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PATHOLOGY MATTERS

Giovanni Di Guardo: Animal Models and Pathogenetic Insights to Covid-19

As a veterinary pathologist I feel ‘reassured’ by the recent data originating from the autopsies and the ancillary investigations performed on Covid-19-affected patients.

In this respect, the comparative pathology data obtained from experimentally challenged animals such as non-human primates, cats and ferrets, the latter two highly susceptible to experimental infection (Shi *et al.*, 2020), may prove additionally useful in dissecting the pathogenesis of SARS-CoV-2 disease. Indeed, vasculitis and intravascular coagulation, along with pulmonary endoalveolar fibrin leakage, have been reported in the two aforementioned Covid-19 experimental disease models (Shi *et al.*, 2020).

Noteworthy, abnormal coagulation parameters compatible with disseminated intravascular coagulation (DIC) have been linked to a poor prognosis in SARS-CoV-2-infected patients, who may suddenly develop very severe forms of disease leading to death (Tang *et al.*, 2020). This most likely results from viral targeting of endothelial cells, as the virus likely gains access to host cells through angiotensin-converting enzyme 2 receptors (Lan *et al.*, 2020), which are widely expressed by endothelial cells (Donoghue, 2000). The viral damage to the inner vascular wall throughout the body, including the blood–brain-barrier endothelium, may well explain the DIC and ‘cytokine storm’ experienced by those individuals developing very severe disease forms. Endothelial cells are, in fact, immunologically active, with heparin having been indicated as a drug efficiently counteracting the DIC associated with SARS-CoV-2 infection (Lin *et al.*, 2020).

In other words, the ‘popular’ view of Covid-19 as a ‘viral pneumonia’ is being progressively comple-

mented by that of a disease characterized by DIC and an excessive immune response, causing in turn a severe and swift ‘multiorgan dysfunction’.

We should give special thanks to pathologists who, I believe, are not being given the credit they deserve by the media in Italy and in many other countries.

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