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Fatal Eosinophilic Myocarditis in a Healthy 17-Year-Old Male with Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2c)

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ABSTRACT

Background: Cardiac damage is frequently referred to in patients with SARS-CoV-2, is usually diagnosed by enzyme elevations, and is generally thought to be due to underlying coronary artery disease. There are references to cardiomyopathies accompanying coronavirus, but there has been no histologic confirmation.

Case report: A previously healthy 17 year male old presented in full cardiac arrest to the emergency department after a 2 day history of headache, dizziness, nausea and vomiting. Autopsy demonstrated an enlarged flabby heart with eosinophilic myocarditis. There was no interstitial pneumonia or diffuse alveolar damage. Postmortem nasopharyngeal swabs detected severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) known to cause coronavirus disease 2019 (COVID-19). No other cause for the eosinophilic myocarditis was elucidated.

Conclusion: Like other viruses, SARS-CoV-2 may be associated with fulminant myocarditis.

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COVID 19; coronavirus disease 2019; severe respiratory syndrome coronavirus 2; SARS-CoV-2; eosinophilic myocarditis

Introduction

Myocardial damage, myocarditis, and cardiomyopathy is often referred to in patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1–6]. The etiology is often attributed to underlying cardiac disease in adults and is often defined by elevation of cardiac enzymes rather than histologically, frequently as an anecdotal report [7]. Minimal gross [8] or histologic descriptions [9, 10] exist. There is little information regarding cardiac complications in children [11–13]

We present a previously healthy 17 year male old dying suddenly with an eosinophilic myocarditis (EM) in which a nasopharyngeal swab detected SARS-CoV-2 at autopsy (Figs. 1 and 2).

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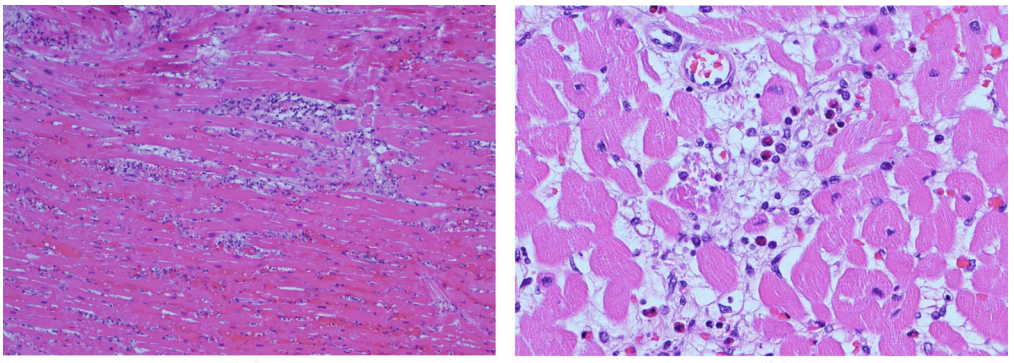

Figure 1. A. Myocardium with a mixed interstitial inflammatory infiltrate with focal areas of rarefaction. B. Higher power highlighting the eosinophilic infiltrate and the disruption of myocytes (A: Hematoxylin and eosin, 100×, B: Hematoxylin and eosin, 400×).

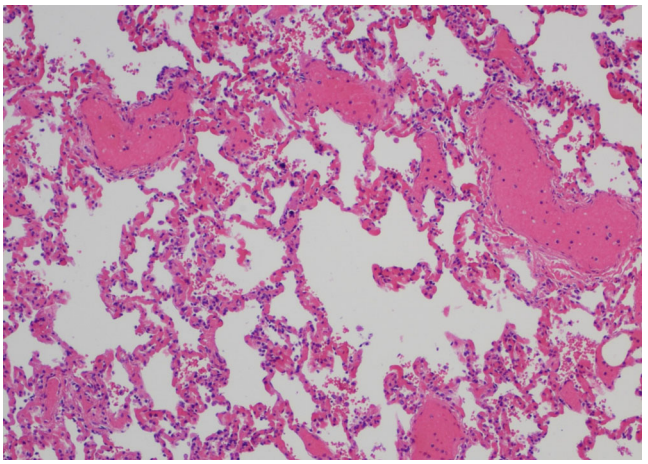

Figure 2. Lung with congestion but no interstitial infiltrate, increased hemosiderin laden macrophages, vasculitis, or eosinophilic infiltrate (Hematoxylin and eosin, 100×).

Case report

In March of 2020 during the SARS-CoV-2 pandemic, this 17 year old healthy African American male was residing with a relative because his mother was a healthcare worker with exposure to patients with coronavirus disease 2019 (COVID-19). In the weeks prior, he pursued his normal activity, including participation in the school's football practice. He developed severe headaches, dizziness, nausea and vomiting, and collapsed 2 days after the beginning of these symptoms. There was no documented fever, shortness of breath, or cough. Emergency Medical Services found him pulseless, and resuscitation attempts at the hospital were unsuccessful. In November 2019, he was seen in the emergency room with a dry cough and flu-like symptoms, with no fever, and the influenza A and B PCR tests along with a throat culture were all negative. No complete blood count was performed at that time or during the present illness.

Autopsy findings

The heart was 500 grams (expected for age- 262-295 grams), was soft and rubbery, and had a mottled parenchyma. There were 80 mls of pericardial fluid. Microscopically, there were diffuse inflammatory infiltrates composed of lymphocytes, macrophages, with prominent eosinophils. This inflammation was primarily in the interstitium, was associated with multiple foci of myocyte necrosis, and was present in both right and left ventricles. It did not localize to the subendocardium, and the subendocardium was not thickened. There was no prominent perivascular infiltrate, no vascular inflammation, fibrinoid necrosis, vascular thrombi or endothelial prominence, nor was there a granulomatous component. There was minimal if any interstitial fibrosis.

The lungs were heavy and congested (right 1030 grams- expected 451-604 grams, left 900 grams - expected 411-564 grams). Microscopically, there was congestion, focal acute hemorrhage and edema, but no interstitial inflammation, diffuse alveolar damage, increased intra-alveolar hemosiderin-laden macrophages, viral inclusions or viral cytopathic changes, eosinophilic infiltrates, vasculitis, or intraparenchymal lymphoid hyperplasia. The bronchi had slightly thickened basement membranes, and the surrounding submucosa showed a mild chronic inflammation with only occasional eosinophils.

There was no peripheral edema, periorbital edema, pleural effusions or ascites.

The liver showed centrilobular congestion with minimal steatosis. There were no increased eosinophils in the bone marrow or other organs. No central nervous system lesions were identified.

Postmortem nasopharyngeal swabs were positive for SARS-CoV-2. There was no molecular evidence in the respiratory tissue for influenza A and B, parainfluenza 1-4, and RSV. Postmortem CSF cultures grew *Staphylococcus epidermidis*, considered a contaminant. Postmortem blood culture was sterile. Postmortem toxicology contained caffeine and naloxone; a drug given during resuscitation. Postmortem vitreous did not detect glucose or acetone.

Note: The first COVID-19 related death in our community was on March 14, 2020 in a 58-year-old African American male with comorbidities. This young patient died 8 days later and remains the youngest person with COVID-19 examined by our office at this time of submission. Due to scarcity of test availability at this "early "time, and concerns for conservation, our postmortem testing was highly selective.

Discussion

There are frequent references to myocardial disease complicating COVID-19 disease in adults. In adults hospitalized with COVID-19, myocardial damage was considered as the cause of death in 7%, or contributed to death in 33%, based only clinical and laboratory findings [1]. In other studies, coronary artery disease was present in 8% of patients [2], 7.3% had cardiac complications [3], and while troponin levels were increased in 8-12% in one series[4], this increase was not a significant predictor of mortality [14]. There is a single report of a fulminant COVID-19 myocarditis that responded to steroids and human immunoglobulin [5], but this was not confirmed by histology.

Presentation with cardiac arrest was noted in 3 patients [14], although in this reference, these patients were excluded from further study, as the focus was on other clinical characteristics.

Pathologic examinations are limited. One gross picture of a cross section of the left heart at autopsy was described as" gray red fish like" [8]. In a patient dying of respiratory failure, one heart showed only a few lymphocytes without other findings [10], demonstrated by postmortem biopsy. There are cardiac histology photomicrographs of interstitial fibrosis and scant interstitial inflammation, mostly of monocytes with a few CD34 cells- features of a longer standing myocardial injury which may or may not be related to the SARS-CoV-2 infection [9].

Eosinophilic myocarditis is defined histologically as inflammation containing prominent eosinophils along with myocyte necrosis. EM is not thought to represent a single entity but can be seen with different diseases. Ten percent of EM affect children. Etiologies include hypersensitivity reactions (most often drug exposure related), eosinophilic granulomatosis with polyangiitis, hypereosinophilia syndromes, infections, malignancies, and idiopathic [15]. In this 17-year-old, there was no history of drug exposure, and caffeine and naloxone only were detected from postmortem blood. The inflammatory infiltrate was limited to the heart, was not angiocentric, not granulomatous, and not associated with vasculitis. Tissues from other organs, including the bone marrow, or within the vasculature did not show frequent eosinophils, suggesting this was not a hypereosinophilia syndrome or an eosinophilia associated with a myeloproliferative disorder. There was no increased interstitial fibrosis, suggesting this was an acute event. There was no increased subendocardial fibrosis as with Loeffler's endocarditis. The conclusion was that this was either an idiopathic or infection related eosinophilic myocarditis.

Hypereosinophilia can be associated with thrombosis but thrombi were not seen in our patient.

It is well known that acute myocarditis may develop after a variety of viral infections and may either be fulminant or chronic. The lack of peripheral edema, periorbital edema, pleural effusions, ascites, hemosiderin-laden intra-alveolar macrophages, or myocardial interstitial fibrosis suggests the cardiac dysfunction was acute. This may represent a fulminant course, or a compensated subacute course until the final cardiac arrest.

This eosinophilic myocarditis may not be a specific entity and may not be specific to SARS-CoV-2 infection. This report should arouse the suspicion that the heart may be affected in COVID-19, as it can be in other viral infections. The question of whether this is a direct complication of SARS-CoV-2 infection, or if this is an idiopathic eosinophilic myocarditis in which the stress of the COVID-19 contributed to the cardiac decompensation cannot be answered definitively at this time. Case series from institutions performing autopsies on COVID-19 patients may at future time further define myocardial pathology as seen in this patient.

Since the acceptance of this article, there has been several other articles appearing in the literature associating fulminant myocarditis with COVID-19 [16–22]. One occurred in a 21 year old [19]. One report states that despite the infection, there was no respiratory symptoms in a patient with myocarditis and SARACoV-2 infection [20], as in our patient. None of these reports had histologic confirmation.

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