Histopathological findings in fatal COVID-19 severe acute respiratory syndrome: preliminary experience from a series of 10 Spanish patients

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INTRODUCTION

Novel coronavirus-associated disease (COVID-19) was first detected in Spain on 31 January 2020, with more than 204 178 cases subsequently identified in 3 months.1 Severe COVID-19 is associated with high circulating levels of inflammatory cytokines akin to a cytokine release syndrome that frequently results in respiratory failure. To date, scant histopathological information of infected patients is available. Few descriptions of histopathological findings have mainly reported pneumonitis and diffuse alveolar damage (DAD).2–5 To advance in the knowledge of COVID-19-associated tissue damage is important to understand the mechanisms of damage caused by SARS-CoV-2.

METHODS

Postmortem multiorgan biopsies in 10 patients who died with SARS-CoV-2 infection were performed after oral authorisation of a first-degree relative. Biopsies were obtained without ultrasound guidance with the patient’s corpse still on the hospital bed. See online supplementary files for a detailed description of methods.

RESULTS

Clinical characteristics are summarised in online supplementary table 1. Chest CT findings and images are shown in figure 1 and online supplementary table 1. Pathological characteristics are summarised in online supplementary table 2.
respiratory syndromes produced by other coronaviruses.6,7 When found, the inflammatory component in our biopsies was generally of a chronic type, mostly confined to T lymphocytes, (CD3 positive). Signs of inflammation were absent (four cases), mild (four cases) or moderate (two cases). The four patients, who did not receive immunomodulatory drugs (corticosteroids and/or tocilizumab), showed similar histopathological findings than those who did receive these drugs. The absence of cellular infiltrates is consistent with a cytokine release syndrome, in what appears to be the hyperinflammmatory stage of COVID-19.2,8 Small pulmonary artery thrombosis was evident in different stages of evolution (figure 2). According to the disseminated intravascular coagulation (DIC) standard of care, all our patients received prophylactic low-molecular-weight heparin. Despite heparin and in concordance with other studies, vascular thrombosis was highly prevalent. The precise mechanisms for the coagulopathy, whether a classic DIC, a pulmonary specific COVID-19 vasculopathy,9 or mediated by a diffuse endothelial damage via endothelitis,10 still requires further investigation.

Most patients had radiological features compatible with COVID-19, that is, diffuse, peripheral ground-glass opacities and air bronchogram, which has been associated with a worse prognosis. The only patient with unilateral, right sided, involvement had spent most of the time in a right lateral-decubitus position for several years due to advanced Alzheimer disease.

Regarding the biochemical cardiac derangement frequently seen in infection by SARS-CoV-2, it is remarkable that there was no clinically relevant right ventricle volume overload. On histopathological examination, myocardiocytes showed neither signs of inflammation or fibrosis, nor signs of pulmonary volume overload. Two cases showed myocardial hypertrophy, most likely not associated with COVID-19. We only found mild myocarditis in one patient, who happened to have the greatest elevation in troponin. This patient also had a follicular-cell lymphoma and received chronic immunosuppressive medication due to kidney transplantation. A previous study found that reversible, subclinical diastolic left ventricular impairment appears to be common in acute SARS-CoV-1 infection, even among patients without underlying cardiac disease,11 suggesting that left ventricular dysfunction in the acute phase might be attributable to the cytokine release syndrome. In the same report, an isolated postmortem examination was performed, and no evidence of interstitial lymphocytic infiltrate or necrosis of myocardial cells was found.

The main limitation of our study is the tissue sample size due to the postmortem biopsy technique used. However, autopsies in COVID-19 patients were only allowed under strict biosecurity regulations.
To our knowledge, this is the first report where RT-PCR for SARS-CoV2 has been tested in all organ samples from each patient. It is remarkable that 9 out of the 10 patients had at least one organ with significant amount of SARS-CoV2 RNA, being most prevalent in lung tissue.

Correction notice This article has been corrected since it was published Online First. The first author’s name has been amended.

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REFERENCES