In the post-acute phase of COVID-19, there is an increased risk of neurologic sequelae that affect the central nervous system (CNS), such as anosmia, dizziness, headache, stroke, cognitive and memory disorders, extrapyramidal and movement disorders, mental disorders, and encephalitis or encephalopathy, as well as the peripheral nervous system (PNS), such as sensory disorders, polyneuropathy, Guillain–Barré syndrome, orthostatic intolerance, and syncope. In this retrospective study, the authors from the United States presented patients diagnosed with a new-onset small fiber neuropathy (SFN) after COVID-19. SFN was diagnosed with a skin punch biopsy, a reliable diagnostic tool.

Patients diagnosed with SFN experience neuropathic symptoms like distal symmetric burning pain, allodynia, impaired temperature sensation, paresthesia, and numbness. The manifestations of autonomic paralysis in SFN include anhidrosis, orthostatic hypotension, lack of tears and saliva, impaired control of heart rate, weak bowel and bladder sphincters with overflow incontinence, and weakness and dilatation of the esophagus and colon. It was reported that symptoms of dysautonomia in SFN are associated with autoantibodies to trisulfated heparin disaccharide (TS-HDS) or fibroblast growth factor receptor 3 (FGFR3).

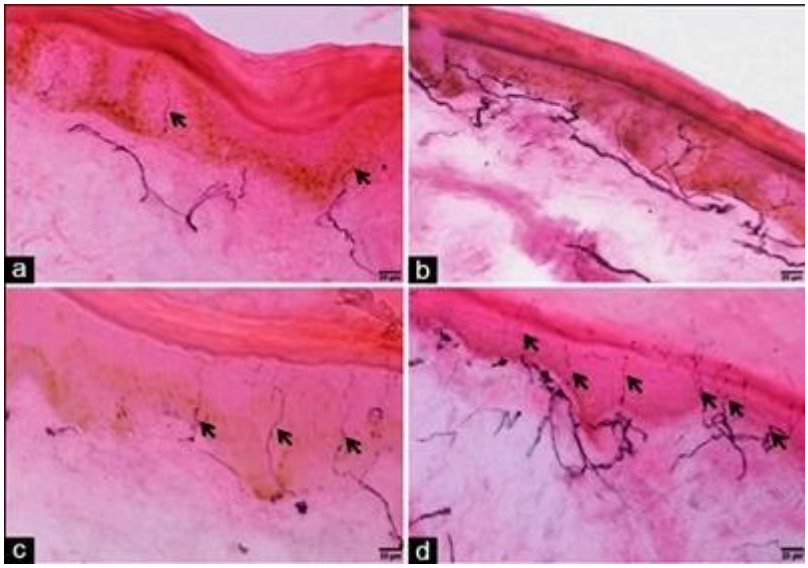
It is assumed that immune dysregulation during infection with severe acute respiratory

syndrome coronavirus 2 (SARS-CoV-2) may contribute to small fiber nerve damage. A recent study found neurological sequelae as decreased density and length of corneal nerve fibers in patients with long COVID syndrome more than 20 months after acute infection. https://discovermednews.com/reduced-corneal-innervation-increased-dendritic-cell-density-long-covid-patients/

About the study

This retrospective study enrolled 16 individuals diagnosed with post-acute/long COVID syndrome and new-onset SFN. The majority of patients had mild COVID-19, and 38% were hospitalized during the acute infection, but none needed intensive care. The median age was 47 years (from 40 to 58), and 75% were women.

The inclusion criteria were as follows: a diagnosis of post-acute/long COVID syndrome based on the World Health Organization definition, a diagnosis of new-onset SFN using punch skin biopsy, no prior diagnosis of neuropathy, and negative electrodiagnostic and laboratory tests for neuropathy of any other cause. The onset of SFN symptoms after COVID-19 vaccination and a previous diagnosis of neuropathy from any other causes were considered the exclusion criteria.



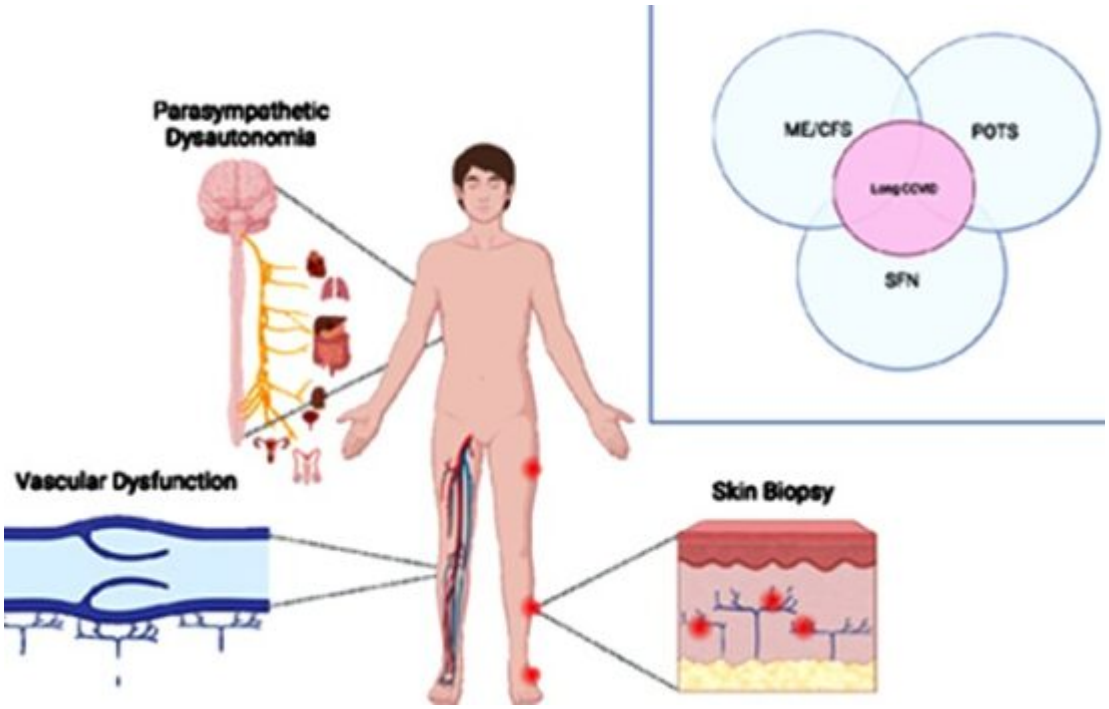
Results

In individuals diagnosed with a new-onset SFN and post-acute/long COVID syndrome, the symptoms of neuropathy such as numbness, paresthesia, and allodynia occurred at a median of 2.5 weeks after the onset of COVID-19. The participants also reported symptoms of dysautonomia as follows: 69% of them reported orthostatic hypotension, 77% reported altered sweating, and 85% had a labile heart rate.

92% of participants reported post-exertional malaise, a characteristic symptom of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). Cardiopulmonary exercise testing (iCPET), performed on six patients who experienced post-exercise malaise and dysautonomia, demonstrated neurovascular dysregulation and dysautonomia consistent with ME/CFS.

Three of 16 individuals diagnosed with a new-onset SFN were positive for autoantibodies to TS-HDS, while three others were positive for autoantibodies to FGFR3. Six of nine patients tested for autoantibodies for sensory neuropathy were positive.

Eight patients were treated with intravenous immunoglobulin (IVIG) for a median of 9.5 months (3 to 18.5 months). Most of them (63%) experienced resolution of neuropathic symptoms. In the remaining 37%, the intensity and duration of their symptoms were significantly reduced. Importantly, patients without complete resolution of neuropathic symptoms were subsequently diagnosed with diabetes or pre-diabetes.



Original illustration from the study of McAlpine LS et al, 2023

Conclusion

This study presented 16 patients diagnosed with post-acute/long COVID syndrome and new-onset SFN. The authors concluded that further studies are necessary to investigate the underlying pathophysiology of small nerve fiber damage after COVID-19, and the link between SFN and ME/CFS. Also, larger clinical trials should demonstrate the efficacy of IVIG in treating SFN that developed after the SARS-CoV-2 infection.

This study was published on a preprint server and is currently being peer-reviewed.

Journal Reference

McAlpine LS et al. Small Fiber Neuropathy after COVID-19: A Key to Long COVID. medRxiv preprint. https://doi.org/10.1101/2023.11.07.23297764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