

Adrenal Vascular Changes in COVID-19 Autopsies

To the Editor.—For the past 2 months, New York City has been the epicenter of the ongoing pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2 virus). The disease (coronavirus disease 2019 [COVID-19]) most acutely and severely affects the lungs, requiring mechanical ventilation in a subset of cases. Other organs, including the heart, kidneys, liver, and gastrointestinal tract, can also be involved. The pathophysiology and the extent of multiorgan involvement is poorly understood. We report pathological findings in the adrenal glands of the first 5 postmortem examinations of patients with COVID-19 diagnosed on clinical grounds with confirmatory real-time polymerase chain reaction testing of nasopharyngeal swab. Two patients were brought to the emergency room in cardiac arrest and could not be resuscitated. Three were briefly hospitalized, 2 for 24 hours and 1 for 72 hours. There were 4 males and 1 female, ranging from 59 to 90 years of age and with the following co-morbidities: hypertension (5 of 5), diabetes (3 of 5), ischemic cardiomyopathy (3 of 5), chronic lung disease (2 of 5, 1 with chronic obstructive pulmonary disease and 1 with interstitial lung disease), prostate carcinoma (2 of 5), and recent spinal surgery (1 of 5). Blood cultures were negative in the 3 patients tested. On microscopic examination, acute fibrinoid necrosis of small vessels, mainly arterioles in adrenal parenchyma, adrenal capsule, and in the immediately adjacent periadrenal adipose tissue, was identified. Subendothelial vacuolization and apoptotic debris were present (Figure, A–C). No significant inflammation, adrenal parenchymal infarcts, or thrombi were appreciated. The vascular pathology was disproportionately conspicuous in adrenal and not as easily identified in other organs examined.

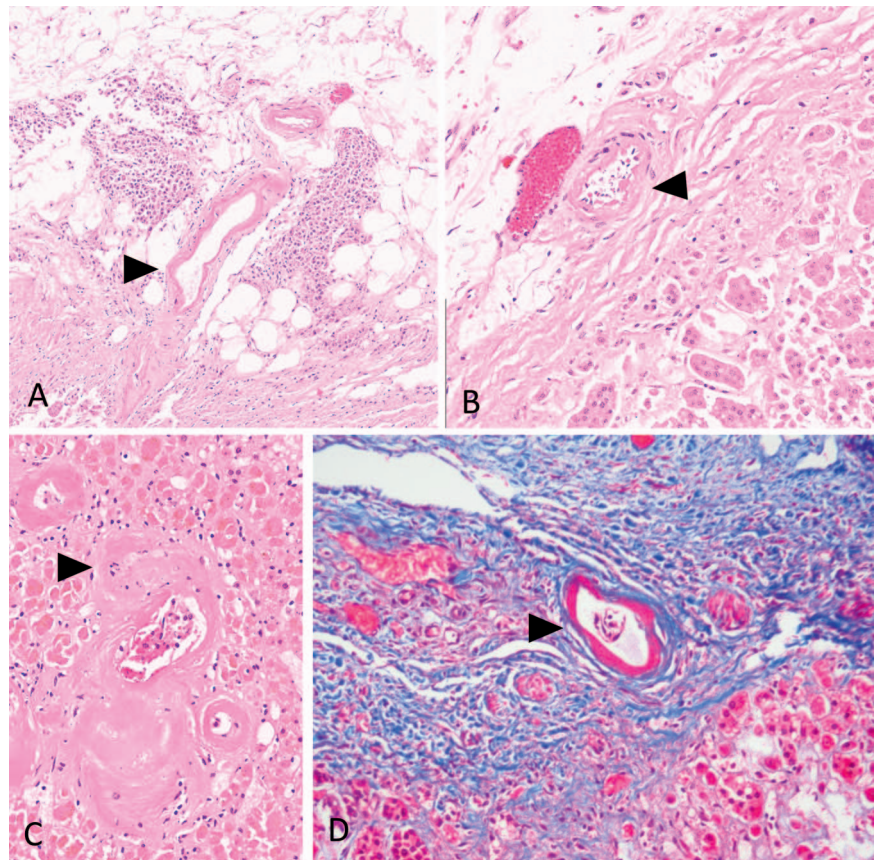
Fibrinoid necrosis describes vessel wall necrosis with fibrin and serum protein accumulation conveying an eosinophilic amorphous appearance on histology. With Masson's trichrome stain, the amorphous fibrinoid material is red, unlike collagen that

stains blue (Figure, D). Arteriolar hyalinosis is another term used to describe the accumulation of pink amorphous material in vessel walls. This is thought to relate to hypertension, but is not typically associated with vessel necrosis and endothelial apoptosis. Hyalinosis may explain some of the histopathology; however, many of the vessels we observed were either necrotic or associated with apoptosis. It is unclear if the adrenal vasculopathy is because of hypoxia, abnormal vascular reaction and blood flow patterns, direct viral cytopathic effect, an immune-mediated injury, or a combination of events. Acute fibrinoid necrosis is classically described in malignant hypertension (first by Volhard and Fahr¹ in 1914), mainly in kidneys, and in immune-mediated vasculitides. While SARS-CoV-2 infection seems to more severely affect patients with a history of hypertension,² most critically ill patients with COVID-19 need vasopressors for per-

sistent hypotension.³ Two of 3 hospitalized patients described had recorded high blood pressure values and 1 was hypotensive on arrival. Localized fibrinoid necrosis is also mentioned in a report of pathological findings in SARS virus infection.⁴ SARS-CoV-2 virus gains entry to the cell via the angiotensin-converting enzyme 2 receptor,⁵ which is most abundant in lung alveolar cells, but also present in endothelia and other tissues, providing a possible mechanism for vascular injury.⁶

Adrenal hormones are involved in modulating inflammatory responses⁷ and adrenal gland dysfunction has been described in patients with community-acquired pneumonia.⁸

In general, adrenal function is not routinely assessed in an intensive care unit setting. The most common indication for corticosteroid administration in an intensive care unit is refractory hemodynamic shock. According to several critical care societies, acute respiratory distress syndrome manage-



(A) Fibrinoid hyaline vasculopathy in periadrenal vessels indicated by black arrow head (hematoxylin and eosin stain [H&E] ×10 magnification). (B) Apoptosis in periadrenal and adrenal vessels (black arrow head points to apoptotic endothelial cells; H&E stain, ×20 magnification). (C) Necrotic vessel with karyorrhectic debris at black arrow head (H&E stain, ×20 magnification). (D) Masson's trichrome stain highlights fibrinoid hyaline material in red, indicated by the black arrow head (Trichrome stain, ×20 magnification).

ment can include corticosteroids, as they may decrease the time on a ventilator and reduce mortality.⁹ Corticosteroids are also administered if there is suspicion of adrenal insufficiency or if they are indicated because of an underlying condition. Currently, the World Health Organization and major critical care and infectious diseases associations advise against routine corticosteroid use in COVID-19 patients, mainly out of concern for slowing viral clearance. However, early reports from China and Europe suggested that corticosteroids are useful in severe COVID-19 and some experts posit that severe cytokine release syndrome seen in some patients warrants the use of corticosteroids or other targeted immunosuppressants.⁹⁻¹²

It is interesting to consider that adrenal insufficiency secondary to the vasculopathy described here may contribute to the cytokine storm observed in patients with severe COVID-19. Clinical studies to further assess adrenal function in COVID-19 may help in understanding the pathogenesis of disease in severely affected patients and hopefully lead to therapeutic protocols that may rescue an increased number of patients.

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Creation and Benefits of the “COVID Autopsy Listserve”

To the Editor.—I am writing to commend many members of the autopsy pathology community (including hospital and forensic practitioners) who have come together to help shape and deliver quality postmortem care during the initial wave of the novel coronavirus disease 2019 (COVID-19) pandemic. In March 2020, as new cases were rapidly escalating in New York City and around the world, most autopsy pathologists likely appreciated that decedent management and autopsy practice would have to quickly and adeptly evolve in response to the pandemic. Staff questioned where to put increasing numbers of decedents who were incessantly arriving in morgue spaces. Attending and resident pathologists were concerned about the potential infectivity of COVID-19 at autopsy. I realized I did not have sufficient information with which to effectively navigate the unfamiliar territory into which postmortem care was rapidly transitioning amid the evolving pandemic.

So, on March 20, 2020 I drafted an email to a group of colleagues around the country asking their opinions on managing COVID-19 at autopsy and in the morgue. I also encouraged them to spread the word about this fledgling “COVID Autopsy Listserve (the “listserv”—really just an email distribution list) to anyone involved with postmortem care. That day ended with 55 inaugural participants, and by the end of March more than 100 people from around the United States and some international locations were engaging on the listserv. Today, there are nearly 200 members on the listserv, mostly autopsy pathologists but also some researchers and clinicians. All are welcome, and new people join each week. The goal of the listserv is to disseminate knowledge and experience so we can safely and effectively expand medical knowledge through autopsy, while compassionately caring for decedents and their families.

The members of the listserv have addressed and continue to deal with myriad issues relating to COVID-19 in the postmortem realm. However, one of its most rewarding successes was its empowering pathologists who have appropriate facilities, supplies, and experience to autopsy COVID-19 decedents. I developed and disseminated through the listserv 2 surveys, 1 each at the end of March and April 2020. Around 50 pathologists responded to each survey (51 in March, 49 in April). Interesting perspectives and practice trends documented in these surveys over the initial weeks of the pandemic include the following:

1. Most respondents felt that existing guidelines¹ allow for the safe performance of COVID-19 autopsies (84% March and 92% April);
2. More institutions performed or were preparing to perform COVID-19 autopsies in April (63%) than in March (35%);
3. More respondents had autopsied a COVID-19 decedent in April (51%) than had in March (6%); and
4. Respondents’ support for resident involvement in COVID-19 autopsies increased from March (55%) to April (82%).

“Experientia docet” (experience teaches) and through the COVID Autopsy Listserv we continue to educate and reassure each other, collaborate on research, and optimize our