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Acute type a aortic dissection in a hemodialysis patient in the early period after COVID-19 infection

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Abstract

The novel coronavirus spread all over the world in 2019 and became a serious international health concern of this century. Coronavirus disease 2019 (COVID-19) had a wide range of clinical manifestations; mostly affecting the respiratory system, but cardiovascular involvement has also been reported, including acute coronary syndromes, thromboembolic events and one of the deadly complication named aortic dissection. Among other cardiovascular complications of COVID-19, aortic dissection has been a significant yet underrated problem. Herein, we report a type a aortic dissection in a hemodialysis patient in the early period after COVID-19 infection.

KEYWORDS: post covid; hemodialysis; aorta

Introduction

Type A acute aortic dissection (AAD) is a serious clinical condition that requires urgent surgical intervention as it is associated with high mortality and morbidity. Aortic dissection is the blood passage into the aortic media as a result of the rupture in intimal layer of the aortic wall [1]. Consequently, separation of the intimal layer from the outer layers occurs, and hence a false lumen appears. The ascending aorta is reported to be the most common site of aortic dissection, as 65% of the dissections originate in this region [2].

Numerous major risk factors contribute to increased risk of aortic dissection, including hypertension and smoking, genetic factors, vasculitis. Numerous articles mentioned COVID-19 infection as a strong inflammatory syndrome [3]. Moreover, there are multiple cases of COVID-19 patients with hyper-inflammation who have had cardiac manifestations [4].

There are several similarities between molecular pathways and markers of aortic dissection and COVID-19. For instance, the level of Von Willebrand Factor (VWF) Increases in COVID-19 patients, which is indicative of extensive endothelial cell activation [5]. The major factors include Transforming growth factor beta (TGF-β), total plasma homocysteine Y (tHCy), and Matrix metalloproteinases (MMPs) [6,7,8,9].

Some studies suggested that COVID-19 infection down-regulates angiotensin-converting enzyme 2 and activates renin–angiotensin–aldosterone system, causing the hypertensive state which may lead further towards aortic dissection. Aortic dissection remains the deadliest manifestation of acute aortic syndromes with mortality as high as 1% per hour for acute type A aortic dissections [6]. The presentation can vary, and the classical symptoms may be absent or inconsistent [10]. This can paint a diagnostic dilemma for the clinician.

Results

A 50-year-old male with Lupus Nephritis and CKD stage 5 presented to the emergency room with the chief complaint of sudden onset of substernal chest pain radiating to his back. He denied any recent trauma. The patient had a history of hospitalization for ten days in the ICU due to COVID-19 infection with severe lung

involvement, with his polymerase chain reaction (PCR) being positive. The patient had been discharged at 17 days. Additionally, he had received steroid treatment due to ongoing respiratory symptoms (dexamethasone 6mg). 2 days after his hospital leave, he had sudden onset of chest pain firstly radiating to his back, and then to his epigastrium. Chest pain has quite been relieved. Physical exam was significant for reproducible midepigastric pain, without guarding or rebound. The patient had a mild leukocytosis, elevated amylase. His ECG showed normal sinus rhythm with a rate of 80 beats/minute. Abdominal US was negative for cholelithiasis. He was treated with pain killers, plasmolytic drugs and bowel rest for presumed acute pancreatitis diagnosed clinically because of elevated amylase and epigastric pain. An abdominal CT scan to assess the severity of pancreatitis was not indicated to be performed as the patient's clinical symptoms were stable. Throughout his admission, his pain never fully resolved. On day 5, he decided to leave the hospital. Next day, he referred cardiologist in another clinic. He was evaluated with transthoracic echocardiography and chest CT angiography tests. His ECG showed normal sinus rhythm with a rate of 69 beats/minute. T/A-167/86mmHg, RR-23' paO2-95%. Chest CT angiography revealed a dissection line starting from the ascending aorta and progressing to the infrarenal segment of abdominal aorta, a diagnosis of Stanford type A aortic dissection was made. On transthoracic echocardiography, left ventricular hypertrophy, the ejection fraction was 45%, and a dissection flap in the ascending aorta was observed. Pathological finding was observed in the heart valves: moderate mitral valve regurgitation 2+/4+; moderate tricuspid valve regurgitation 2+/4+; aortic stenosis (AV PG mean 15mmHG). IVC 2.0<50%; PAP 48 mmHg. Preoperative blood parameters were as follows: lactate dehydrogenase: 2.7 mmol/L; aspartate aminotransferase: 17; alanine aminotransferase: 17; gamma-glutamyl transferase: 128 U/L; troponin I – 39.3; urea: 78.2 mg/dL; creatinine: 590.1 μmol/L; white blood cells: 10.46 10^9/L; neutrophils: 88.2 %; lymphocytes: 5.6 %; hematocrit: 29.3%; platelets: 101 10^9/L; erythrocytes: 2.97 10^12/L; Hb: 9.1 g/dl; erythrocyte sedimentation rate: 40 mm/h; C reactive protein: 58.0 mg/l. Aortic valve replacement combined with replacement of the ascending aorta and the underside of the aortic arch with a Dacron graft was made. Also Aortocoronary venous bypass was held and during the operation there weren't complications. Separation from cardiopulmonary bypass after cardiac surgery was challenging, on TEE right ventricular akinesis was revealed and inotropic/vasopressor support was started. Sol. Noradrenaline – 0,46mcg/kg/min, sol. Adrenaline-0.48mcg/kg/min. sol. Dobutamine-20-27mcg/kg/min. Patient was nonstable and passed away 24 h after the operation.

Discussion

Aortic dissection is a form of acute aortic syndrome that is more prevalent in men (2:1) and has a peak incidence in the sixth and seventh decades of life. It is known that the incidence of aortic dissection increases in cold seasons and places with lower climate temperature. Some studies have demonstrated increase in the incidence of aortic dissection, along with other cardiovascular manifestations such as myocardial infarction and aortic aneurysms in the first wave of COVID-19 [16].

The COVID-19 is known to cause increased risk of several cardiovascular complications; including acute myocardial injury, arrhythmias, cardiogenic shock, acute coronary syndrome, and venous thromboembolism. Among the cardiac complications, aortic dissection is an important yet underrated problem in COVID-19 patients. Even though few articles indicate that the rate of aortic dissection has been increased during the course of pandemic, no comprehensive studies have been conducted about the molecular basis and coincidence rate of COVID-19 and aortic dissection [18].

Numerous major risk factors contribute to increased risk of aortic dissection, including hypertension and smoking, and genetic factors such as Marfan Syndrome (MFS) and Ehlers Danlos. Vasculitis is also a notable factor that increases the risk of aortic dissection, as in Takayasu arteritis, Behcet's disease, and syphilis infection. Interestingly, numerous articles mentioned COVID-19 infection as a strong inflammatory syndrome [3]. Moreover, there are multiple cases of COVID-19 patients with hyper-inflammation who have had cardiac manifestations such as coronary microvascular dysfunction and peripheral artery thrombosis [11].

Among the risk factors, hypertension is one of the most prevalent causes of increased risk of aortic dissection. Some studies suggested that COVID-19 infection down-regulates angiotensin-converting enzyme 2 and activates renin–angiotensin–aldosterone system, causing the hypertensive state which may lead further towards aortic dissection. These findings, along with other molecular findings discussed earlier, intensify the role of COVID-19 in predisposing patients to aortic dissection.

There are several similarities between molecular pathways and markers of aortic dissection and COVID-19. For instance, the level of Von Willebrand Factor (VWF) Increases in COVID-19 patients, which is indicative of extensive endothelial cell activation [5]. Multiple molecular factors are known to be correlated in MFS and aortic dissection that are also elevated in COVID-19 patients. The major factors include Transforming growth factor beta (TGF-β), total plasma homocysteine Y (tHCy), and Matrix metalloproteinases (MMPs) [7, 8, 9].

Several reports illustrated that excessive activation of TGF-β in MFS patients is correlated with aortic root dilation and predisposition to aortic dissection [8]. Ghazavi et al. indicated that in a study of 63 COVID-19 patients and their matched controls, the level of TGF-β increased in COVID-19 patients. Furthermore, TGF-β in this study was significantly higher in patients with severe form of COVID-19 compared to the patients with mild form. With these findings, one may assume that the COVID-19 can possibly increase the probability of aortic root dilation and henceforth aortic dissection. It is worthy to mention that in MFS patients, treatment with β-blockers decreases the TGF-β levels.

According to the literature, the tHCy is described as a marker of the level of aortic atherosclerosis. Moreover, in a study of one hundred and seven patients, Giusti et al. concluded that higher levels of tHCy in MFS patients is correlated with the incidence rate of aortic dissection and other cardiovascular complications [8, 11]. In case of COVID-19, it has been shown that tHCy can be used as a predictive value for the severity of the disease, as the higher levels of tHCy corresponds to more severe pneumonia in imaging evaluations.

One of the major similarities between MFS patients with aortic dissection and COVID-19 patients, is the imbalance between MMP and Tissue inhibitor of metalloproteinase (TIMP).

Prior studies have demonstrated that macrophage infiltration in the media layer of aorta may result in excessive production of MMPs, specifically MMP-1, MMP-9 and MMP-12. As a result, collagen and elastin degeneration leads to aortic aneurysms and aortic dissections [12]. One of the molecular characteristics of MFS is known to be increased expression of MMPs that ensues an imbalance between MMP and TIMP levels [8]. Speaking of MMPs in COVID-19, several studies have reported an increase in MMPs expression. Shi et al. studied sixty-two cases of COVID-19 and their matched controls, and reported a significant rise in serum MMP3 levels in COVID-19. As mentioned in the article, MMP3 activates other MMPs, including MMP9 [13]. Additionally, Neutrophils response to viral infection is followed by MMP9 release from neutrophil granules [14].

Considering macrophage molecular pathway activation in COVID-19 patients, there are several other markers that are increased; including Ferritin, IL-15, IL-1β, IL-18. There has been a significant difference in Ferritin and IL-15 levels in COVID-19 patients with critically ill situations compared to other patients and healthy individuals [15]. These findings imply that there are several major pathway similarities between aortic dissection and the inflammation caused by COVID-19 infection.

Inflammation plays an important role in the development of aortic dissection, as found in many patients. Although dissection may occur due to collagen tissue diseases, it is often caused by the rupture of an atherosclerotic plaque as the blood passes

through the intima-media layers and progresses distally. Serum proinflammatory cytokines are elevated in coronavirus cases, resulting in lung damage and an increase in microthrombotic events. Furthermore, neutrophil infiltration has been demonstrated in lung tissues in COVID-19 cases during autopsies [17].

There is a concern about the relationship between a viral infection and aortic dissection. Recently an increased admission for aortic dissection and higher in hospital mortality of urgent aortic dissection surgery during the influenza season compared with noninfluenza season were noticed. It has been detected that the number of patients with acute aortic dissection were increased in winter months, regardless of climate. Inflammatory, immune-mediated injury, increased sympathetic activity or medication uses are some of the reasons that may contribute to aortic dissection [16].

In previous coronavirus pandemics, accelerated rate of cardiovascular complication occurred; therefore the association of the new coronavirus with cardiovascular complications such as aortic dissection should be suspected. Although the rapid mortality rate, low incidence and limitation of detecting cases in aortic dissection, may cause difficulty in confirming this association [16].

However, our case was a known COVID-19 patient that was hospitalized, and soon after the COVID-19 infection, the case was complicated by aortic dissection. Presentation of this case was challenging, because symptoms were very similar to pancreatitis. The presentation of acute pancreatitis in the setting of aortic dissection poses a diagnostic challenge, as some of the cardinal symptoms of aortic dissection, such as hypertension and pain, overlap with acute pancreatitis. Acute pancreatitis is a clinical diagnosis, but without an easily identifiable cause, such as gallstones, alcohol abuse, or hypertriglyceridemia, further imaging may be warranted if the patient does not clinically improve. Due to its lethal complications, physicians should be aware and should have a high index of suspicion for aortic dissection when evaluating a patient with presumed acute pancreatitis.

Acute pancreatitis presenting as acute aortic dissection is a rare entity with less than ten well-documented cases reported so far. It is hypothesized that the pancreas can be susceptible to hypoperfusion as seen in cardiopulmonary bypass surgery [3]. We present a case misdiagnosed as only acute pancreatitis based on clinical symptoms and later correctly diagnosed as an aortic dissection when symptoms did not improve.

We do not know whether COVID-19 was a trigger for the aortic dissection or if it was a coincidental finding.

Conclussion

The ongoing COVID-19 epidemic represents a healthcare crisis in the world. Hence, it is currently not possible to fully predict the problems that may be caused by COVID-19. Aortic dissection may be a relatively rare but important complication in COVID-19 patients. In our case, we think that the inflammatory process caused by COVID-19 may have been a triggering factor for the development of an aortic dissection. Further studies are required to obtain confirmation regarding this hypothesis.

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