PAIN MEDICINE CASE REPORTS

ISSN 2768-5152

Volume 8, Number 7, pp. 253-256

Use of Neuromodulation to Treat Post-COVID Neuropathic Pain: A Case Report

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Background: Post-COVID-19 neuropathic pain is a difficult-to-treat condition seen in approximately one-third of patients with long COVID. It has been shown to be resistant to many first-line therapies as well as over-the-counter and prescription medications.

Case Report: We present the case of a 27-year-old man who developed bilateral upper extremity neuropathic pain in conjunction with a severe COVID-19 infection. He failed occupational therapy, multiple medications, and a stellate ganglion block. A dorsal column stimulator was placed and provided the patient with both pain relief and improved functionality.

Conclusions: Given the results of this case and the history of neuromodulation in effectively treating neuropathic pain, we submit that neuromodulation is a viable option for patients with refractory post-COVID-19 neuropathic pain.

Key words: Neuromodulation, neuropathic pain, post-COVID-19 syndrome, dorsal column stimulation, case report

BACKGROUND

The virus responsible for COVID-19, SARS-CoV-2, has been implicated in causing chronic disease involving multiple systems throughout the body, which can be seen for months after a patient has recovered from a COVID-19 infection (1,2). These residual effects have been termed "long COVID" and can be resistant to first-line therapies. One system, in particular, that is affected in about one-third of patients with long COVID is the nervous system. The etiology of post-COVID-19 neuropathic pain is still being elucidated but seems to be related to increased nociceptor excitability and peripheral/central sensitization after COVID-19 infection. From a demographics standpoint, younger patients, men, those with depression, and those with more severe disease requiring an intensive care unit stay were more prone to develop neuropathic pain (1,3).

Neuropathic pain is the pain that results due to any lesion or disease of the somatosensory nervous system, as per the International Association for the Study of Pain (4). The mechanisms behind neuropathic pain after viral infection are multiple but seem to be mainly immune-related involving the release of proinflammatory cytokines and other inflammatory mediators, such as tumor necrosis factor-alpha (1,2,5,6). Prior to COVID-19, other human coronaviruses were known to infect the nervous system through similar immune-mediated mechanisms. There may also be some direct neural invasion, as seems to be the case with the effect of coronavirus on the olfactory system (2).

Neuropathic pain is particularly troublesome among COVID-19-induced pain states because it has been shown to be quite challenging to effectively treat (7,8). In general, patients start with over-the-counter analgesics, which have not been shown to be overly beneficial in this population. Prescription medications, such as gabapentinoids, serotonin and norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants,

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Disclaimer: There was no external funding in the preparation of this manuscript.
Conflict of interest: Each author certifies that he or she, or a member of his or her immediate family, has no commercial association (i.e., consultancies, stock ownership, equity interest, patent/licensing arrangements, etc.) that might pose a conflict of interest in connection with the submitted manuscript.
Patient consent for publication: Consent obtained directly from patient(s).
This case report adheres to CARE Guidelines and the CARE Checklist has been provided to the journal editor.
Accepted: 2024-07-10, Published: 2024-11-30

and topical therapies (such as lidocaine and capsaicin) tend to be the next steps but have only been shown to be modestly beneficial (7,8). Opioid medications, such as tramadol and full mu agonists like hydrocodone and oxycodone, have been used in refractory cases, but also have not shown notable benefit in these patients and come with their own set of side effects and problems (2,7,8). Reliable pain control for post-COVID-19 neuropathic pain has been difficult to achieve with conservative therapies, which have opened the door to more specialized and invasive/implantable therapies as a potential to improve patient pain and quality of life while decreasing overall disability.

CASE PRESENTATION

We present the case of a 27-year-old man who initially presented to our clinic to discuss bilateral neuropathic hand pain that started in conjunction with a COVID-19 infection about 2 years prior. Informed consent was obtained from the patient to utilize his case presentation and submit as a case report. He reported that with his initial COVID-19 symptoms of congestion, body aches, and fevers, he also started to have severe burning pains in his bilateral hands. The patient was hospitalized for a short time with his COVID-19 symptoms, but did not require intubation or intensive care. Since that time, his pain symptoms worsened and he also developed other symptoms, including skin color changes, temperature changes in the hands, and fluctuating edema. He had been seen prior at the University of Texas-Houston by a specialist on post-COVID-19 syndrome who was unsure on the exact cause of his symptoms and whether they were related to his COVID-19 infection. The patient localized the majority of his pain to the area of the metacarpophalangeal joint of the thumb and the skin between the first and second digits bilaterally. He characterized the pain as a constant, throbbing, pulsating, stabbing pain. The pain was worsened with exercise, lifting, cold, and repetitive tapping activities, such as typing or texting. The pain improved with heat and rest. He denied allodynia. In addition to the reported symptoms of pain, skin color changes, and edema, his physical exam demonstrated edema in the carpometacarpal joint and lateral wrists bilaterally, visible redness/skin discoloration in the medial hands and wrists, and tenderness in the medial wrists and fingertips with repetitive light tapping/palpation.

At the time of his initial visit with us, he had a working diagnosis of Raynaud's disease. He had vascular studies that demonstrated postexercise arterial spasm in the palmar arch as well as postexercises arterial spasm in the first and second digits and light spasm noted in digits 3 through 5. However, his presentation was certainly unusual for Raynaud's disease because of the lack of progressive color changes. From a vasomotor standpoint, he was experiencing more of a redness in the dorsal and palmar aspects of the hands, and he did not experience pallor or blue/dusky skin color changes. In addition, while cold did occasionally worsen his symptoms, this was not reliably reproducible, and his main aggravating factor was repetitive tapping motions with his fingers. There was also concern for carpal tunnel syndrome, although this was lower on the differential given the myriad of symptoms he was experiencing. He did have an electromyogram, which demonstrated mild findings of median nerve entrapment bilaterally. Cervical magnetic resonance imaging was nonconcerning. He had been trialed on multiple different medications, including amlodipine, sildenafil, and gabapentin, which gave him minimal relief. The gabapentin seemed to be the most helpful, but he had dose-limiting side effects, including lethargy.

Our differential diagnosis included Raynaud's disease, carpal tunnel syndrome, complex regional pain syndrome (CRPS) type I, post-COVID-19 syndrome, and thoracic outlet syndrome. Based on his clinical presentation and timing of symptoms, Raynaud's disease and spontaneous post-COVID-19 thoracic outlet syndrome or carpal tunnel syndrome seemed less likely while CRPS type I and/or post-COVID-19 neuropathic pain seemed to be more likely. He certainly met the International Association for the Study of Pain's revised criteria (Budapest Criteria), including reported symptoms of sensory changes of hyperesthesia, vasomotor skin color changes, as well as sudomotor changes, including edema. Signs in all 3 of these categories were also noted on physical exam in the clinic.

Initially, we scheduled the patient for a stellate ganglion block with the hope that he would get relief from either a vascular pain or sympathetically maintained pain. Unfortunately, he denied getting noticeable benefit from this procedure. We also tried other oral medications, including duloxetine which did not provide much benefit, and low-dose naltrexone (LDN) 4.5 mg daily, which did seem to help. He was working with occupational therapy (OT) as well and the combination of OT with LDN did help him make some progress with his symptoms. However, his pain remained and

was causing a significant decrease in his quality of life. Given the fact that he had failed adequate trials of medications from multiple different classes, including gabapentinoids, SNRIs, nonsteroidal anti-inflammatory medications, calcium channel blockers, phosphodiesterase-5 inhibitors, acetaminophen, and LDN, as well as failure of our interventional stellate ganglion block and inadequate benefit from OT, we elected to proceed with neuromodulation for intractable neuropathic pain of the bilateral upper extremities, chronic pain syndrome, and CRPS type 1.

Spinal cord stimulator workup was reassuring, including updated imaging and psychological evaluation. We pursued a Nevro device (Nevro, Redwood City, CA) with cervical lead placement. A single lead trial with lead tip at the C2/C3 interspace provided excellent relief. He reported an improvement in functionality, increased ability to participate in physical therapy, and a > 70% decrease in baseline pain. With this response, we elected to pursue a spinal cord stimulator implant procedure. Two leads were placed during the implant procedure with one lead at the C2/C3 interspace and the other lead staggered at the C3 vertebral body level. He has recovered well from his stimulator placement and is now > 6 months postop. He reports a 50% improvement in his baseline pain with improvement in functionality, including improved ability to lift weights and perform repetitive motions. Although similar activities, such as texting and typing, do cause him discomfort, he recovers from any flare in the pain much quicker than he previously would. Overall, he is quite pleased with his response to the device and is doing well.

DISCUSSION

The chronic effects of long COVID are varied and can be difficult to treat. Whether the issue is shortness of breath, chronic fatigue, or chronic pain, a multitude of problems have been ascribed to previous COVID-19 infections. According to a systematic review by Williams et al (1), 34.3% of patients with long COVID suffer from neuropathic pain. Persistent neuropathic pain after COVID-19 has been well-documented, although there are few (if any) case reports describing CRPS as a result of COVID-19. Our case details the history and treatment of a patient who developed chronic neuropathic pain symptoms that meet the Budapest Criteria that started within days of a severe COVID-19 infection.

Effective treatment options for neuropathic pain, in general, are limited and neuropathic pain secondary to COVID-19 seems particularly difficult to treat (7,8). Studies on the effectiveness of first-line medications, such as gabapentin and amitriptyline, in the COVID-19 population are scarce, making it difficult to follow any sort of tested treatment algorithm. In addition, the economic burden related to lost productivity, physician office visits, and medications average over $25,000 per year per patient when looking at direct and indirect costs to the patient, their insurance, and society (9). Because of this, and because of the disability associated with neuropathic pain, implantable therapies should potentially be considered sooner in a patient's treatment plan.

At this time, the main indications for neuromodulation are postlaminectomy syndrome type 2, CRPS, refractory angina pectoris, ischemic limb pain, and intractable neuropathic pain of the trunk and extremities (10). There is long-standing quality evidence of the effectiveness of dorsal column stimulation for the treatment of CRPS and other neuropathic pain issues (11-16), but because of the complexity of post-COVID-19 neuropathic pain, it was far from assured that this patient population would respond to neuromodulation in the treatment of their symptoms. Fortunately, in our case, the patient responded nicely to the therapy and his pain has been steadily improving for at least 6 months postimplant.

Limitations of the study include those inherent to case reports, including lack of generalizability, inability to establish a cause-effect relationship, retrospective design, and potential for overinterpretation of findings.

CONCLUSIONS

Neuromodulation does seem to be more effective at treating chronic neuropathic pain and chronic musculoskeletal pain. With the prevalence of chronic neuropathic post-COVID-19 pain, our hope is that this case will help expand the use of neuromodulation therapy to help treat these patients, particularly when more conservative treatments have failed. We believe neuromodulation should be considered as a potential therapy to treat persistent neuropathic pain thought to be related to previous COVID-19 infection, particularly when a patient meets the criteria for CRPS.

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