Lymphocytic Myocarditis

Lily Mahler, MD and Brandi McCleskey, MD†*

Key Words: viral myocarditis, pediatric sudden death, gastric ischemia, forensic pathology

(*Am J Forensic Med Pathol* 2022;43: e12–e14)

CASE BACKGROUND

A 2-year-old African American boy presented to the hospital after experiencing increasing respiratory distress and a febrile illness with nausea and vomiting for approximately 1 week before presentation. His medical history was pertinent for asthma. The patient died shortly after being arriving at the hospital and was sent for autopsy.

The decedent measured greater than 99th percentile for both height and weight (39.5 in., 49 lbs). External examination was unremarkable other than an umbilical hernia. Upon internal examination, the heart weighed 100 g (expected weight 56 g[1]) and was opened along the flow of blood revealing a dark maroon discoloration of the myocardium, especially along the interventricular septum of the left ventricle (Fig. 1). The chambers of the heart did not appear dilated. The liver was enlarged at 630 g (expected weight, 394 g[1]). The gastric mucosa had multiple, small, well-demarcated areas of thinning without erythematous edges (Fig. 2). The brain mass was 1390 g (expected, 1064 g[1]).

Microscopic examination of the heart was notable for diffuse lymphocytic infiltrate, as well as foci of myocytolysis with lymphohistiocytic infiltrate. Karyorrhectic debris were also present (Figs. 3A–B). Sections of the right lung revealed focal mucus plugging of terminal bronchioles in the lower lung with associated atelectasis. No significant inflammatory infiltrate was seen throughout sections of both lungs. Sections of the stomach revealed areas of focal mucosal ulceration consistent with ischemic damage (Figs. 4A–C).

The cause of the child's death was certified as lymphocytic myocarditis likely viral in origin. Additional molecular testing was performed on formalin-fixed heart tissue for severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) testing and found to be negative (the polymerase chain reaction [PCR]-based testing method on formalin fixed tissue was approved for research purposes only). Fresh-frozen brain and liver tissue, blood in ethylenediaminetetraacetic acid tube, and formalin-fixed heart tissue were also submitted for a full PCR-based viral panel and found to be negative for adenoviruses, cytomegalovirus, EBV, enterovirus, influenza A virus, mumps virus, parvovirus, rubella, and RSV. This testing if positive would have been an indirect evidence of infection, but the optimal specimen, fresh-frozen heart tissue, was not available. The negative viral panel does not exclude a likely viral pathogen in this case.

Manuscript received July 30, 2021; accepted September 10, 2021.
From the *Department of Pathology, Beth Israel Deaconess Medical Center, Boston, MA; and †Division of Forensics, Department of Pathology, University of Alabama School of Medicine, Birmingham, AL.
The authors report no conflict of interest.
Reprints: Brandi McCleskey, MD, Division of Forensics, Department of Pathology, University of Alabama School of Medicine 1515 6th Ave S #220, Birmingham, AL 35233. E-mail: bmccleskey@uabmc.edu.

ISSN: 0195-7910/22/4302–0e12
DOI: 10.1097/PAF.0000000000000730

DISCUSSION

Myocarditis is an inflammatory disease of the myocardium that is an established cause of sudden death for both adult and pediatric populations alike. The clinical presentation of myocarditis varies drastically from asymptomatic to cardiogenic shock and sudden death. Myocarditis can present as nonspecific symptoms, such as shortness of breath, nausea/vomiting, and tachycardia, but it can also mimic acute coronary syndrome.[2] The clinical outcomes for myocarditis are also broad: a portion of patients have a full recovery, some require circulatory support or cardiac transplantation, and some develop long term sequelae such a dilated cardiomyopathy. The most common causes of death due to myocarditis are heart failure and dysrhythmia.

Because of the heterogeneous nature of myocarditis, diagnosis can prove difficult and the true incidence of the disease is likely to be higher than reported cases. The rate of histologically proven myocarditis in 1516 pediatric cases sent to autopsy over 10 years was higher at 2%; this cohort of patients also had a sudden death rate of 57%.[3] Given that the clinical presentations of myocarditis are heterogeneous and often overlap with other cardiac diseases, this type of case is quite challenging for both the forensic pathologist and the clinician. Outside of autopsy, the criterion standard for clinical diagnosis of myocarditis is the endomyocardial biopsy (EMB). The diagnostic power of EMB has been strengthened by using PCR in the detection of viral genomes within biopsy samples.[4]

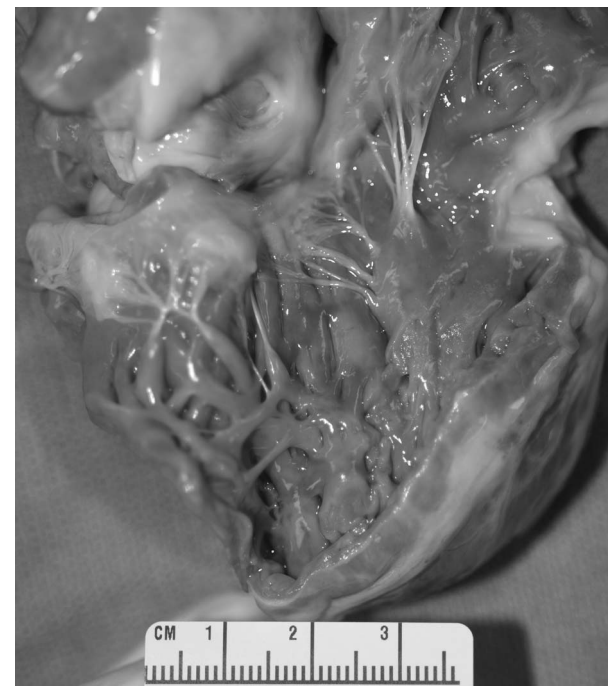

FIGURE 1. Mottling of septum.

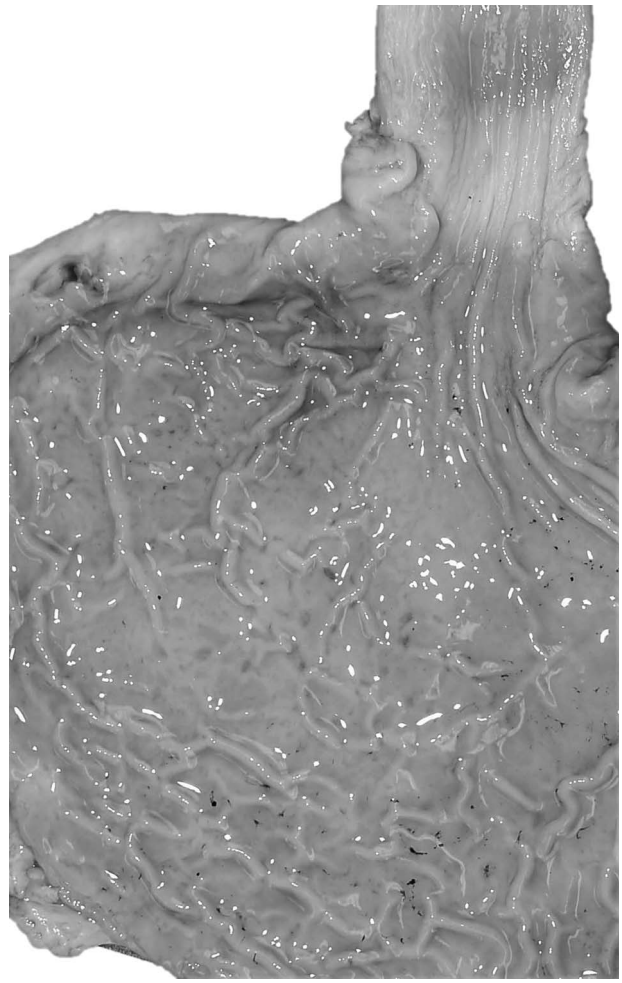

FIGURE 2. Gastric wall with well-demarcated thinning of the mucosa.

The most common etiology of myocarditis in the United States is viral infection. Commonly identified viruses implicated are enteroviruses (specifically Coxsackie B serotype), parvovirus B19, human herpesvirus 6, and adenovirus. In total, approximately 20 different cardiotropic viruses have been associated with myocarditis.[4] Other etiologies of myocarditis include bacterial infection, drug-induced hypersensitivity or toxicity, and autoimmune forms. Since late 2019, the SARS-CoV-2 has spread worldwide, and although most manifestations of the infection are respiratory in nature, a number of case series have been associated with severe cardiac sequalae as well. Numerous case reports have described clinical presentations of acute myocarditis in association with COVID-19.[5–8] Unfortunately, few of the current case reports on COVID-19–related myocarditis have histological confirmation. According to a *Journal of American College of Cardiology* review in January 2021, EMB was performed in 9 cases of COVID-19–positive patients, 2 of which met diagnostic criteria for myocarditis; all 9 cases lacked evidence of SARS-CoV-2

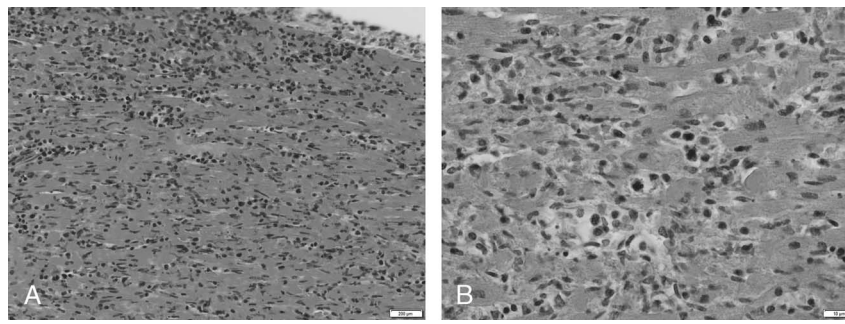

FIGURE 3. A, Diffuse myocardial lymphocytic infiltrate and myocyte necrosis (20×; hematoxylin and eosin stain). B, Diffuse myocardial lymphocytic infiltrate and myocyte necrosis (40×, hematoxylin and eosin stain).

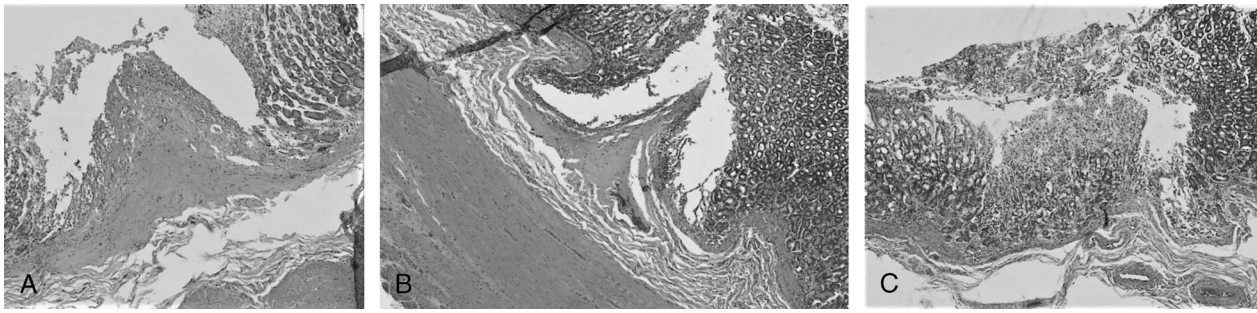

FIGURE 4. A, Gastric mucosal ulceration (4×; hematoxylin and eosin stain). B, Gastric mucosal ulceration (4×; hematoxylin and eosin stain). C, Gastric mucosal ulceration (4×; hematoxylin and eosin stain).

within cardiomyocytes.[9] In a systematic review performed in September 2020 analyzing cardiac autopsy findings of COVID-19–positive decedents, few cases revealed myocarditis upon postmortem examination.[10] The majority of cardiac pathology included cardiac dilatation, ischemia, or thrombosis, whereas only 1.5% of cases demonstrated myocarditis.[10]

This case highlights a spectacular example of lymphocytic myocarditis with associated ischemic gastric ulcers, which have not been described in the literature and occur because of severe myocardial dysfunction and resultant cardiogenic shock. A decrease in myocardial contractility leads to diminished cardiac output and subsequent poor perfusion of peripheral tissues. In an attempt to compensate for the decreased circulation, peripheral vasoconstriction transiently improves cardiac function and increases stroke volume until the burgeoning afterload overwhelms the damaged myocardial tissue resulting in end-organ damage and ischemia. Ischemic changes disproportionately affect the gastrointestinal system due to prioritization of systemic over mesenteric circulation. The gastric tissue is further subjected to damage mediated by gastric acid following the compromise of the gastric mucosa. This results in mucosal necrosis/ulceration and loss of glandular architecture, with severe ischemic damage extending into the lamina propria and beyond.[11] This case effectively illustrates the pathophysiology of gastric ischemic ulceration secondary to myocarditis-induced cardiogenic shock, as well as the diagnostic challenges in a clinically diverse disease process, such as myocarditis, especially in the unprecedented setting of the 2019 SARS-CoV-2 epidemic.

REFERENCES

1. Gilbert-Barness E, Debich-Spicer DE. *Handbook of Pediatric Autopsy Pathology*. Berlin, Germany: Springer Science & Business Media; 2008.
2. Klugman D, Berger JT, Sable CA, et al. Pediatric Patients Hospitalized with Myocarditis: A Multi-Institutional Analysis. *Pediatr Cardiol*. 2010; 31(2):222–228.
3. Weber MA, Ashworth MT, Risdon RA, et al. Clinicopathological features of paediatric deaths due to myocarditis: an autopsy series. *Arch Dis Child*. 2008;93(7):594–598.
4. Biesbroek PS, Beek AM, Germans T, et al. Diagnosis of myocarditis: current state and future perspectives. *Int J Cardiol*. 2015; 191:211–219.
5. Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA*. 2020;323(11):1061–1069.
6. Guo T, Fan Y, Chen M, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). *JAMA Cardiol*. 2020;5:811–818. Published online March 27, 2020.
7. Ho JS, Sia CH, Chan MY, et al. Coronavirus-induced myocarditis: a meta-summary of cases. *Heart Lung*. 2020;49(6):681–685.
8. Beri A, Kotak K. Cardiac injury, arrhythmia, and sudden death in a COVID-19 patient. *HeartRhythm Case Rep*. 2020;6:367–369. Published online May 13, 2020.
9. Kawakami R, Sakamoto A, Kawai K, et al. Pathological evidence for SARS-CoV-2 as a cause of myocarditis: JACC review topic of the week. *J Am Coll Cardiol*. 2021;77(3):314–325.
10. Sertogullarindan B, Ozbay B, Gumrukcuoglu HA, et al. A case of viral myocarditis presenting with acute asthma attack. *J Clin Med Res*. 2012; 4(3):224–226.
11. Bailey RW, Bulkley GB, Hamilton SR, et al. The fundamental hemodynamic mechanism underlying gastric "stress ulceration" in cardiogenic shock. *Ann Surg*. 1987;205(6):597–612.