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COVID-19 nephropathology: what could pathologist say?

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The pathogenetic mechanism of renal involvement in coronavirus disease 19 (COVID-19) is still unclear. It is supposed to result from a combination of several contributing factors, such as state of dehydration, leading to pre-renal failure with acute tubular necrosis, toxic tubular damage, induced by cytokine storm or rhabdomyolysis, cytopathic action induced by the virus that invades ACE2-expressing kidney cells and drug-induced nephrotoxicity.

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Coronavirus disease 19 (COVID-19) is a newly described pandemic infectious disease (1,2) mainly involving the respiratory tract, with alveolar and interstitial pneumonia in most serious conditions. Genomic analysis studies and pairwise protein sequence analysis highlighted a SARS-related coronavirus, the SARS-CoV-2 (severe acute respiratory syndrome-coronavirus-2), as the causative pathogen agent. The virus seems to have a probable bat origin and exploits the receptor-angiotensin converting enzyme II (ACE2) for entering the cells (3). ACE2 is a membrane-associated aminopeptidase expressed in several human tissues including respiratory tract, small intestine, vascular endothelia, renal and cardiovascular tissues (4). A rebus of COVID-19 is the onset of anosmia and ageusia probably secondary to a central nervous system (CNS) involvement. Some authors have suggested that the neurotropism of the virus may involve the brainstem and the respiratory center, as observed in SARS-CoV in both patients and experimental models (5). Thus, the disease shows a multi-organ involvement with a large spectrum of clinical manifestations. The severity of symptoms is extremely variable and the highest morbidity and mortality rate is detected in elderly men with chronic diseases (heart disease, diabetes, and hypertension). Kidney represents an important target organ of COVID-19 (2). As reported in a recent case series (6), the main manifestations of

the renal involvement include proteinuria, elevated plasma creatinine and blood urea nitrogen, hematuria and, less frequently, acute kidney injury (AKI). The development of AKI during hospitalization seems related to a previous kidney disease and associated with higher in-hospital mortality. The pathogenetic mechanism of renal involvement is still unclear. It is supposed to result from a combination of several contributing factors, as clearly summarized by Mubarak and Nasri (7). These mechanisms could be mainly related to 1) state of dehydration, leading to pre-renal failure with acute tubular necrosis, 2) toxic tubular damage, induced by cytokine storm or rhabdomyolysis, 3) cytopathic action, induced by the virus that invades ACE2-expressing kidney cells, and 4) drug-induced nephrotoxicity. SARS-CoV-2 mechanism of action in kidney is debated. In particular, the questions related to the pathogenesis of kidney damage reflect those that underlie the COVID-19: how much the clinical manifestations are attributable to the virus itself or to the immune response triggering a cytokine storm? What is the role of previous systemic pathologies on the course of the disease? The autopsic practice could give an important contribution to carefully study the histopathological lesions associated with the infection. The examination of organs and tissues could clarify the role of the various pathogenic noxae in triggering kidney damage, as happened in several kinds of glomerulopathies related to viral infections, such

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as collapsing glomerulopathy during HIV. Furthermore, nephrologists take advantage of an extremely useful technique, the electron microscopy (EM), often used in their diagnostic practice. The use of transmission and scanning electron microscopy for the identification of viral particles in autoptic specimens has been reported in the literature (8). It could allow us to investigate if SARS-CoV-2 shows a tropism for a specific renal cell and to explore if the kidney damage results from a direct viral cytopathic effect or if it is exclusively secondary to a systemic involvement of the disease. The recent detection of the viral RNA in urine samples strongly supports the evidence of viral tropism in renal tissue but the specific target is still unknown. The ultrastructural studies could be also applied for the examination of other organs or tissues, such as the CNS. While the contribution of molecular investigations is of undeniable advantage, not less important is the value of EM. Although molecular analysis provides fast identification of the viral RNA, EM could have the advantage to provide additional morphological data concerning the virus localization in cellular and subcellular sites. The evidence of specific cellular and subcellular involvement by EM and immunogold could allow us to better understand specific fine structure changes and biologic circuits, a powerful way to discover target therapeutic approaches. The questions regarding the pathogenetic mechanisms underlying COVID-19 exceed the answers so far. In this complex scenario, pathologists could give an important contribution in unravelling this enigmatic and unpredictable disease, thus supporting an evidence-based practice.

Authors' contribution

FF and FP prepared and revised the manuscript equally.

Conflicts of interest

Authors declare no conflict of interest.

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