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Perspective

The COVID-19 pandemic: Pathologists support the clinical infectious diseases team

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ABSTRACT

The pathologist is involved in many diagnostic steps together with the clinical infectious disease team in the management of COVID-19-affected patients. In particular, cytological and histopathological procedures as well as autoptic findings may represent useful tools to better understand the pathobiology of the disease as well as to correctly define causes of death. Moreover, pathologists have been forced to reconsider the usual laboratory workflow and introduce adequate guidelines against virus diffusion in the COVID-19 pandemic, requiring high biosafety levels.

Introduction

The severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2) virus has produced a worldwide diffusive disease (COVID-19), which was defined by the World Health Organization (WHO) as a pandemic in March 2020. Consequently, many governments have adopted a series of public health measures in order to promote social distancing and reduce the spread of COVID-19. Therefore, cultural and political meetings have been cancelled; schools, universities and gyms have been closed; smart working from home has been recommended; avoiding frequenting bars and restaurants has been advised; and travel between different countries has been advised to be avoided. However, analysing the clinical course of COVID-19, the WHO has considered 3% of cases as critical and requiring intensive care (ICU), 15% as severe and needing hospitalisation and 82% as mild and being sufficient to undergo quarantine and home therapy (Yang et al., 2020; Vetter et al., 2020).

Safety in the pathology laboratory

There is no doubt that pathologists have to be included in all healthcare systems, mainly because they are involved in many diagnostic steps from cytology and histopathology processes, to autopsy of COVID-19 cases in order to better understand the pathobiology of the disease and correctly define cause of death. Therefore, in this pandemic, pathology laboratories have had to reconsider the usual workflow, introducing adequate guidelines against virus diffusion among staff personnel and also requiring typical biosafety level 2 (Barbareschi et al., 2020; Carpenito et al., 2020; Kaufer et al., 2020; Pambuccian, 2020). Nevertheless, the main fixatives that are used in pathology laboratories are represented by alcohol solutions of >70% and formalin; both are considered to be extremely effective in destroying COVID-19. Obviously, protective equipment and additional measures (hand-washing with sanitizers, wearing gloves, etc.) have to be respected together with decontamination of all working surfaces (Centers for Disease Control and Prevention, 2020).

Cytology procedures

The first impact for pathologists concerning COVID-19 patients is the cytological approach. In fact, sputum and bronchoalveolar lavage fluid (BAL) should be the first relevant laboratory step, especially when nasopharyngeal/oropharyngeal swabs have already been performed with negative results. Nevertheless, cytological findings encountered in the above-mentioned cytological samples are generally unspecific, reflecting lung injuries; therefore, the presence of macrophages (frequently in aggregates) with characteristic foamy cytoplasm and ground glass nuclei, together with a variable component of granulocytic neutrophils, multinucleated cells, damaged alveolar elements and squamous metaplastic bronchial epithelium has repeatedly been reported (Damiani et al., 2021; Parada et al., 2020; Reusken et al., 2020;

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Vasquez-Bonilla et al., 2020). However, although the cytological features are inconclusive for the diagnosis of COVID-19 disease, it must be stressed that some fixatives characterised by a weaker alcohol concentration used in thin preparations (PreservCyt, CytoLyT, SurePath) may probably be inadequate to inactivate the virus. It is therefore mandatory to apply greater caution in the cytology laboratory (Pambuccian, 2020).

Histopathology approach

It is well known that SARS-CoV-2 determines histologic changes in lungs, producing acute respiratory distress syndrome and presenting diffuse alveolar damage (DAD) (Al Nemer, 2020; Damiani et al., 2021). In detail, DAD is associated with oedema, vascular congestion, proteinaceous exudates constituting hyaline membranes as well as inflammatory infiltration of various entity, with the presence of fibrin thrombi and vascular injuries and various degrees of fibroblastic organised plugs (Konopka et al., 2020; Polak et al., 2020). Moreover, viral particles have been detected, by electron microscopy, in type I and II pneumocytes, tracheal biopsies and bronchial mucus (Bradley et al., 2020; Prieto-Pérez et al., 2020). Additionally, other relevant pathologic findings induced by COVID-19 have been documented outside of the respiratory tract, including some organs such as the heart, liver, kidney and central nervous system; the characteristics of these lesions came from autoptic post-mortem examinations (Damiani et al., 2021; Vasquez-Bonilla et al., 2020). Consequently, the central role of the pathologist to ascertain this peculiar kind of diffusive pathology is furtherly highlighted.

Autopsy information

For suspected or affected COVID-19 patients a specific autopsy protocol should be applied, taking into consideration measures provided by governments, ministries of health and local regional advice. The autopsy room and the procedures of internally managed biological samples need a safety level 3, as designed by the Centers for Disease Control and Prevention (Centers for Disease Control and Prevention, 2020). In detail, the autopsy room needs to be at a negative pressure, with a minimum of 6–12 air changes per hour for existing or new structures, and having an efficient adequate particulate filter (Centers for Disease Control and Prevention, 2020). Although the details about technical execution of autopsy are out of scope of this paper, it must be noted that any COVID-19-affected or suspected deceased patient should be preliminary investigated by a swab for molecular detection of SARS-CoV-2 by PCR (Carpenito et al., 2020; Centers for Disease Control and Prevention, 2020). Moreover, an early performed autopsy has been suggested, specifically before the routine $\geq$16 hours expected after death, in order to avoid post-mortem phenomena and likewise to obtain high-quality biological samples to perform immunohistochemical, ultrastructural and biomolecular investigations (Carpenito et al., 2020).

Many series of autopsies concerning patients affected by COVID-19 coming from different countries have been reported, and all of them have stressed the viral cytopathic effect not only in lungs but also in different organs and parenchyma (Ackermann et al., 2020; Calabrese et al., 2020; Pesaresi et al., 2020). From many of these reports it can be argued that SARS-CoV-2 infection represents a multiorgan pathology, in which together with DAD some additional lesions have been encountered in the heart (lymphocytic myocarditis, thrombotic vascular occlusion), brain (encephalitis, ischaemic or haemorrhagic infarcts, vasculitis), kidney (tubular injury, arterionephrosclerosis), liver (steatosis, lymphatic lobular infiltration), lymph nodes and bone marrow (histiocytosis, haemophagocytosis) (Calabrese et al., 2020; Damiani et al., 2021; Vasquez-Bonilla et al., 2020). Therefore, all the reported post-mortem findings suggest a central role for pathologists in order to better understand and explain the pathological impact of SARS-CoV-2 infection.

Conclusions

The knowledge of pathological lesions in different organs and the analysis of their peculiar tissue characteristics may greatly contribute to critically examining the interactions between human host and virus, addressing a more accurate therapeutic approach against symptoms and complications during the COVID-19 pandemic.

Conflict of interest

None declared.

Ethical approval

Not applicable.

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