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Case Report: Effects of Sars-CoV-2 on Marfan syndrome with resulting acute aortic dissection

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Marfan syndrome is one of the most common inherited connective tissue disorders that affects the heart, eyes, blood vessels, and bones. It occurs in approximately 1-2 per 10,000 individuals annually. Many patients with Marfan syndrome eventually develop aortic wall abnormalities, often resulting in aortic dilatation, which increases the risk of acute aortic dissection. Recent studies involving SARS-CoV-2 propose that individuals with connective tissue disorders such as Marfan syndrome can have additional associated conditions that could impose a higher risk for morbidity and mortality from SARS-CoV-2. The purpose of this article is to discuss the interrelationship between Marfan Syndrome, Acute Type A Aortic Dissection in a patient with Sars-CoV-2 infection. Pertinent review of these conditions, diagnostic findings, treatment, and the patient's clinical course will be discussed. There is minimal research focused on the connection between this novel virus, Marfan Syndrome, and compounding risk for aortic dissection.

Background

This case report will describe the interrelationship between Marfan Syndrome, Acute Type A Aortic Dissection in a patient with Sars-CoV-2 infection. Pertinent review of these conditions, diagnostic findings, treatment, and the patient's clinical course will be discussed.

Marfan Syndrome

Marfan Syndrome (MFS) affects 1-2 per 10,000 individuals with approximately 200,000 individuals in the United States.[3] Males and females experience similar rates of MFS, however males experience death and aortic pathology earlier in life. Understanding of MFS has dramatically improved over the last 20 years with the identification of the FBN1 gene. The FBN1 gene encodes for the large extracellular matrix glycoprotein fibrillin-1 which provides elasticity and structural support for connective tissues.[4,5] Anomalies in the FBN1 gene vary and this accounts for the phenotypic expression of individual patient symptoms and disease presentation.

Diagnosis of MFS relies on the presence of two cardinal features: aortic root aneurysm and extopia lentis. In the absence of family history of MFS the presence of both cardinal features is sufficient for an unequivocable diagnosis. In the absence of the two cardinal features the Ghent Nosology should be utilized for diagnosis. The Ghent Nosology is the defined clinical criteria that was established in 2010 to improve accurate and timely diagnosis of MFS. Identification of the FBN1, family history, and a systemic score calculation is required for diagnosis. A systemic score of ≥ 7 is consistent with a diagnosis of MFS. The systemic score assigns point values for the following: wrist and/or thumb sign, anterior chest wall deformity, hindfoot deformity, history of pneumothorax, dural ectasia, protrusion acetabulae, reduced upper segment/lower segment ratio (US/LS) and increased armspam/height ratio, scoliosis or thoracolumbar kyphosis, reduced elbow extension, distinctive facial features, skin striae, myopia, and mitral valve prolapse.

Improved diagnostic criteria, genetic testing for the FBNI1 gene, and surgical advances has accounted for a dramatic increase in the life expectancy of patients with MFS. In 1972 the mean age of death for patients with MFS was 32 years for both males and females and the current life expectancy is approaching age 70.[4] Increasing life expectancy now places the impetus for further exploration on how MFS impacts acute and chronic health conditions and quality of life.

Aortic dissection

Aortic dissection is a life-threatening condition with an overall in-hospital mortality rate of 27.4%.[8] Aortic root aneurysm significantly increases the risk of acute aortic dissection and is the lead-

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ing cause of morbidity and mortality for patients with MFS. Acute aortic dissection (AAD) is a disruption in the integrity in the intima of the aorta. This disruption of the vasculature can result in rupture or a dramatically increased aortic diameter. This damage coupled with the elastic and structural impairment experienced by patients with MFS compounds their risk of experiencing AAD as well as subsequent or recurrent dissection. Aortic dissections are categorized by the location of the aorta affected using the Stanford criteria. Stanford Type A affects the ascending and descending aorta and Stanford Type B affects the descending aorta.

Patients with MFS present with Stanford Type A dissections at a rate of 63.6% of cases and Type B dissections occur at a rate of 36.4% of cases. There is a significant correlation with increase of AAD in patients with MFS of all ages and an even greater correlation of AAD in patients less than 40 years of age.[3]

Sars-CoV-2

Sars-CoV-2 is a viral illness that is highly contagious and is associated with upper and lower respiratory manifestations. Sars-CoV-2 contagion has proven to be variable as the virus experiences epigenetic drift and shift. Sars-CoV-2 is responsible for over 5.4 million deaths worldwide and has dramatically impacted the healthcare landscape.[7] Much like other viral respiratory illnesses such as influenza, Sars-CoV-2 infection pathogenesis is related to the development of oxidative stress in combination with an excessive immune/inflammatory reaction amplifying cytokine storm.[1,6] The cytokine storm consequently leads to tissue/organ hypoxia, endothelial (vascular wall) damage, and hypercoagulation thus leading to venous thromboembolism and an increased risk of Acute Type A Aortic Dissection.[2]

Patient Presentation

A 49-year-old Caucasian female called her primary care clinic after members attending the same church service came down with confirmed Sars-CoV-2 infection despite social distancing and mask wearing. The patient reported symptoms of headache, but denied cough, shortness of breath, and lack of taste/smell. Sars-CoV-2 testing was ordered and detailed instructions of when/how to obtain emergency care were given however, the patient did not obtain testing.

Two days later the patient experienced cold like symptoms; sinus congestion, mild cough, and fever. Six days after onset of symptoms the patient reported to the emergency department with worsening shortness of breath, headache, fatigue, fever, and mental status changes.

Past medical history

Marfan Syndrome, hypertension, paroxysmal atrial fibrillation, heart failure, systolic dysfunction with defibrillator insertion and EF 35%, and severe mitral and aortic insufficiency with root repair delayed due to pandemic but anticipated in the near future.

Past surgical history

Type A&B dissection repair, atrial cardioversion, phacoemulsification of lens and insertion of intraocular lens.

Table 1
Diagnosis of MFS based on the 2010 revised Ghent Nosology.

Family history of MFS	No family history of MFS
Presence of any of the following: • Aortic root dilation • Ectopia lentis • Systemic score ≥7	Aortic root dilation or dissection **AND** any of the following: • Ectopia lentis • FBN1 pathogenic variant • Systemic score ≥7

Medications

Apixaban, bumetanide, carvedilol, losartan, rosuvastatin, and spironolactone.

Physical exam was essentially unremarkable except for presence of atrial fibrillation and faint bilateral rales. The diagnostic workup in the emergency department revealed community acquired pneumonia (CAP), hypoxia, acute kidney injury with stage III chronic kidney disease, elevated troponin, and hyponatremia.

The CAP was treated with cefepime 2g IV every 8 hours, solumedrol 80mg IV every 8 hours. Gentle hydration was ordered for the acute kidney injury and hypoxia required BiPap per respiratory service. Elevated troponin with no symptoms of chest pain or EKG changes was thought to be troponin leak due to hypotension and hypoxia. Hyponatremia was corrected in the Emergency Department. Sars-CoV-2 PCR was subsequently obtained. Day two of hospital admission revealed positive Sars-CoV-2 PCR, cefepime and solumedrol were stopped and remdesevir 200mg IV x 1 dose followed by 100mg IV daily and dexamethasone 6mg IV every 24 hours were initiated. Patient's respiratory status continued to decline, patient was mechanically ventilated, placed in prone position, and transferred to a tertiary care center.

The patient continued to decline on day 3 of her hospital stay. Chest x-ray demonstrated worsening pneumonia. Echocardiogram was performed and was consistent with previous findings. Hospital course day 4, mechanical ventilation continued and sepsis protocols were initiated. Significant clinical decline ensued with hemodynamic instability, ST segment depression and T wave changes on EKG, thus stat CT scan was ordered. CT results demonstrated Acute Type A Aortic Dissection distal to previous repair. Due to patient's worsening respiratory status, hemodynamic instability, and complex comorbidities the patient was not deemed a surgical candidate. As a result husband withdrew care, and patient expired.

Discussion

This patient referenced in this case report had several variables that could have impacted her outcome. Delayed aortic root repair may have increased her likelihood of aortic dissection. The patient's fear of being exposed to Sars-CoV-2 delayed recommended testing, which subsequently postponed prompt diagnosis and the use of evidenced based medical therapy. The pathophysiologic sequelae of Sars-CoV-2 in this patient with MFS may have increased her risk of morbidity and mortality (Tables 1–3).

Table 2
Vital signs & measurements.

T: 36.2 C° (Temporal Artery)	HR: 61 (Monitored)	RR: 16	BP: 84/41 (NIBP)	Sp02: 95%	HT: 177.88 cm	WT: 75.3 kg

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Table 3
Emergency department laboratory results.

Lab	Results and Normal Values
BUN	52 mg/dL (7mg/dL-18mg/dL)
Creatinine	1.9 mg/dL (0.55mg/dL-1.02 mg/dL)
eGFR	27 (>60)
Glucose	161mg /dL (75mg/dL-115 mg/dL)
Sodium	132 mEq/L (136 mEq/L-145 mEq/L)
Procalcitonin	2.10 ng/mL (<0.1ng/mL)
Lactic Acid	1.8 mmol/L (0.5mmol/L-2mmol/L)
LDH	464 unit/L (90 unit/L-246 unit/L)
C-Reactive Protein	3.0 (0mg/dL-1mg/dL)
D-Dimer	3434 ng/mL (<0.5ng/dL)
ABG	pH 7.493; pO^2 192.3; pCo^2 24.0, O^2 Sat 99.8; O^2 flow rate 4.0L, HCO^3 18.4
Troponin	0.046 (0ng/mL-0.03 ng/mL)
CKMD	<0.2 (0.5ng/mL-3.6 ng/mL)
Hemoglobin	10.9 gm/dL (12gm/dL-15gm/dL)
Hematocrit	33.3% (35.3%-43.6%)
Urinalysis	No evidence of infection
Chest X-Ray	Impression: Chronic pulmonary vascular congestion; hazy ground glass opacities in the lower lungs likely atelectasis, low grade edema; hazy basilar opacities could indicate inflammation

Conclusion

MFS patients have known increased risk for aortic dissection and viral syndromes such as influenza have been shown to increase this risk. Sars-CoV-2 is associated with respiratory illness, cytokine storm, oxidative stress, and venous thromboembolism, which could subsequently confer increased risk of Acute Type A Aortic Dissection in patients with MFS. Additionally, delayed care, fear to access healthcare resources, and overwhelmed healthcare systems have impacted the health of patients, specifically those with complex health needs. Investigating this potential relationship is essential to protect this vulnerable population in an ever-changing pandemic. Further understanding of this potential relationship will serve to support patients in making informed healthcare decisions.

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