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Lung fibrosis: an undervalued finding in COVID-19 pathological series

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With the COVID-19 pandemic having reached tremendous proportions, post-mortem series are under the limelight to explain many of the peculiar clinical findings. Pathological descriptions of disease are fundamental for understanding pathogenetic features and might inform new treatments. Indeed, the widely discussed identification of thrombosis in patients with COVID-19 has garnered much interest, and has resulted in new treatment strategies, with anticoagulants now part of patient management.

In their Article, Luca Carsana and colleagues¹ describe the lung findings of 38 patients who died with COVID-19 and show that early-phase or intermediate-phase diffuse alveolar damage is the main pathological finding, as well as fibrin thrombi in small arterial vessels.¹ Other autopsic series, composed of fewer cases, also show thrombotic events to be findings specifically related to COVID-19.^{2,3} The fibrotic changes seen in patients who died with COVID-19 who had severe disease of long duration have been, however, only briefly touched upon in published studies, and no complete pathological description of these cases is available.

Between April 16, and May 4, 2020, we collected lung tissue using a cryobiopsy approach from eight patients in our institution who died in intensive care with COVID-19 (unpublished). Patients died after a mean disease duration of 31.3 days (SD 8.3), a much longer duration of illness than reported in the study by Carsana and colleagues, in which the mean time from symptom onset to death was 16 days (SD 6). Tissues obtained by cryobiopsy are comparable to specimens from live patients as the procedure is done within 30 min of death. We observed marked fibrotic lung parenchymal remodelling, characterised by fibroblast proliferation, airspace obliteration, and micro-honeycombing in many of the available cryobiopsies (appendix). This aspect has been described in other series,¹⁻³ but we feel it has not received as much attention as it should.

Presumably, the fibrotic pathological findings are unlikely to regress in patients with severe COVID-19 who survive, although prospective studies are necessary to identify long-term functional impairment.⁴ Whether the cause of fibrotic findings in the lungs is viral infection, the secondary cytokine cascade, related to treatment or ventilation, or a mixture of all these things is unknown; however, tissue collection must be part of, and indeed become the basis for, more in-depth studies.⁵

As more pathological information is being collected from COVID-19 post-mortem series, a clearer picture of the disease, and its possible short-term and long-term complications, will emerge and hopefully aid treatment.

We declare no competing interests.

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- 5 Burnham EL, Janssen WJ, Riches DW, Moss M, Downey GP. The fibroproliferative response in acute respiratory distress syndrome: mechanisms and clinical significance. *Eur Respir J* 2014; **43**: 276–85.

See Online for appendix