

TIBIAL NERVE MONONEUROPATHY POST-COVID-19 AND SUCCESSFUL MANAGEMENT WITH PERIPHERAL NERVE STIMULATION: A CASE REPORT

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Background: Infection with COVID-19 has evolved from a novel health crisis into an entity with a myriad of increasingly recognized sequelae. Among these, peripheral neuropathy is often an underrecognized and underdiagnosed complication. Neuropathic pain can be challenging to treat with many cases being refractory to conservative management, often requiring advanced techniques. Neuromodulation has become an important tool for the treatment of the refractory cases.

Case Report: We present a case of a 43-year-old woman with refractory right tibial mononeuropathy secondary to COVID-19 infection who was treated successfully using peripheral nerve stimulation.

Conclusions: The use of peripheral neuromodulation represents a pivotal strategy for the management of difficult cases. Our case highlights the first use of neuromodulation to treat neuropathic pain secondary to COVID-19 infection. We hope that this case sparks further research on the topic, which could lead to better clarification of this condition and potential expansion of treatment strategies.

Key words: Neuromodulation, peripheral nerve stimulator, long COVID, tibial neuropathy, neuropathic pain

BACKGROUND

COVID-19, caused by the SARS-CoV-2 virus, rapidly emerged as a global health crisis, primarily recognized for its respiratory implications. However, accumulating evidence suggests a broader impact. Neurological manifestations associated with COVID-19 range from mild symptoms like anosmia and ageusia to more severe complications, such as encephalitis, stroke, and various types of neuropathies. Among these, peripheral nerve involvements, including mononeuropathies, represent a less explored yet significant aspect of the virus's neurological impact. As the link between COVID-19 and peripheral neuropathies becomes more recognized (6), we anticipate that patients with this diagnosis to increase in number in our practices, which leads to the

question of what would be the best approach when dealing with these patients and whether therapies that have been proven to be beneficial with other type of neuropathies will be effective in treating the ones secondary to COVID-19 infection.

Mononeuropathy involves the dysfunction of a single nerve, often leading to motor, sensory, or autonomic symptoms. As is well understood, this type of pain can be debilitating and can become a significant burden given its impact on quality of life. This can affect other aspects of life, sometimes leading to depression, anxiety, and sleep disorders as it often takes away the patient's independence. In the context of COVID-19, the exact mechanisms leading to mononeuropathy are not entirely understood, but are thought to involve direct or

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indirect effects of the virus on the peripheral nerves. The involvement of systemic inflammation, immune responses, and potential vasculopathies are all considered to be contributing factors (1,2). In regards of the timing, the literature suggests that neuropathic pain after an infection can be an immediate consequence of it and, in other cases, it can present as a delayed complication (3).

Even though efforts have been made to delineate the prevalence of this type of complication, the evidence seems to suggest that although in the hospitalized population the prevalence has been reported to be below 10%, when the patients are evaluated in the context of long COVID, up to one-third of patients, or more specifically, 34.3% suffer from this syndrome (3).

This case report represents an uncommon instance of tibial nerve mononeuropathy in a patient following a COVID-19 infection. The rarity of this specific neuropathy in relation to COVID-19 and the successful application of a peripheral nerve stimulator for pain relief mark a notable addition to the current medical literature. This case not only contributes to the growing body of evidence concerning the neurological sequelae of COVID-19, but also highlights the potential of innovative therapeutic approaches in managing such complications.

CASE PRESENTATION

A 43-year-old right-handed woman with a medical history of hypertension, diabetes, depression, and anxiety, presented to our clinic with persistent symptoms of right-foot pain following a severe COVID-19 infection in April 2020; this involved a 4-week hospitalization, including mechanical ventilatory support for close to 3 weeks (Table 1). After she was weaned off the ventilator, she began experiencing pain and numbness on the plantar surface of her right foot. This neuropathic pain was characterized as constant numbness and pins-and-needles sensation, which was rated 7/10 in intensity on the Numeric Rating Scale. In addition, the discomfort extended into all 5 toes and the spaces in between. The pain was aggravated by standing, walking, sitting, and wearing enclosed socks, while relief was found when resting the foot on fluffy pillows or cold surfaces. Additionally, she reported changes in nail growth on her right great toe without alterations in temperature or color, and no symptoms of allodynia or hyperpathia. Notably, the patient reported being in pain 75% of the time and denied any history of trauma or casting of the affected limb.

In regards of workup, the patient underwent an

extensive multidisciplinary diagnostic evaluation (Table 1). Diabetic neuropathy was considered a less likely cause given the stable glycosylated hemoglobin of 5.8% and the lack of typical distribution of neuropathic symptoms. Hypovitaminosis, including vitamin B12, folate, vitamin D, and other causes like thyroid disorders, anemia, and chronic alcoholism were all ruled out. On rheumatologic examination, she was found to have positive antinuclear antibodies in the setting of family history of this condition. Rheumatologic workup was then performed, which yielded no association with her symptomatology. Electromyography showed small amplitude of the right more than left tibial nerves. In essence, given the temporal relation with the symptom development and the lack of another explanation for her symptoms, the most likely cause was deemed to be the COVID-19 infection.

Since the start of the process, she had an extensive trial and failure of multiple medications, including gabapentin, pregabalin, duloxetine, tramadol, and memantine, which yielded minimal benefits (Table 1). In addition, she underwent multiple diagnostic and therapeutic interventional procedures, which included intravenous (IV) lidocaine infusion, ketamine infusion, capsaicin treatment, and eventually a right posterior tibial nerve block. This block provided a temporary 20% improvement of her pain. Taking into account the lack of success with oral therapies and interventional procedures, we offered and performed a trial with spinal cord stimulation, which was also unsuccessful (Table 1).

After multiple discussions with the patient and a multidisciplinary discussion of her case, we decided to offer a trial of right posterior tibial nerve percutaneous stimulation, which the patient agreed to have. This trial procedure was performed, in September 2023, using fluoroscopic and ultrasound techniques to guide a single lead to its destination in close proximity to the posterior tibial nerve (Fig. 1, Table 1). The agreed-upon trial period was 7 days. To our surprise, the trial resulted in significant improvement of her pain, with over 75% reduction in her right-foot discomfort. Encouraged by this positive response, she underwent permanent peripheral nerve stimulator implantation and has experienced positive results to this date from the implantation (Table 1).

It is important to highlight the positive impact that this intervention has had in this patient's life. She has been able to engage more actively in her personal life, has improved her associated psychosocial challenges, and has

Table 1. Timeline of event occurrence.

COVID-19 infection with ICU admission	April 2020
Development of symptoms of right-foot peripheral neuropathy	May 2020
Extensive diagnostic evaluation for potential other causes of peripheral neuropathy	May 2020-2021
Trial and failure of multiple medication modalities and peripheral nerve block (tibial nerve)	2021-2022
SCS trial (unsuccessful)	August 2022
Posterior tibial nerve peripheral nerve stimulator trial (successful)	September 2023
Permanent implantation of peripheral nerve stimulator	November 2023

Abbreviations: ICU, intensive care unit; SCS, spinal cord stimulation.

changed her perspective about the future. Interestingly, at the time of this publication, she is currently working on sharing her experience online in hopes to reach other individuals with similar experiences after COVID-19 infection with the hope of facilitating their course and raising awareness of the options available for them.

DISCUSSION

In this case report detailing tibial nerve mononeuropathy in a post-COVID-19 patient, the first question that comes to mind is whether COVID-19 alone, another etiology, or a combination of factors was the genesis of this condition. At this point in time, COVID-19 neuropathy continues to be a diagnosis of exclusion. As presented, our patient underwent an extensive multidisciplinary evaluation, which yielded no other reasonable explanation for her symptoms. We anticipate that as the neurologic sequelae of COVID-19 continues to be more recognized, more patients will be identified and diagnosed with this condition. At the time of this publication, there is no established diagnostic tool or criteria in the literature reviewed.

In regards of treatment, our case highlights the implementation of peripheral nerve stimulation (PNS) as a pivotal and innovative aspect of the treatment strategy. Neuropathic pain is a prevalent symptom among long COVID patients, with a pooled prevalence of 6.7% in hospitalized patients during the acute phase and 34.3% in long COVID patients (3). Our patient's persistent symptoms of pain and numbness on the plantar surface of the right foot, coupled with the characteristic pins-and-needles sensation, typify neuropathic pain

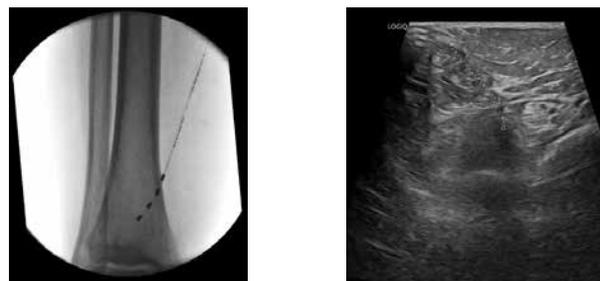


Fig. 1. Fluoroscopic and ultrasound images showcasing the placement of PNS trial leads. PNS, peripheral nerve stimulation.

symptoms, indicative of nerve damage. Her extensive treatment history, encompassing IV lidocaine and ketamine infusions, a range of oral medications, and nerve blocks, mirrors standard neuropathic pain management strategies. However, the limited and temporary relief experienced by our patient is not unusual, reflecting the complex nature of treating neuropathic pain, particularly when it emerges in the aftermath of COVID-19.

PNS has emerged as a promising technique in managing such chronic pain conditions. By delivering controlled electrical impulses directly to the affected peripheral nerve there is modification or inhibition of the transmission of pain signals to the brain. The efficacy of PNS in managing neuropathic pain can be attributed to its targeted approach, which allows for the direct modulation of pain pathways at the peripheral nerve level. This method of pain control can be particularly effective in cases where neuropathic pain is localized and persistent, as seen in our case of tibial nerve mononeuropathy (4).

The successful application of a peripheral nerve stimulator in our patient, leading to significant pain relief, underscores the potential of this technology in managing post-COVID-19 neuropathic pain. This aligns with emerging literature that emphasizes the importance of innovative pain management strategies in the post-COVID-19 context, where peripheral neuropathies are increasingly recognized (5,6). Additionally, the use of PNS in our case is significant in highlighting the role of advanced therapeutic options in the management of COVID-19-related neuropathies, which can often be resistant to conventional pain medications. It opens up avenues for further research into the efficacy and long-term outcomes of PNS in similar neuropathic conditions post-COVID-19.

CONCLUSIONS

Peripheral neuropathy secondary to COVID-19 is and will continue to be more recognized as an important sequela after an infection. Regardless of the etiology, peripheral neuropathy is a condition that many times is difficult to treat and is refractory to multiple medication and interventional strategies. The use of advanced techniques like peripheral neuromodulation represents

a pivotal strategy for the management of difficult cases. Our study highlights the first instance of usage of neuromodulation to treat neuropathic pain secondary to COVID-19 infection. We hope that cases like these spark further research in the topic, which could lead to further clarification of this condition and potential expansion of treatment strategies.

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