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

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Received: 14 April 2021
Accepted: 12 November 2022
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DOI 10.5001/omj.2023.75

Abstract

Since the first cases were reported in Wuhan, China, Coronavirus Disease 2019 (COVID-19) has spread swiftly around the world and is caused by severe acute respiratory syndrome coronavirus 2 (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, the 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. A number of oncogenic (HBV, HCV, HPV, EBV, HIV) and oncolytic viruses (Coxsackie Virus, Reovirus, Vaccinia Virus, 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.

Keywords: Coronavirus Disease 2019 (COVID-19); SARS-CoV-2; Cardiac Injury; Viral Myocarditis; Echocardiogram; Thyroid Gland Follicular Neoplasm; Hemodialysis.

Introduction

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 ICU admission, respectively [2].

• COVID-19 mortality rates vary between various countries with genetic factors and climates differences between countries had been 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 special 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 versus 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 trice weekly (4).

A recent study including 1590 COVID-19 positive patients in China showed cancer as one of the more serious comorbidities that increase risk with respect to COVID-19 (6, 7). Human leukocyte antigens (HLA) 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 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 outcome (6, 9, 10, 11).

Case Report

A 38-year-old Omani male with known case of hypertension and ESKD on a regular trice weekly hemodialysis session since January 2011.

He was diagnosed with COVID on the 19th of July 2020 after he presented with fever and diarrhea. He presented with mild to moderate infection, so he was not admitted to hospital, but he was remained at home. He was quarantined for two weeks and attended the medical center trice weekly for dialysis in an isolated room at our dialysis center. 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 artificial limbs were done so functional capacity could not be full assessed by the attending clinician. His electrocardiogram showed a normal sinus rhythm with left ventricular hypertrophy by voltage criteria.

His chest x-ray revealed a cardiomegaly with no abnormalities in both lungs. A new echocardiography, compared to an old 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 left ventricular (LV) functions with dilated dimension, concentric left ventricular hypertrophy (LVH), dilated left atrium (LA), RWMA in the form of hypokinesia of the whole anterior wall, basal IVS, basal inferior wall, basal posterior wall, grade I diastolic dysfunction, impaired systolic function, and an EF of 35%.

The cardiologist impression was a Dilated Cardiomyopathy (DCM) with deterioration of left ventricular (LV) functions which could be due to Acute Viral Myocarditis or Coronary Artery Disease (CAD). On the 26th of August 2020, he underwent coronary angiography (CAG) which revealed normal coronary arteries.

The myocyte necrosis markers showed a high troponin level of 200 ng/L (normal range <50 ng/L), and creatine kinase level of 223 U/L (N:<190 u/l)). The 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 was changed, so he was referred to ENT clinic. By examination of the neck, enlarged thyroid lobes and cervical lymph nodes were identified. Neck ultrasound scan showed bulky thyroid gland with heterogenous texture fairly defined hypoechoic nodules in right and left lobes with multiple cervical lymph nodes calcifications. The neck CT scan showed enlarged thyroid lobe and calcified cervical lymph nodes. FNA/FNAC (Fine Needle Aspiration/FNA Cytology) was taken from right and left nodule reported as: thyroid follicular cells with cytologic atypia are seen. Also, an initial FNA taken from level III left cervical lymph nodes reported as nonspecific. However, the differential diagnosis includes parathyroid lesion versus thyroid gland follicular neoplasm. Parathyroid scan was done and was negative for parathyroid adenoma. Repeated FNA revealed thyroid gland follicular neoplasm. He denied any alcohol use, tobacco use, or illicit drug use and denied any family history of cardiac disease. He had an interesting past medical history. It started in 1993, when he was 11 years old age, and he was found to have an osteosarcoma of the right tibia and he underwent right below knee amputation. Then, in 2000- when he was 18 y old age- he developed the osteosarcoma in his left femur and underwent left above knee amputation and got chemotherapy.
This was complicated by chronic kidney disease (CKD) that progressed gradually into ESKD and started hemodialysis in the early of 2006. Later that year, he underwent a kidney transplant. His kidney function was suboptimal, and CKD progressed again towards ESKD. He underwent kidney graft nephrectomy in December 2010 after recurrent graft infection, and he was reinitiated on hemodialysis since then.

**Time line showed the chronological progress and prognosis by dates.**

<table>
<thead>
<tr>
<th>Event</th>
<th>Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>COVID-19 infection</td>
<td>2 weeks before 2019/7/2</td>
</tr>
<tr>
<td>Voice change and ENT consultation</td>
<td>16/8/2020</td>
</tr>
<tr>
<td>CT thyroid and FNA(9/9/2020)</td>
<td></td>
</tr>
<tr>
<td>Improved cardiac state by ECHO in (28/2/2021)</td>
<td></td>
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<tr>
<td>Chest pain and cardiac consultation</td>
<td>1/8/2020</td>
</tr>
<tr>
<td>Coronary angiography</td>
<td>26/8/2020</td>
</tr>
<tr>
<td>Total thymectomy</td>
<td>21/1/2021</td>
</tr>
</tbody>
</table>

**Discussion**

We presented an unusual yet complicated medical case where he developed acute viral myocarditis in patient 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 level of troponin and creatine kinase and normal coronary angiography.

Infection with viral pathogens, such as influenza and parvovirus B-19, has been widely described as the most common infectious cause of acute myocarditis. So, viral infection has been widely described 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. reported the first direct evidence of myocardial inflammation by endomyocardial biopsy (EMB) in a COVID-19 patient. EMB revealed diffuse T-lymphocytic inflammatory infiltrates with significant interstitial edema and limited focal necrosis (13).

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 ejection fraction (EF). In severe cases, the patient had echo changes (DCM) and high troponin (14).

For patients with a ventricular motion abnormality, elevated troponin, and with 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 would provide more information than an echocardiogram, its use is
limited because of prolonged acquisition time, the need for breath-holding and 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 LA, RWMAs in the form of hypokinesia at presentation) and confirmed COVID-19 infection two weeks back. 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 infection) revealed thyroid gland follicular neoplasm. This neoplasm associated with COVID as last year (2019) he was referred for assessment multiple lymphadenopathy with Positrone Emission Tomography + Computer Tomography (PET/CT) 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 (HBV, HCV, HPV, EBV, HIV) and oncolytic viruses (Coxsackievirus, reovirus, vaccinia virus, 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, 20, 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 tumor site to the viral infection site (20).

Prognosis: The patient underwent total thyroidectomy on the 21st of Jan 2021 and he was maintained on thyroid replacement therapy. Also, his echocardiography was repeated on the 28th Feb-2021 that showed an improved left ventricular EF of 45%. The patient presently on follow up and he is doing quite well.

Conclusion

Among 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.

References


