

STELLATE GANGLION BLOCK FOR HEADACHE PAIN AND COGNITIVE IMPAIRMENT ASSOCIATED WITH LONG COVID PERSISTING OVER 12 MONTHS: A CASE REPORT

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Background: Postacute sequelae of COVID-19 (PASC) are debilitating health conditions affecting over 7% of the US population. Clinical PASC manifestations are variable, but consistently involve dysautonomia and elevated inflammatory biomarkers. Common symptoms include pain, fatigue, cognitive impairment, sensory loss, and orthostatic intolerance. As neuroimmune hyperactivation and reductions in cerebral blood flow are each implicated in PASC pathophysiology, stellate ganglion block (SGB) represents a promising treatment option due to its ability to reset autonomic activity and reperfuse the brain. We sought to retrospectively assess the potential of SGB to treat head and neck pain, cognitive impairment, and fatigue associated with PASC persisting over 12 months.

Case Report: We reviewed and analyzed case data from 2 middle-aged female patients with painful, longstanding PASC managed with repeat unilateral SGB. Procedures were performed under ultrasound guidance, with 3 mL 0.5% bupivacaine + 12 mg betamethasone as the injectate. Each patient received 2 SGBs, with all procedures being tolerated well. No complications occurred. One patient had a recurrence of migraine pain following the blocks, while the other experienced durable relief. Both patients saw improvements in cognitive function and fatigue postoperatively, which were sustained.

Conclusions: Most literature on SGB for PASC management concerns its ability to reverse sensory loss, rather than relieve chronic pain. This case report provides preliminary evidence supporting the effectiveness of SGB for managing pain and cognitive impairment in PASC. As PASC symptoms with longer durations tend to be less effectively managed with SGB, we speculate that chronicity of the patients' symptoms hampered SGB-mediated pain relief.

Key words: Stellate ganglion block, COVID-19, long COVID, headache pain, cognitive impairment, case report

BACKGROUND

Pain and cognitive impairment are among the most common symptoms of postacute sequelae of COVID-19 (PASC) (1), a condition that affects 7.3% of the US adult population (2). Commonly known as "long COVID," PASC is defined broadly as SARS-CoV-2 symptoms that persist > 3 months following acute infection (3).

Current literature (4,5) suggests that PASC occurs following ~30% of symptomatic COVID-19 cases. While PASC symptomatology is diverse (6), cases consistently involve dysautonomia (7,8) and elevated proinflammatory cytokine levels (9,10) indicative of chronic immune-mediated neuroinflammation. Reductions in

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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.

Ethics Statement: Informed consent for procedures and publication of data and images was obtained from both patients included in this case report. Procedures involving human patients were performed in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration, its later amendments, and comparable ethical standards. This report was declared exempt from ethical review requirements by the Wright State University Institutional Review Board, Study ID#: IRB-2024-687, in January 2024.

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cerebral blood flow have been reported as well (11,12), contributing to common symptoms, such as headache, cognitive impairment, anosmia, dysgeusia, chronic fatigue, and orthostatic intolerance (3,7). A recent analysis (13) of > 34,000 COVID-19 patients identified 4 reproducible PASC subphenotypes, one of which encompasses these stereotyped musculoskeletal and nervous system symptoms (neuro-PASC). Considering the chronic and debilitating nature of neuro-PASC, investigations of management strategies are essential to mitigating lasting public health effects of the COVID-19 pandemic.

As neuroimmune hyperactivation persisting after the acute phase of COVID-19 infection and resulting dysautonomia have been implicated in neuro-PASC, stellate ganglion blocks (SGBs) have intuitively emerged as a treatment avenue (7,14). By briefly interrupting neural propagation in the sympathetic chain, SGB triggers a “resetting” of autonomic activity, followed by an increase in cerebral blood flow (7,15). This mechanism has shown significant benefits for many indications, from chronic upper extremity pain to migraine and posttraumatic stress disorder (16,17). While evidence indicating SGB for PASC is promising, most studies to date (18-21) have focused on SGB’s potential to reverse sensory loss, rather than manage PASC-associated chronic pain. Recent evidence (7,14) also indicates that SGB can reduce PASC-related fatigue and cognitive impairments. Here, we present 2 cases of painful neuro-PASC with cognitive impairments managed using 2 unilateral SGBs. This report serves to emphasize SGB as a viable PASC management strategy, and inform patient and physician expectations when considering this treatment.

CASE REPORT

Case #1

A 44-year-old female patient presented with severe facial pain described as dull, deep, and burning. The pain manifested as migraines centered on the maxillary branch of the trigeminal nerve, accompanied by anterior neck pain. The migraines were exacerbated by screen time, focused cognitive tasks, and dietary changes. Additionally, the patient suffered executive dysfunction, vestibular dysfunction, and working memory issues that caused her to reduce everyday activity levels. The patient also had difficulties carrying out her work as a family medicine physician. Both the migraines and cognitive deficits arose suddenly during a SARS-CoV-2 infection

in June 2022 and did not subside, representing a clear case of PASC.

The patient had addressed symptoms with sumatriptan, ubrogepant, atogepant, ondansetron, guanfacine hydrochloride, naproxen sodium, acetaminophen, and diphenhydramine—without sufficient relief from daily pain and cognitive difficulties. After 18 months of steady symptoms, the patient presented to explore other treatment options. The patient was determined to be a good candidate for SGB, and preemptively discontinued blood thinners. Viscous lidocaine was prescribed, with minimal benefit.

A right-sided SGB was performed after obtaining informed consent. The patient was placed in the supine position, and skin was prepped with ChlorPrep™ solution (Becton, Dickinson and Company, Franklin Lakes, NJ). An ultrasound probe was placed transversely over the cricoid cartilage, then moved laterally to identify the C6 Chassaignac’s tubercle, the ipsilateral carotid artery (CA), and C7 vertebral artery (Fig. 1). Color Doppler was used to locate vascular structures. Skin over the C6 transverse process was anesthetized with 1% lidocaine. The spinal needle was then advanced to the stellate ganglion, above the longus colli muscle and below the CA. The needle was aspirated and negative for heme and cerebrospinal fluid. A solution of 6 mL 0.25% bupivacaine + 12 mg betamethasone was injected in slow increments. Vital signs remained stable throughout and signs of sympathetic blockade were monitored. The patient tolerated the procedure well, and Horner’s syndrome was confirmed. The patient reported an almost complete resolution of pain, as well as a rapid improvement in cognitive clarity.

Despite the procedure’s short-term effectiveness, the patient followed-up 2 weeks later with a recurrence of migraines. Visual Analog Scale (VAS) and Brief Pain Inventory (BPI) scores were improved from the patient’s first visit (Table 1), and cognitive improvements were sustained. The patient reported 40% pain relief following SGB. Additionally, the patient had been using the Visible app (22) for activity pacing and saw her overall score improve from 3 to 5, suggesting a return to near-normal capacity levels for physical activity. The patient was scheduled for a repeat right-sided SGB the following week, which was performed using a reduced injectate volume with higher bupivacaine concentration (3 mL, 0.5%). The procedure was tolerated well with the patient endorsing > 50% pain relief postoperatively. Two weeks after the second block, the patient reported

another recurrence of migraine pain, which was as severe as before the SGBs. Nonetheless, the patient saw sustained cognitive improvements and reported a 50% overall improvement in the BPI's "Enjoyment of Life" item (Table 1). The patient is considering neurostimulation options for the management of PASC-related migraines.

Case #2

A 46-year-old female patient presented with chronic pain of the neck and shoulders, described as tightness, aching, and cramping. The pain was constant but variable in severity, causing tension-type headaches (TTH) that worsened at night. The patient had comorbid anxiety disorders, major depression, hypothyroidism, type 2 diabetes mellitus, and diabetic neuropathy. Additionally, the patient had chronic low back and hip pain, which was managed with a transcutaneous electrical nerve stimulation unit and unrelated to her chief complaints. The patient's upper extremity pain emerged rapidly in May 2023 following a SARS-CoV-2 infection, and symptoms remained unchanged for 12 months. Along with chronic pain symptoms, the patient developed extreme fatigue and new cognitive deficits, including delayed verbal responsiveness, diagnosed by her primary care physician as a mild cognitive impairment (MCI), as facets of her PASC symptomatology. PASC-related pain and fatigue left the patient unable to walk more than one block at a time, and they required

a walker or cane for everyday mobility. The patient had discontinued work entirely.

Upon presentation to our practice, the patient was managing PASC symptoms with gabapentin, modafinil,

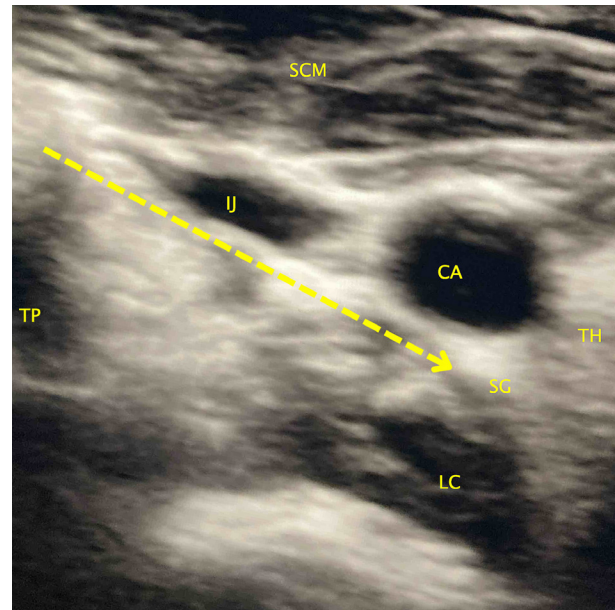


Fig. 1. Medial view of SGB needle path and anatomical markers.

SG = stellate ganglion, SGB = stellate ganglion block, CA = carotid artery, IJ = internal jugular, LC = longus colli, SCM = sternocleidomastoid, TP = transverse process. Dotted arrow indicates the needle path.

Table 1. Changes in VAS pain intensity and BPI interference with daily activities.

	Pain (VAS)	General Activities	Mood	Walking Ability	Work	Relations With Others	Sleep	Enjoyment of Life
Case 1								
Baseline	5	5	5	1	10	3	6	10
SGB #1	3	-	-	-	-	-	-	-
2-Week Follow-up	2	5	5	0	5	2	3	7
SGB #2	-	-	-	-	-	-	-	-
2-Week Follow-up	6	8	5	0	5	4	1	5
Case 2								
Baseline	6	10	9	9	10	9	10	9
SGB #1	-	-	-	-	-	-	-	-
2-Week Follow-up	2	4	2	0	3	0	1	1
6-Week Follow-up	4	3	1	2	7	1	3	3
SGB #2	-	-	-	-	-	-	-	-
1-Week Follow-up	0	4	3	3	3	0	3	3

Abbreviations: VAS, Visual Analog Scale; BPI, Brief Pain Inventory; SGB, stellate ganglion block.

and lorazepam, though without significant relief. The patient was prescribed low-dose naltrexone, which was effective, and determined to be a good candidate for SGB. After obtaining informed consent, a right-sided SGB was performed 2 weeks after the patient's initial visit. The procedure was uneventful, and performed using identical techniques to Case 1, though with 3 mL 0.5% bupivacaine, instead of 6 mL 0.25% bupivacaine + 12 mg betamethasone as the injectate. Horner's syndrome was confirmed postoperatively, and the patient endorsed immediate > 50% pain relief.

The patient continued to follow-up over the next 6 weeks, noting improvements in pain that peaked from one to two weeks after the SGB. Additionally, the patient demonstrated steady improvements in cognitive function with each follow-up visit, which were also noted by the patient's physical therapist and speech therapist. The patient reported an improved ability to perform activities of daily living and increased levels of physical activity. Three months after the first SGB, the patient received a repeat right-sided SGB to address lingering musculoskeletal pain of the neck, again endorsing > 50% pain relief. Sharp decreases in chronic pain severity were reflected in the patient's BPI and VAS scores (Table 1). PASC-related deficits in speech and cognition were durably improved from the first SGB.

CONCLUSIONS

This case report serves to emphasize the potential of SGB to restore cognitive function and alleviate headache pain associated with neuro-PASC persisting > 12 months. Both patients in this retrospective case report sustained both cognitive improvements and increased physical abilities after several weeks post-SGB. However, PASC-associated pain was less durably improved than cognition or energy levels. Two weeks after the second SGB, the patient in Case 1 had worse migraine pain than when she first presented, despite $\geq 50\%$ improvements in the pain's interference with the "Work," "Sleep," and "Enjoyment of Life" BPI items (Table 1). The patient in Case 2 reported a complete resolution of pain on the VAS, but still noted minor pain-related interference on most BPI items (Table 1). While cognition and overall quality of both patients' lives improved as a factor of treatment with SGB, chronic pain symptoms were only brought under control for the patient in Case 2.

Physiological underpinnings of the observed discrepancy between SGB's effectiveness in treating pain and cognitive PASC symptoms are unclear. Though both sets

of symptoms are within the umbrella of dysautonomia (8,15), it is possible that PASC-related pain and other neurological symptoms (e.g., MCI, fatigue) arise through disparate pathophysiological mechanisms. Dysautonomia in PASC is attributed to excess inflammatory cytokine release in the peripheral nervous system (7-9), which can then trigger a central neuroimmune response via the vagus nerve (23). Autonomic "resets" from SGB procedures may owe their durability to vagally mediated effects on the central nervous system (24), in tandem with established effects like increased cerebral blood flow (15) and the interruption of hyperinflammatory positive feedback loops (9). The proportionate roles and interplay of PASC-related neuroinflammation and vasculopathy in generating chronic pain and cognitive impairment have yet to be elucidated.

As prior studies (12,15) have observed, the presentation of neuro-PASC has significant overlap with other types of dysautonomia, namely myalgic encephalomyelitis/chronic fatigue syndrome and postural orthostatic tachycardia syndrome, which can also be effectively managed with SGB. Migraine commonly manifests as a symptom of dysautonomia (8), and has also long been treated with SGB (16). Cases of effective neuro-PASC management with SGB highlight shared pathophysiologies between dysautonomic conditions. However, PASC is still broadly defined and poorly understood; not all cases may be appropriate candidates for SGB.

It has been suggested that PASC headache is a distinct condition, the onset of which is triggered by postinfection immune hyperactivity, which, in turn, causes trigeminovascular system activation and migraine or TTH (25). The cases described here fit this proposed PASC subphenotype well, with one patient suffering migraines and the other TTH. The migraines in Case 1 being less effectively managed than TTH in Case 2 could indicate that PASC-related migraines are more difficult to address with SGB. Considering SGB efficacy for migraine management (16), however, it is more likely that the duration of PASC symptoms preceding SGB determined its effectiveness as a pain management procedure. This is supported by data (14,19) indicating PASC symptoms with longer durations tend to be less effectively managed with SGB. Plausibly, the longer a COVID-19-related inflammatory response is sustained, the more irreversible damage to the nervous system accrues. Since Case 1 had PASC symptoms persisting 6 months longer than Case 2, we speculate that PASC duration played the most salient role in Case 1's comparatively poor outcome.

Our case report is limited by its small sample, as well as the fact that the 2 cases described did not have identical PASC symptomologies. Both patients declined to fill out select questionnaires issued by our practice throughout standard operations, including the Neck Disability Index, the data from which would have been illuminating. Additionally, as the drasticity of cognitive improvements seen in both cases was unforeseen, no cognitive testing was utilized. Future studies on this topic will be advantaged to utilize more specialized questionnaires, quantitative outcome assessments, and larger, controlled designs. The determination of clearer PASC subphenotypes will

be crucial to future understandings of which cases are indicated for SGB.

SGB is a viable treatment option for pain and cognitive impairment associated with neuro-PASC. The success of SGB in managing these symptoms gives credence to notions of PASC as a fundamentally dysautonomic condition. In the 2 cases we described, patients saw lasting neurological benefits from 2 right-sided SGBs, which included dramatic improvements in cognition and energy levels. However, one patient did not have lasting relief from PASC-related migraines, which we speculate was a factor of their long duration of symptoms prior to receiving treatment.

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