

# Spectrum of histopathological findings in coronavirus disease-19, Middle East respiratory syndrome and severe acute respiratory syndrome

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Clinical manifestations of coronavirus disease-19 (COVID-19) suggest multiorgan disease involvement. Patients with severe COVID-19 develop acute respiratory distress syndrome, acute kidney injury, cardiac dysfunction and arrhythmia, shock, gastrointestinal symptoms, lymphocytopenia, and liver dysfunction.<sup>[1,2]</sup> The underlying mechanisms of organ involvement and whether it is related to direct viral infection or not are unclear at this point.

In *The Lancet Respiratory Medicine*, Xu *et al.*<sup>[3]</sup> presented the first description of the postmortem histopathological findings of a severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in a 50 years old male. Although the pathological analysis was limited to tissue from the lung, heart, and liver and utilized only light microscopic examination, the histopathological findings were similar to those described in SARS-CoV<sup>[4,5]</sup> and Middle East respiratory syndrome coronavirus (MERS-CoV).<sup>[6]</sup> These data suggest similarities in the pathogenesis and the mechanisms of tissue damage and inflammatory response to coronaviruses infections.

Xu *et al.*<sup>[3]</sup> histopathological findings of heterogeneous acute alveolar damage (DAD), predominantly lymphocytic interstitial

inflammation and the identification of reactive pneumocytes and multinucleated syncytial cells are similar to those we described in a 33-year-old male who expired secondary to MERS.<sup>[6]</sup> In our case with MERS, the extent of lung tissue damage appeared to be more extensive than the case described by Xu *et al.*, and confluent parenchymal necrosis was evident. However, our patient has co-existing bacterial pneumonia. In the patient with MERS, we managed to ultrastructurally identify the viral particles in both the pneumocytes as well as the pulmonary macrophages, which was compatible with a direct viral cytopathic effect. It would be interesting to examine tissue by electron microscopy in SARS-CoV-2 infection as finding viral particles in these types of cells would emphasize the coronavirus localization.

SARS-associated portal and lobular hepatitis was linked to SARS-CoV RNA positivity in liver tissue.<sup>[7]</sup> Although portal and lobular hepatitis was described in both MERS-CoV<sup>[6]</sup> and COVID-19,<sup>[3]</sup> it is still not clear whether this is due to direct viral infection or secondary to other causes, such as drug-induced hepatitis or ischemia/hypoperfusion. Further studies are needed to establish whether the virus has a direct cytopathic effect on the liver. Similar to our patient with MERS,<sup>[6]</sup> there were no obvious histological changes in heart tissue in the case reported by Xu *et al.*,<sup>[3]</sup> suggesting

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that the observed clinical cardiac dysfunction and the high incidence of arrhythmia reported in one study with COVID-19<sup>[2]</sup> may not be related to direct SARS-CoV-2 infection of the myocardium.

Acute renal failure and kidney injury are commonly encountered in patients with SARS-CoV and MERS-CoV infections, and electron microscopy examination demonstrated viral particles in the renal tubular epithelial cells in SARS patients<sup>[5]</sup> and in our patient with MERS.<sup>[6]</sup> These findings may explain the deterioration in renal function in a substantial number of patients with SARS and MERS. The effect of SARS-CoV-2 on kidneys is yet to be explored, but emerging data suggest that the kidney may be an important target organ for SARS-CoV-2.<sup>[8]</sup>

Myopathy in the form of macrophagic infiltrate and myofiber necrosis and regeneration was described in SARS patients with RT-PCR reported positive in few cases, but neither viral antigen nor virus particles were identified.<sup>[9]</sup> In addition to the myopathic changes and lymphohistiocytic infiltrate, we ultrastructurally localized the viral particles in our MERS case.<sup>[6]</sup> No data on the SARS-CoV-2 effect on skeletal muscle are available until now.

Further histopathological data are required on SARS-CoV-2 to better characterize the involvement of organs that are affected clinically and that has high expression of angiotensin-converting enzyme 2, including kidney, gastrointestinal tract capillaries, lymph nodes, spleen, and muscles.

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## Conflicts of interest

There are no conflicts of interest.

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