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Histopathological Correlates of Long COVID: Emerging Patterns and Mechanisms.

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Introduction

The coronavirus disease 2019 (COVID-19) pandemic, caused by *Severe Acute Respiratory Syndrome Coronavirus 2* (SARS-CoV-2), has generated a significant subset of patients experiencing persistent or recurrent symptoms long after acute infection — a condition now termed *Long COVID* or *Post-Acute Sequelae of SARS-CoV-2 infection* (PASC). While clinical presentations such as fatigue, cognitive dysfunction, dyspnea, and myalgia are widely reported, the histopathological underpinnings of Long COVID remain an emerging area of investigation.

Histopathology offers a unique lens to identify structural and cellular alterations in affected tissues, providing critical insight into disease mechanisms [1, 2, 3, 4, 5]. Recent autopsy and biopsy studies have revealed sustained microvascular damage, low-grade inflammation, and aberrant immune responses in multiple organ systems. Notably, persistent endothelial injury, microthrombosis, and immune cell infiltration have been observed in lung, brain, cardiac, and skeletal muscle tissues. These pathological changes may be linked to viral persistence, dysregulated immune signaling, and autoimmune phenomena triggered by the initial infection.

Emerging evidence also highlights mitochondrial dysfunction and chronic inflammatory infiltrates as central contributors to ongoing symptoms. The overlap between histopathological patterns in Long COVID and other post-viral syndromes suggests shared mechanistic pathways, but the unique endothelial and vascular signatures of SARS-CoV-2 infection may explain its broader systemic impact. Understanding these correlations is crucial for developing targeted interventions and prognostic biomarkers.

Conclusion

The histopathological landscape of Long COVID reveals a complex interplay between persistent inflammation, microvascular pathology, and immune dysregulation. Although studies are still in early stages, recurring patterns — including endothelial damage, microthrombi, and chronic inflammatory cell presence — are consistently reported across organ systems. These findings reinforce the need for multidisciplinary approaches, combining histopathology, molecular profiling, and clinical phenotyping to clarify causative mechanisms. As our understanding deepens, histopathological insights will be vital in guiding the development of diagnostic markers, individualized therapeutic strategies, and preventive interventions for the long-term sequelae of COVID-19.

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