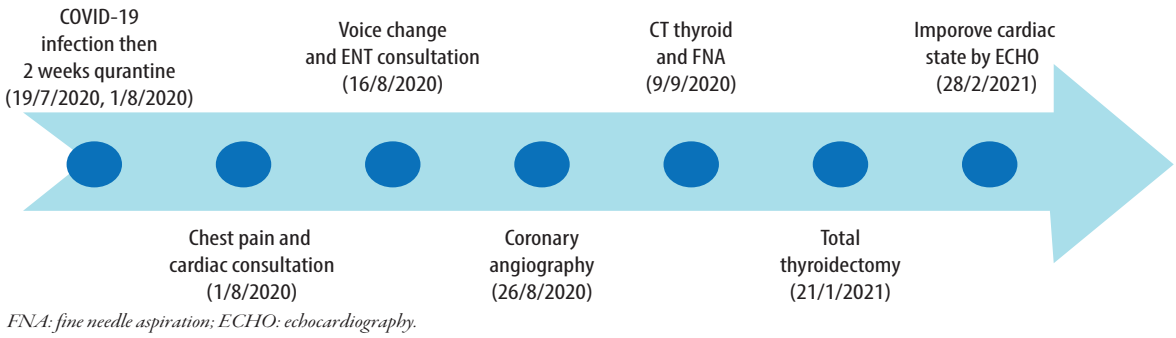
The cardiologists impression was a dilated cardiomyopathy with deterioration of LV functions which could be due to acute viral myocarditis or coronary artery disease. On 26 August 2020, he underwent coronary angiography which revealed normal coronary arteries.

The myocyte necrosis markers showed high troponin levels of 200 ng/L (normal range < 50 ng/L), and creatine kinase level of 223 U/L (normal range < 190 U/L). Myocarditis is a diagnosis by exclusion (clinical presentation, elevated level of markers of myocyte necrosis, and normal coronary arteries). So, the final diagnosis was acute viral myocarditis associated with COVID-19 infection.

One month later, his voice changed, so he was referred to the ENT clinic. A neck examination identified enlarged thyroid lobes and cervical lymph nodes. Neck ultrasound scan showed a bulky thyroid gland with heterogenous texture and defined hypoechoic nodules in the right and left lobes with multiple cervical lymph nodes calcifications. The neck computed tomography scan showed enlarged thyroid lobe and calcified cervical lymph nodes. Fine needle aspiration (FNA)/FNA cytology was taken from the right and left nodules and thyroid follicular cells with cytologic atypia were seen. Also, an initial FNA taken from level III left cervical lymph nodes was reported as nonspecific. However, the differential diagnosis includes parathyroid lesion versus thyroid gland follicular neoplasm. A parathyroid scan was done and was negative for parathyroid adenoma. Repeated FNA revealed thyroid gland follicular neoplasm. He denied the use of any alcohol, tobacco, or illicit drugs and denied any family history of cardiac disease. He had an interesting medical history. In 1993, when he was 11 years old, he was found to have osteosarcoma of the right tibia and he underwent right below-knee amputation. In 2000, when he was 18 years old, he developed osteosarcoma in his left femur and underwent left above-knee amputation and got chemotherapy. This was complicated by chronic kidney disease which progressed gradually into ESKD and started hemodialysis in early 2006. Later that year, he underwent a kidney transplant. His kidney function was suboptimal, and chronic kidney disease progressed again towards ESKD. He underwent a kidney graft nephrectomy in December 2010 after recurrent graft infection, and he was reinitiated on hemodialysis. Chronological progress and prognosis by date are shown in Figure 1.

DISCUSSION

We present an unusual yet complicated medical case in which the patient developed acute viral myocarditis



FNA: fine needle aspiration; ECHO: echocardiography.

Figure 1: Chronological progress and prognosis by date.

with COVID-19 infection on dialysis. He presented with shortness of breath and retrosternal chest pain with elevated levels of markers of myocyte necrosis including high levels of troponin and creatine kinase and normal coronary angiography.

Infection with viral pathogens such as influenza and parvovirus B19, has been widely described as the most common infectious cause of acute myocarditis. Viral infection has been extensively discussed as one of the most common infectious causes of myocarditis.[12] As with other coronaviruses, SARS-CoV-2 can elicit the release of multiple cytokines and chemokines that can lead to myocardial inflammation. Sala et al,[13] reported the first direct evidence of myocardial inflammation by endomyocardial biopsy in a COVID-19 patient. Endomyocardial biopsy revealed diffuse T-lymphocytic inflammatory infiltrates with significant interstitial edema and limited focal necrosis.

In patients with SARS-CoV-2 infection, the most important features that suggest myocardial injury are electrocardiogram changes and troponin elevation coupled with echocardiography showing signs of subclinical left ventricular diastolic impairment or even reduced EF. In severe cases, the patient had echo changes (dilated cardiomyopathy) and high troponin.[14]

For patients with a ventricular motion abnormality, elevated troponin, and no acute coronary syndrome, possible diagnoses include stress cardiomyopathy and clinically suspected myocarditis as prescribed in this case report.[15]

If myocarditis is suspected, an echocardiogram should be done because it is more accessible than other imaging modalities. Although cardiac magnetic resonance imaging would provide more information than an echocardiogram, its use is limited because of prolonged acquisition time, the need for breath-holding given that COVID-19 is highly contagious, and the requirement for deep cleaning after use.[16]

The patient had exertional breathlessness associated with retrosternal chest pain suggestive of pericarditis, evidence of myocardial injury (elevated troponin and deterioration of LV functions with dilated dimension, concentric LVH, dilated left atrium, regional wall motion abnormalities in the form of hypokinesia at presentation) and confirmed COVID-19 infection two weeks prior. The elevated level of troponin is known to occur in about 35% of myocarditis cases.[17] The myocardial biopsy was not done as "patients with unexplained new-onset cardiomyopathy and/or cardiogenic shock often have dilated ventricles with thin walls leading to a higher risk of perforation and dysrhythmias".[18]

Work-up of enlarged thyroid and cervical lymph nodes (one month post COVID-19 infection) revealed thyroid gland follicular neoplasm. He was referred for assessment, multiple lymphadenopathy with positron emission tomography/computed tomography scan, which revealed a few mildly sub centimeter bilateral level I/II cervical lymph nodes showing preserved fatty hilum, most likely reactive. A number of oncogenic (hepatitis B virus, hepatitis C virus, human papilloma virus, Epstein-Barr virus, and HIV) and oncolytic viruses (coxsackievirus, reovirus, vaccinia virus, and adenovirus) are known to cause and regress various cancer types. There are other viruses with unknown roles in cancer regression or growth, one of them is SARS-CoV-2. Conflicting results for the link between cancer subtypes and viral infections have been reported in clinical and pre-clinical studies.[19–21] For instance, a faster growth of melanoma was observed in mice challenged with lymphocytic choriomeningitis virus and PR8/

H1N1/influenza A, respectively, compared to the uninfected controls.[20,22] This was attributed to the shunting of anti-cancer cytotoxic $CD8^+$ T cells from the tumor site to the viral infection site.[20]

The patient underwent a total thyroidectomy on 21 January 2021 and maintained on thyroid replacement therapy. His echocardiography was repeated on 28 February 2021 and showed an improved left ventricular EF of 45%. The patient is presently on follow-up and is doing well.

CONCLUSION

Among the hemodialysis population, COVID-19 can induce an acute myocardial injury leading to acute myocarditis and could be associated with neoplasms, such as thyroid gland follicular neoplasm. Prompt diagnosis and management may improve the outcome of patients with such presentations.

Disclosure

The authors declared no conflicts of interest. Informed consent was obtained from the patient.

REFERENCES

1. Bennett J, Dolin R, Blaser MJ. Mandell, Douglas, and Bennett's principles and practice of infectious diseases. 9th ed. Elsevier; 2019. p. 1151-1164.
2. Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72314 cases from the Chinese center for disease control and prevention. JAMA 2020 Apr;323(13):1239-1242.
3. Valeri AM, Robbins-Juarez SY, Stevens JS, Ahn W, Rao MK, Radhakrishnan J, et al. Presentation and outcomes of patients with ESKD and COVID-19. J Am Soc Nephrol 2020 Jul;31(7):1409-1415.
4. Wu C, Chen X, Cai Y, Xia J, Zhou X, Xu S, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med 2020 Jul;180(7):934-943.
5. Kliger AS, Silberzweig J. Mitigating risk of COVID-19 in dialysis facilities. Clin J Am Soc Nephrol 2020 May;15(5):707-709.
6. Guan WJ, Liang WH, Zhao Y, Liang HR, Chen ZS, Li YM, et al; China Medical Treatment Expert Group for COVID-19. Comorbidity and its impact on 1590 patients with COVID-19 in China: a nationwide analysis. Eur Respir J 2020 May;55(5):2000547.
7. Hanna TP, Evans GA, Booth CM. Cancer, COVID-19 and the precautionary principle: prioritizing treatment during a global pandemic. Nat Rev Clin Oncol 2020 May;17(5):268-270.
8. Hotchkiss RS, Moldawer LL. Parallels between cancer and infectious disease. N Engl J Med 2014 Jul;371(4):380-383.
9. Alqahtani FY, Aleanizy FS, Ali El Hadi Mohamed R, Alanazi MS, Mohamed N, Alrasheed MM, et al. Prevalence of comorbidities in cases of Middle East respiratory syndrome coronavirus: a retrospective study. Epidemiol Infect 2018 Nov;147:e35.
10. Martínez A, Soldevila N, Romero-Tamarit A, Torner N, Godoy P, Rius C, et al; Surveillance of Hospitalized Cases of Severe Influenza in Catalonia Working Group. Risk factors associated with severe outcomes in adult hospitalized patients according to influenza type and subtype. PLoS One 2019 Jan;14(1):e0210353.
11. Mauskopf J, Klesse M, Lee S, Herrera-Taracena G. The burden of influenza complications in different high-risk groups: a targeted literature review. J Med Econ 2013;16(2):264-277.
12. Fung G, Luo H, Qiu Y, Yang D, McManus B. Myocarditis. Circ Res 2016 Feb;118(3):496-514.
13. 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 May;41(19):1861-1862.
14. 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 Mar;323(11):1061-1069.
15. 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 Jul;5(7):802-810.
16. Siripanthong B, Nazarian S, Muser D, Deo R, Santangeli P, Khanji MY, et al. Recognizing COVID-19-related myocarditis: the possible pathophysiology and proposed guideline for diagnosis and management. Heart Rhythm 2020 Sep;17(9):1463-1471.
17. Smith SC, Ladenson JH, Mason JW, Jaffe AS. Elevations of cardiac troponin I associated with myocarditis. Experimental and clinical correlates. Circulation 1997 Jan;95(1):163-168.
18. Aghdassi A, Gupta A. Endomyocardial biopsy: examining indications and trends in use - more native heart biopsies to come? Cardiology 2019;142(2):102-104.
19. Cooksley CD, Avritscher EB, Bekele BN, Rolston KV, Geraci JM, Elting LS. Epidemiology and outcomes of serious influenza-related infections in the cancer population. Cancer 2005 Aug;104(3):618-628.
20. Kohlhapp FJ, Huelsmann EJ, Lacek AT, Schenkel JM, Lusciks J, Broucek JR, et al. Non-oncogenic acute viral infections disrupt anti-cancer responses and lead to accelerated cancer-specific host death. Cell Rep 2016 Oct;17(4):957-965.
21. Newman JH, Zloza A. Infection: a cause of and cure for cancer. Curr Pharmacol Rep 2017;3(6):315-320.
22. Kohler M, Rüttner B, Cooper S, Hengartner H, Zinkernagel RM. Enhanced tumor susceptibility of immunocompetent mice infected with lymphocytic choriomeningitis virus. Cancer Immunol Immunother 1990;32(2):117-124.