Case of Myocarditis, Pericarditis, and Fatal Aortic Dissection following Covid-19 mRNA Vaccination

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Abstract:

We present a case study of a 34-year-old male who was in good health prior to his COVID-19 mRNA vaccination. Sixteen days after his first dose, he experienced acute inflammation, sudden thoracic aortic dissection, and pericardial tamponade, rapidly leading to his death. Studies suggest that young males, in particular, appear to be at increased risk of adverse cardiac events following COVID-19 mRNA vaccination. Although the incidence of such complications are believed to be low, we propose that information gaps exist in the criteria and findings that inform both public health agencies and the public on incidence rates of even severe myocarditis and cardiac adverse events following COVID-19 vaccination. This view is shared within many COVID-19 vaccine myocarditis studies and is evident within the findings of this case of Myocarditis, Pericarditis, and Fatal Aortic Dissection presented here.

Introduction: Several adverse events and cardiac complications have been linked to COVID-19 vaccination and are found in case reports, which help to inform the medical community, the public, and public health officials of these findings. [1-6] Studies suggest that young males, in particular, appear to be at increased risk of adverse cardiac events following the COVID-19 mRNA vaccination.

Individual case studies and larger cohort studies show mRNA COVID-19 vaccine-related pathogenic and histologic links to myocarditis and pericarditis in some who receive these vaccines. [4][7-10] The CDC also recognizes this risk for young males and advises: “People, especially males ages 12–39 years, should be made aware of the rare risk of myocarditis and pericarditis following receipt of these vaccines…” [11] Pericarditis, Myocarditis, Myocardial Infarction, Takotsubo Cardiomyopathy, and Aortic Dissections are also cardiac pathologies associated with COVID-19 vaccines. [4][8][9]

Case Presentation: Herein, we present a case study of a 34-year-old male who was in apparent good health prior to his COVID-19 mRNA vaccination. Sixteen days after his first dose, he experienced acute inflammation, sudden thoracic aortic dissection, and pericardial tamponade, rapidly leading to his death.

His premorbid cardiac echocardiograms had demonstrated no evidence of aortic root dilation or of aortic aneurysm, although a bicuspid aortic valve was present. No previous reports of aortic dissection in other family members were reported. His autopsy also showed no evidence of aortic aneurysm, and his aortic valves were also noted to be flexible. The intimal tear found at autopsy extended through the aortic media into the adventitial layer of the aorta. This injury formed a pocket that dissected across the aortic arch into the descending aorta. As it grew, it entered the pericardial space, filling it with blood. The subsequent hemopericardium could be expected to have led to cardiac tamponade and then cardiac arrest. Of note, a toxicology drug screen was also performed and failed to find any illicit drugs that could have contributed to such a catastrophic event.

From a clinical perspective, he was at low risk for such a devastating complication given his age, normal blood pressure, and his history as a nonsmoker with unremarkable glucose and lipid levels. He was also found to lack any evidence of genetically linked connective tissue disorders confirmed by postmortem genetic testing.

The patient's pathology, including histology of the heart and pericardial sac, showed lymphocytic infiltrates, indicative of pericarditis and myocarditis, as is seen in other peri and myocarditis cases following COVID-19 mRNA vaccine. Significant eosinophilic infiltrates were also present in his arterial tissues, consistent with a hypersensitivity reaction. **[12-18]** His immunohisto-pathology noted the presence of spike protein in aorta as well as vascular tissues but an absence of staining for nucleocapsid antigens, indicating that the spike protein was vaccine-derived rather than of viral origin. **[19]** Given these findings and a lack of underlying genetic disease, this inflammatory response is suspected to have initiated the deadly vascular and cardiac inflammatory cascade that ultimately took his life. The Pfizer Covid-19 mRNA vaccine is the suspected catalyst for this chain of events.

The postmortem pathology report documented: “Arterial vessels show enlarged intima, lipid deposit areas, and a small perivascular inflammatory infiltration from macrophages and lymphocytes in the area of the vasa vasorum which reaches into the intima media. Circumscribed evidence of SARS- Covid-2 Spike subunit 1 in individual endothelia and macrophages. No evidence of SARS-Cov-2 nucleocapsid.” The lack of nucleocapsid antigens found on immunohistopathologic analysis excludes a natural Covid-19 infection or viral etiology for his myocarditis, pericarditis, or the aortitis, and vascular inflammation found at autopsy and in postmortem histology. **[19]**

Supporting evidence also includes extensive cytokine analysis, in which we see:

1. Acute inflammatory response consistent with elevations of interleukins IL-1, IL-1RA, IL-18, and IL-6. **[20-21]**
2. Coagulopathy as demonstrated with elevations of plasminogen activator inhibitor-1 (PAI-1) and D-dimer levels, typically seen in aortic dissection cases. **[22-24]**
3. Evidence of myocardial injury with significant elevations of myoglobin and fatty acid binding protein 3 (FABP3) indicative of inflammatory infiltration of the myocardium. **[25]**

Each of these abnormalities is a recognized complication of myocarditis or the myocardial effects of COVID-19 mRNA vaccine.

Discussion: As noted in Pfizer document 5.3.6, “Cumulative Analysis of Post-authorization Adverse Events Reports,” 1,441 cardiovascular adverse events had been reported to Pfizer, including aortitis, pericarditis, and myocarditis. **[26]** The CDC website also holds the following notification regarding the causal relationship between vaccination with the COVID vaccines—genetic and protein-based, and the subsequent development of myocarditis and pericarditis: “Evidence from multiple monitoring systems in the United States and globally support a causal association for mRNA COVID-19 vaccines (Moderna or Pfizer-BioNTech) and myocarditis and pericarditis. Cases have occurred most frequently in young adult males within 7 days after receiving the second dose of an mRNA COVID-19 vaccine (Moderna and Pfizer-BioNTech).”

[11] Myocarditis is now well recognized to be a serious adverse reaction associated with Pfizer's mRNA COVID-19 vaccine.

Studies have documented the presence of Spike protein and eosinophilic infiltration in cases of COVID-19 vaccine myocarditis. **[1][6][10-15]** Both of these features are present in this case as well. COVID-19 mRNA vaccines have also been implicated in acute hypersensitivity reactions, coagulopathy, cytokine storm, Takosubo Cardiomyopathy, Vasculitis, Aortitis, Pericarditis, and Myocarditis. **[4][7][10][11][18][27-31]** Any of these mechanisms could have played a role in the sequence of events, leading to aortitis, pericarditis, myocarditis, and ultimately catastrophic aortic dissection.

The pathogenesis of cardiac adverse events linked to COVID-19 mRNA vaccines is studied worldwide. Pfizer's 2022 COVID-19 vaccine internal document on myocarditis states that lipids may activate "immune responses" and "pro-inflammatory processes." **[32-35]** Additionally, the role of the COVID-19 mRNA vaccine LNP is to bring the mRNA to the cells for spike protein production. Animal models and studies since 2015 have shown that mRNA-LNP formulations can travel throughout the body and are not limited to the injection site. **[4][9][10][36]** Studies also show that in several cases in which immunohistochemical staining and biopsy were performed, Spike protein is found to be accompanied by evidence of inflammatory responses in the heart tissue of myocarditis cases after COVID-19 vaccinations, including in the aorta of the young man whose case we present herein. **[1][4][7][34]**

In 2023, Twenty-one Yale physicians published a COVID-19 vaccine myocarditis cytokine research study that details the various cytokine immune responses seen in the cohort of 23 young patients with myocarditis after mRNA vaccine. This study states, "the LNP component of the vaccine alone was found to be highly inflammatory." The study also suggests that "the LNP delivery platform in synergy with vaccine-vectored antigens is more likely the driver of an exaggerated immune cytokine response driving cardiac pathology after vaccination in susceptible individuals." **[4]**

Yale's cytokine myocarditis study referenced Genentech's 2022 study on cytokines in RNA-LNP vaccines, which explains that certain mRNA vaccine components, contaminants, or artifacts in synergy with the lipids are able to elicit inflammatory factors that can lead to cytokine release syndrome (CRS). [9] Genentech's study also states, "…RNA vaccines against COVID-19 (mRNA-1273 by Moderna and BNT162b2 by BioNTech/Pfizer)—which use modRNA with a greatly reduced innate immunostimulatory activity—still elicit systemic adverse events in patients following initial intramuscular administration." **[10]**

In the case of this 34-year-old young man presented herein, at the family's request after his untimely passing following his mRNA COVID-19 vaccine, his perimortem serum was also examined in 2022. His findings of an acute inflammatory cytokine response with concurrent elevations in IL-1 and IL-18 are consistent with Yale's 2023 cytokine myocarditis research study and Johns Hopkins's 2022 cytokine and myopericarditis study as well. **[9]**

In his case, his hospital records show that he was asymptomatic until a few hours before he was rushed to the ER; he was actively walking and talking to paramedics until he collapsed. He presented to the hospital with CPR in progress and died within the hour. Although he was tested for troponin, his levels were not raised. Myocarditis and pericarditis were not investigated by the hospital, and the medical examiner diagnosed "acute aortic dissection." Without the findings gathered in his further immunohisto-pathology, myo and pericarditis, in this case, would not have been documented, and his complete diagnosis would not have been learned. It should be said that in cases of fatality after recent COVID-19 vaccinations, without autopsy and histopathological examinations, a complete patient diagnosis and accurate reporting of the true incidence of vaccine-linked fatal injury, including cardiac events, may not be known.

Conclusion: Myocarditis has been portrayed as a rare complication of Covid-19 mRNA vaccination. However, this may not be accurate. Studies show that when sophisticated techniques are used, such as high-sensitivity troponin assays, magnetic resonance imaging (MRI), or positron emission (PET) heart scanning, it has been shown that these injuries are common even in asymptomatic individuals following COVID-19 mRNA vaccines. **[7][17][30][37]** For example, in Pfizer's February 2022 internal white paper, which elucidates the cause of

myocarditis in mRNA vaccines, Pfizer wrote, "The true incidence of myocarditis after vaccination is likely underestimated because of the subclinical and non-specific clinical manifestations in most cases." **[32]**

There is now a large body of evidence showing that young and apparently healthy individuals have experienced life-changing and life-threatening adverse events subsequent to COVID-19 mRNA vaccination. **[7][11][27-28][30-32][38-46]** For example, in 2022, Patone et al. stated, "The risk of vaccine-associated myocarditis is consistently higher in younger men, particularly after a second dose of mRNA-1273…" The study continues, "An important consideration for this group is that the risk of myocarditis after a second dose of mRNA-1273 was higher than the risk after infection." **[47]** Covid-19 vaccine myocarditis long-term outcomes cannot be predicted; however, studies have shown residual Late Gadolinium Enhancement (LGE) "likely reflecting myocardial fibrosis" in both adults and children following COVID-19 vaccine myocarditis. **[48]** In 2021 and 2022 analyses, two Italian studies also show that abnormal blood pressure findings are not rare after COVID-19 vaccination, even in younger patients. **[49][50]**

However, currently, a standard method of reporting myocarditis and cardiac adverse events, incidence rate, and follow-up findings does not exist, but gaps do exist in many current studies. For instance, myocarditis patients selected for research studies typically restrict the inclusion of patients who have presented with myocarditis within 7 to 14 days of vaccination, and many only include myocarditis cases that take place after the second dose. Yet, it has been shown that myocarditis incidence after COVID-19 vaccination is often known to take place after the first dose, and it can take place within 28 days and sometimes up to 90 days after the second dose. **[47][51][52]**

We should also point out that many studies include only myocarditis participants with raised troponin levels, even though elevated troponin levels have been reported as an unreliable biomarker of myocarditis. **[47][53][54]** For instance, the pathology of the young man whose medical case we present herein shows raised myoglobulin markers without raised troponin markers. Again, the biological markers and the sophisticated imaging techniques described above have revealed even subclinical cases or asymptomatic cases. Still, it is important to remember

that not all cities and communities have access to this testing, and many cases will remain undetected. In the case presented herein and in the relevant data, we found that the above factors can exclude even serious myocarditis cases from research studies, and we also learned that cases may go undetected, untreated, and excluded from statistical analysis. **[47][53]**

We propose that the administration of COVID-19 mRNA vaccinations should be carefully weighed on an individual basis with a full understanding of evolving safety risk data, including undetected and potential subclinical disease presentation, which could prove especially harmful in the younger population under age 39, such as the tragic case we present herein. In-depth histopathology at autopsy upon the death of apparently healthy individuals after COVID-19 vaccination, as well as advanced cardiac testing in all patients with cardiac symptoms such as chest pain and shortness of breath after vaccination, should be performed to avoid future patient harm and to better inform public policy. The benefit to risk appraisal of COVID-19 vaccination is determined by public health agencies who are expected to inform the public of emerging safety data as it is made available to afford complete informed consent, and the public should also expect that each emerging safety concern should prompt timely regulatory investigation and actions that are important for public health.

Acknowledgments- Patient Consent: Written consent was obtained from the patient's family for the case report. We thank them for allowing this important medical information to be presented to the public.

Supplementary Material:

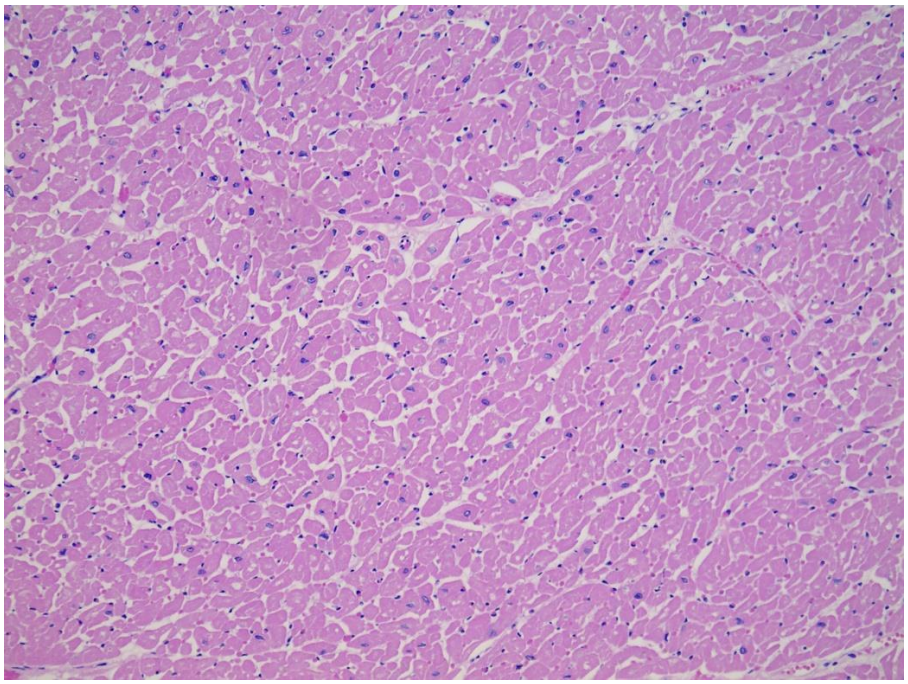

Figure 1 Heart, Histo-and lymphocytic myocarditis. Vacuolation of cardiomyocytes and increased number of interstitial cells, especially macrophages, eosinophilic granulocytes, and small lymphocytes. Magnification 100x, H&E

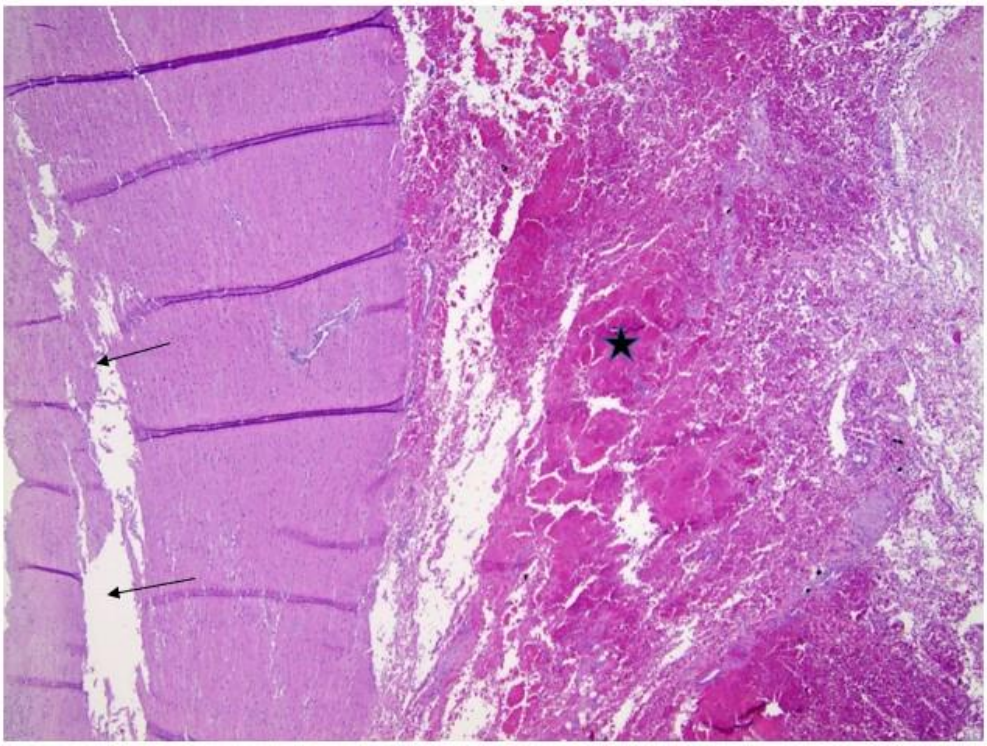

Figure 2 Overview of rupture of aorta with wide underbleeding of adventitia (star) and dissection of intima and media (arrows). Magnification 20x, H&E

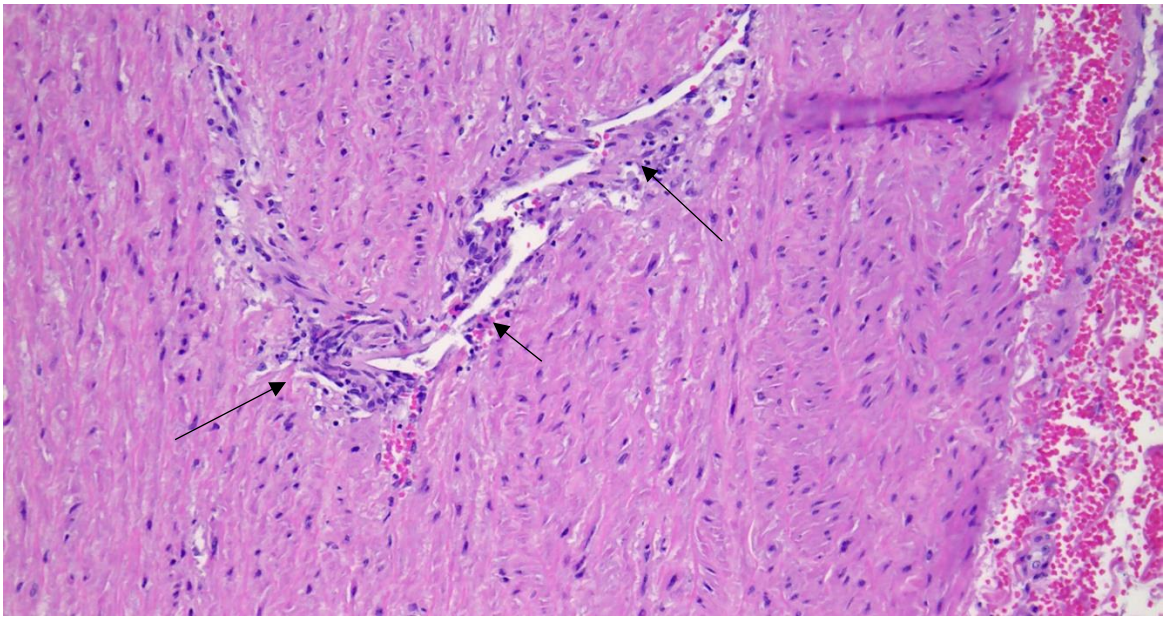

Figure 3 Detail from Figure 2. Vasculitis of vasa vasorum aorta with swelling of the endothelial cells and a perivascular accumulation of macrophages, eosinophil granulocytes, and lymphocytes. Magnification 100x, H&E

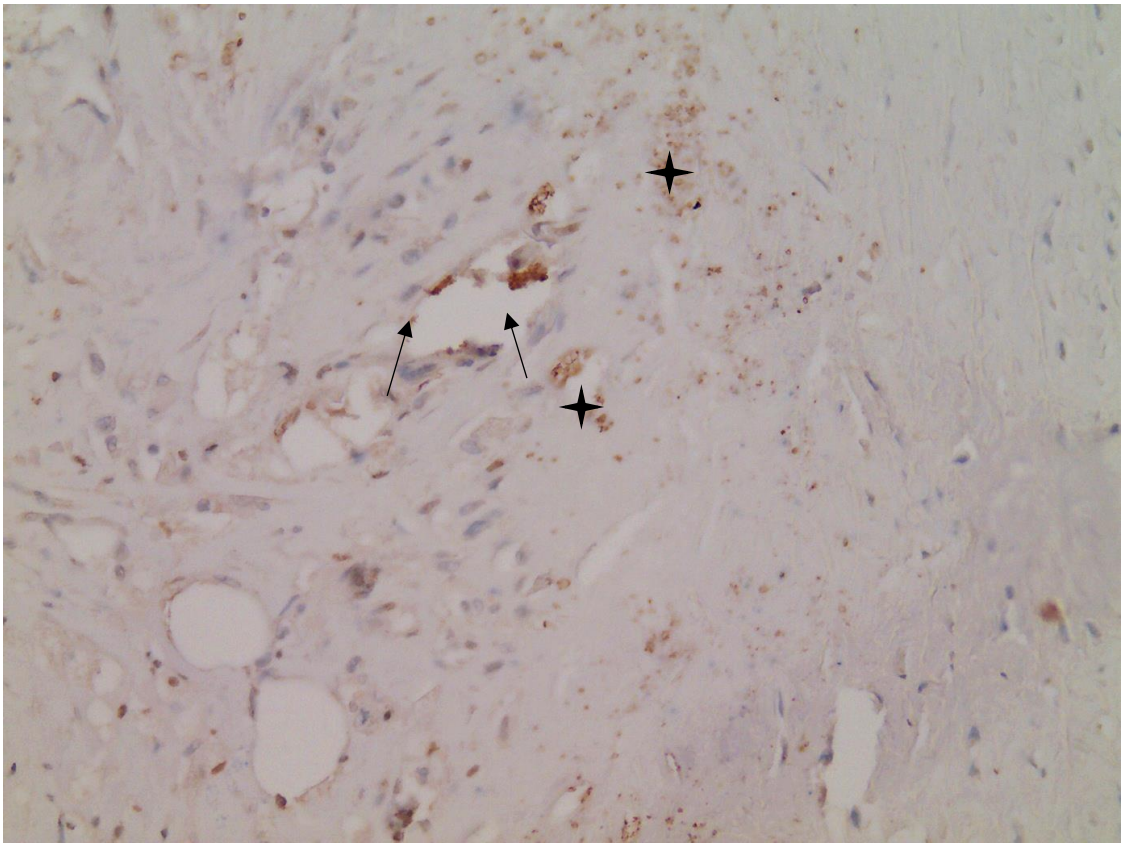

Figure 4 Vasa vasorum aortae. Granular deposition of SARS-CoV2 Spike subunit 1 in endothelial cells (arrows) and perivascular macrophages (stars). Magnification 200x, Immunohistochemistry.

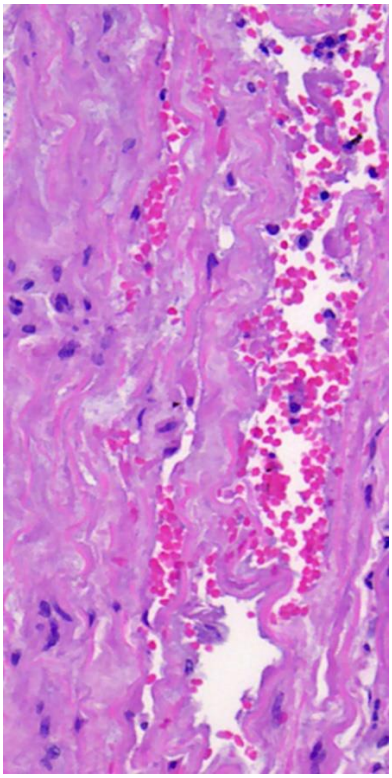

Figure 5 Detail from Figure 2 and 3. Enhanced Close-up. Vasculitis of vasa vasorum aorta with swelling of the endothelial cells and a perivascular accumulation of macrophages, eosinophil granulocytes, and lymphocytes.

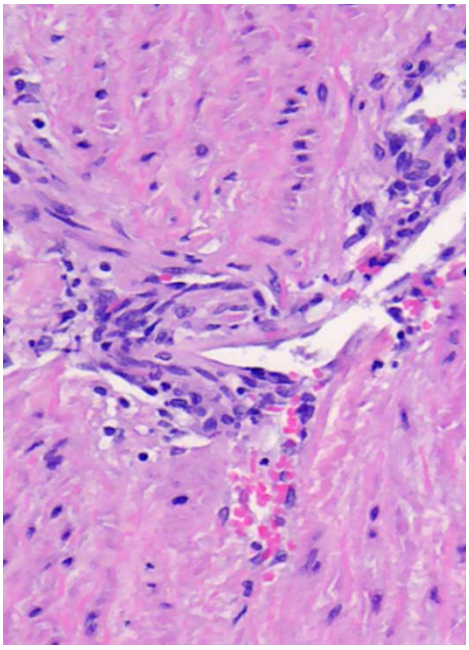

Figure 6 Detail from Figure 2, 3 and 5. Enhanced Close-up. Vasculitis of vasa vasorum aorta with swelling of the endothelial cells and a perivascular accumulation of macrophages, eosinophil granulocytes, and lymphocytes.

Data availability: Not applicable.

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