Commentary

Illuminating COVID-19 lung disease through autopsy studies

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Since the start of the twenty-first century, three zoonotic coronaviruses (CoVs) have caused disease outbreaks in humans. Severe acute respiratory syndrome-CoV (SARS-CoV) emerged in China as a pneumonia outbreak from 2002 to 2003 with a mortality rate of 9.6% and nearly 800 confirmed deaths.1 Cases of Middle East respiratory syndrome-CoV (MERS-CoV) first appeared as respiratory disease in Saudi Arabia and Jordan during 2012 and it remains endemic in Saudi Arabia and the Arabian peninsula with an estimated mortality rate of 34.3% and 858 confirmed fatalities.2 While each of these outbreaks caused regional epidemics, they also revealed the potential for a local outbreak to spread globally via air transportation. Remarkably, coronavirus disease 2019 (COVID-19) emerged in Wuhan China in December 2019 and was declared a global pandemic by the World Health Organization (WHO). In just six months, COVID-19 infection has already left a lasting effect across the globe with over 200 affected countries and more than seven million positive cases confirmed by the WHO (www.who.int – accessed June 9, 2020).

The cause of COVID-19 was identified as a novel coronavirus now called SARS-CoV-2, a betacoronavirus as are SARS-CoV and MERS-CoV.3 In contrast to SARS-CoV or MERS-CoV, SARS-CoV-2 has a lower estimated case fatality rate of 0.8–1.4%,4 but due to its highly efficient transmission between naive individuals and its potential to overwhelm local healthcare facilities, the global death toll attributed to SARS-CoV-2 already exceeds 400,000 (www.who.int – accessed June 9, 2020). Like SARS and MERS, respiratory disease is a common clinical feature of COVID-19; however, observations of involvement by other organ systems and systemic manifestations have complicated our understanding of COVID-19 pathogenesis as well as potential therapeutic options. SARS-CoV-2 uses angiotensin converting enzyme 2 (ACE2) as its cellular receptor, just like SARS-CoV.5 Surprisingly, the clinical disease caused by these viruses, which share the same receptor, are increasingly recognized as not identical, and thus these differences warrant further study.

One of the factors limiting our understanding of COVID-19 has been a lack of published autopsy reports.6 Autopsy (meaning in Greek: “to see for oneself”) is a fundamental element of pathology, a specialized discipline in medicine that studies disease. Pathologists perform autopsies to evaluate tissues for lesions at the macroscopic, microscopic, ultrastructural, and molecular levels. Autopsy is the gold standard for determining how and why deaths happen, and help to clarify pathophysiologic mechanisms underlying clinical disease. For highly contagious and lethal diseases such as COVID-19, biosafety/biosecurity, expertise, technical resources, and cultural practices are some of the potential challenges to safe and effective autopsy performance. Sometimes in these situations, pathologists can only perform a partial autopsy to collect essential organs (e.g. lungs). While these limited autopsies can provide insightful data, COVID-19’s multiorgan to systemic involvement clinically requires a broader picture autopsy to gain a comprehensive view of the disease process. Importantly, study of autopsy reports from multiple institutions and regions are useful to validate commonalities of COVID-19 pathogenesis as well as to distinguish the nonspecific influences of medical therapies, time on ventilator, comorbidities, etc. that can vary between patient, institution, and even stages of the pandemic.

In the current issue of EBioMedicine, Wang and colleagues report their investigation of two autopsy cases (a female and a male) from Wuhan China.7 Both patients had terminal pulmonary/circulatory failure and were confirmed SARS-CoV-2 positive by polymerase chain reaction in lung tissues. The lung tissues had classic features of diffuse alveolar damage (DAD) by computed tomography (CT) and histopathology, similar to that previously seen in SARS and MERS outbreaks.1,2 Additionally, these lung tissues had increased cytokines, macrophages, mucus and desquamated epithelium, with thrombi in vessels. Interestingly, they provide evidence that the SARS-CoV-2 S protein may bind to the surface of macrophages. The field awaits definitive evidence of whether or not this virus enters and completes its replication cycle in alveolar macrophages.

These data add an important piece of the puzzle to the understanding of severe COVID-19. For example, animal model studies have suggested that exuberant cytokine responses to respiratory coronaviruses could cause excessive infiltration by inflammatory monocyte-macrophages into the lungs resulting in severe lung pathology such as DAD.8 Likewise, Wang, et al.7 showed increased cytokines and macrophages in autopsy lungs. The same authors also detected thrombi in some vessels, supporting recent reports of
vascular inflammation and thrombi in other autopsy studies. Uniquely, Wang and colleagues show that COVID-19 lungs have air-spaces partially filled with mucus and desquamated epithelium; some of these features (e.g. mucus) have not been reported by other much larger autopsy studies suggesting it could be related to other factors such as COVID-19 treatments or pre-existing conditions. Finally, we need to continue to acquire more autopsy reports and compare these in triangulation with investigational animal models and clinical studies to gain a more accurate understanding and description of COVID-19 pathophysiology.

Declaration of Competing Interest

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Author contributions

DKM and PBM wrote the manuscript, revised the final manuscript, and are responsible for summarizing all the data.

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