The authors from the United States presented a case series of a new-onset small fiber neuropathy (SFN) after COVID-19. In 16 patients with neuropathic and autonomic symptoms, a skin punch biopsy was used to diagnose SFN. Eight of them were treated with intravenous immunoglobulin (IVIG), and subsequently experienced a significant improvement in their neuropathic symptoms.

More than two years after the global COVID-19 pandemic, it is clear that infection with the severe acute respiratory syndrome coronavirus type-2 (SARS-CoV-2) can lead to a new disease called long-COVID-19 or post-acute COVID-19 syndrome (PACS). Patients diagnosed with long COVID frequently have symptoms of dysautonomia and neuropathy. It was hypothesized that immune dysregulation during a viral infection may result in damage to small fiber nerves, and consequently, in SFN.

Distal symmetric burning pain, allodynia, impaired temperature sensation, paresthesia, and numbness are some neuropathic symptoms in SFN. Anhidrosis and orthostatic hypotension, which are the two most frequent manifestations of autonomic paralysis, occur frequently in SFN. Other autonomic manifestations include a 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. The electrodiagnostic testing is negative in SFN. The skin punch biopsy is a reliable diagnostic tool for diagnosing SFN. Previous studies have found that SFN and symptoms of autonomic dysfunction are associated with autoantibodies to trisulfated heparin disaccharide (TS-HDS) or fibroblast growth factor receptor 3 (FGFR3).

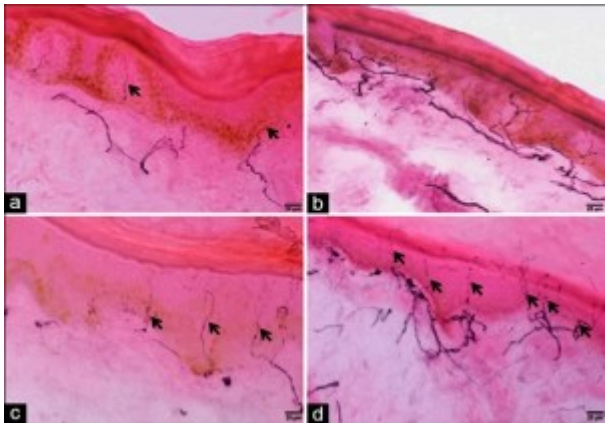
About the study

This retrospective study was conducted on 16 patients who developed new-onset SFN after

a documented COVID-19. The inclusion criteria were as follows: a diagnosis of long COVID based on the definition by the World Health Organization, a positive punch skin biopsy, no prior neuropathy diagnosis, and negative electrodiagnostic and laboratory tests for any other cause of neuropathy. The criteria for exclusion were: the onset of symptoms after anti-COVID-19 vaccination, and a previous diagnosis of neuropathy from any other cause. As there is evidence that immune system dysregulation may be an important factor in some COVID-19- related disorders, eight patients were treated with IVIG for a median of 9.5 months (3 to 18.5 months).

The results

A skin punch biopsy was used to diagnose SFN in 16 patients. The median age was 47 (40 – 58), and 75% of the cohort were women. The majority of patients had a mild COVID-19 illness, and 38% of them were hospitalized during the acute infection, but none needed intensive care. The symptoms of neuropathy, including numbness, paresthesia, and allodynia, occurred a median of 2.5 weeks after the beginning of COVID-19.



Nine patients were tested for autoantibodies for sensory neuropathy, and six of them were positive. Three patients were positive for TS-HDS, while three others were positive for FGFR3.

Dysautonomia in patients with a new-onset small fiber neuropathy after COVID-19 included orthostatic hypotension in 69% of patients, altered sweating in 77% of patients, and labile heart rate in 85% of patients. 92% of patients reported post-exertional malaise, which is characteristic of myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). The

cardiopulmonary exercise test, which assessed neurovascular dysregulation and dysautonomia, was performed in seven patients who showed symptoms of post-exercise malaise and dysautonomia. The results showed a decrease in aerobic capacity, an increase in peak mixed venous oxygen saturation, a decrease in arteriovenous oxygen difference, and low biventricular filling pressures.

Eight patients received IVIG therapy, and 63% of them experienced resolution of symptoms of neuropathy. The remaining 37% of patients experienced a significant reduction in the intensity and duration of their symptoms. It is noteworthy that patients without complete resolution of neuropathic symptoms were diagnosed with diabetes or pre-diabetes.

The authors emphasized the need for further studies to better understand the underlying pathophysiology of small nerve fiber damage after COVID-19, and its link to ME/CFS. Also, a larger clinical trial is needed to further demonstrate the efficacy of IVIG in treating SFN after the SARS-CoV-2 infection.

The results of the study have been published on a preprint server and are 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