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Sphenopalatine Ganglion Block for Postacute Sequelae SARS-CoV-2 Infection Headaches: A Case Report and Review of the Literature

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Background: In a subset of patients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), neurological symptoms including "brain fog" and headache persist beyond the acute phase of the infection, often referred to as postacute sequelae SARS-CoV-2 infection (PASC), or Long COVID.
Current practice supports a multi-modal approach to address PASC symptoms. One technique for chronic headaches not utilized for PASC is sphenopalatine ganglion blocks (SPGB). We evaluate the pathophysiology of PASC headaches, review the utilization of sphenopalatine ganglion blocks in primary headaches, and discuss the potential for SPGB in PASC headaches.

Case Report: We present a patient with PASC headaches who failed various conservative and interventional therapies. Worsening symptoms resulted in pursuing bilateral SPGB, resulting in an 80% improvement in symptoms. To our knowledge, we report the first PASC headache treated with an SPGB via infrazygomatic injection.

Conclusion: SPGB can treat PASC headaches and improve a patient's quality of life.

Key words: Sphenopalatine ganglion block, Long COVID, PASC, headaches, case report

BACKGROUND

The emergence of a novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), as first reported by the World Health Organization (WHO) on December 31, 2019, has brought along a tumultuous disease with symptoms ranging from asymptomatic to death. Distinct from the respiratory manifestations of the virus, over 36% of symptomatic patients have reported neurological symptoms including headaches, migraines, ataxia, impaired consciousness, diminished concentration, hyposmia, fatigue, and myalgia (1). In a subset of these patients, these "brain fog" and fatigue symptoms persist beyond the acute and subacute phases of the infection, lasting more than 2 months as defined by the WHO; these symptoms are also known as postacute sequelae SARS-CoV-2 infection (PASC), or Long COVID syndrome (2).

One prevalent PASC symptom is PASC headaches, which have been reported in 6.5% to 34% of all patients and can be the primary or only neurological symptom (3). Multiple pathophysiological causes of PASC have been suggested, with current research supporting a multimodal therapeutic approach to address the symptoms that encompass PASC (4). O'Kelly et al (5) recently reported that low-dose naltrexone (LDN) improved the activities of daily living, fatigue, concentration, headache, pain, and overall recovery in patients with PASC. LDN requires a particular patient population,

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however, thus necessitating innovative interventions such as sphenopalatine ganglion blocks (SPGB). To our knowledge, we provide the first SPGB to address PASC in a patient via an infrazygomatic injection with fluoroscopy approach. We further evaluate the pathophysiology of PASC headaches, review the utilization of SPGB in primary headaches, and discuss the potential for SPGB in PASC headaches.

CASE PRESENTATION

A patient in her 50s with a past medical history of hypertension, hyperlipidemia, and previous acute COVID-19 infection initially presented to the PASC clinic for functional deficits due to persistent symptoms 5 months after acute COVID-19 infection (Fig. 1). Family history was noncontributory. There was no reported psychosocial history. The patient's PASC symptoms initially included deficits in short-term memory, attention, vision, fatigue, and headaches. A plethora of conservative therapies were initially trialed, including over-the-counter nonsteroidal anti-inflammatory drugs and analgesics, vitamins, reminder phone apps, sleep hygiene, stress reduction, group therapies, and mental health sessions; all had minimal effects. Throughout follow-up PASC visits in the last year, the patient was started on LDN and underwent patient autologous adipose and bone marrow-derived mesenchymal stem cells therapy to target PASC inflammation, with short-term symptom relief. Intravenous nicotinamide adenine dinucleotide therapy was also completed in the last 2 months with no alleviation of symptoms.

A year later, despite continued usage of LDN, the patient was referred from the PASC clinic to the interventional pain clinic. The patient reported worsened initial symptoms and a new loss of taste and smell, sinus congestion, back pain, bilateral eye pain, and blurry vision. In discussion with the patient, the primary concerns at this visit were the worsened anosmia and ageusia and headaches.

A physical exam was significant for palpable tenderness in the soft tissues of the anterior neck along the trachea and postauricular neck. Previous radiographs and computed tomography of the patient's face by outside facilities were unremarkable. At this visit, the patient consented to right and left stellate ganglion blocks, which temporarily relieved most symptoms for 2 weeks and completely resolved the anosmia and ageusia. The patient returned after 2 weeks due to the debilitating nature of the headaches and was amenable to an SPGB via infrazygomatic approach to the right side (Fig. 2).

Consent was obtained and under fluoroscopy the patient underwent an SPGB with a 2 mL solution consisting of 1mL of 10 mg/mL dexamethasone and 1 mL of 0.5% bupivacaine. On follow-up, the patient reported more than an 80% improvement in headaches, blurry vision, and eye pain on the right. The patient additionally reported significant improvement in sinus congestion, concentration, and short-term memory. Given the improvements, the patient requested an SPGB on the left side (Fig. 3), which resulted in similar relief.

DISCUSSION

The pathophysiology of PASC has not been fully elucidated, especially for headaches. Current evidence from previous coronavirus outbreaks and research on basic molecular and cellular coronavirus mechanisms have suggested these PASC symptoms are induced by the continued presence of the virus or viral-elevated immune cell hyperactivation from prolonged inflammatory responses and proinflammatory cytokines

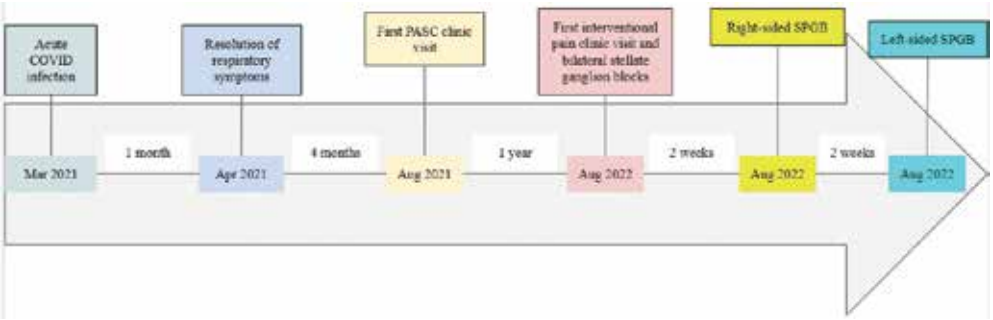

Fig. 3. Patient timeline.
PASC = postacute sequelae SARS-CoV-2 infection; SPGB = sphenopalatine ganglion block.

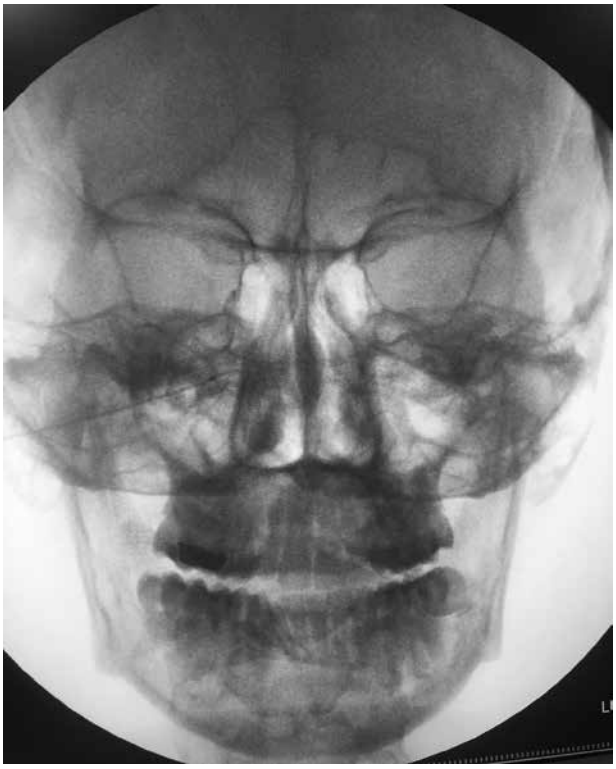

Fig. 1. Sphenopalatine ganglion block via infrazygomatic approach to the right side.

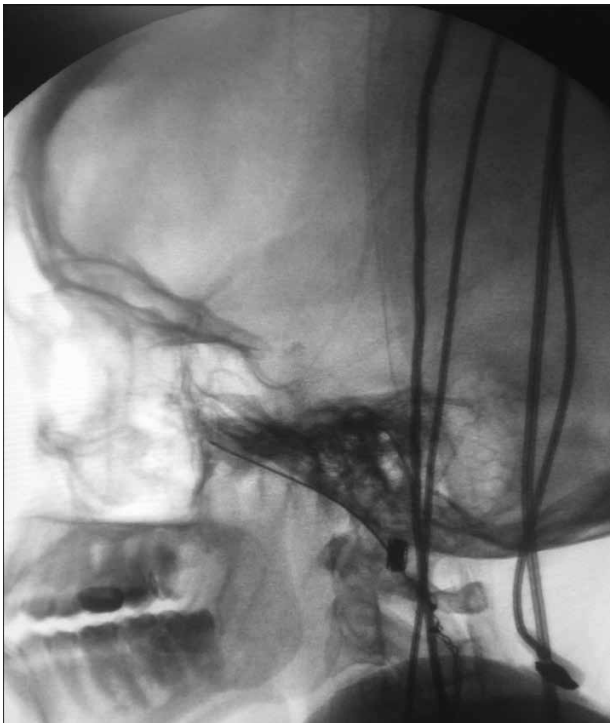

Fig. 2. Sphenopalatine ganglion block via infrazygomatic approach to the left side.

(6-8). This inflammatory imbalance within individuals promotes transforming growth factor beta (TGF-β) activation, leading to further prolonged states of immunosuppression and persistent PASC (9). With similar neuroinvasive pathogenesis to other coronavirus family members, viral protein mimicry with peripheral nerve proteins could also explain the neuromuscular symptoms of PASC (10). Neurotropism of direct musculoskeletal or neurocellular invasion by COVID-19 or its viral proteins via the angiotensin-converting enzyme 2 receptors have been suggested (6-8). In this case, viral breaching could target the blood-brain barrier, the olfactory bulb, the vagus nerve, or any other manner of ganglions, including the sphenopalatine ganglion (11).

The utilization of SPGB is not novel; since its description for sphenopalatine neuralgia by Sluder in 1908 (12), it has been studied in a plethora of facial pain and headache syndromes (13). There are a variety of techniques for how SPGB is accomplished, including transnasal topical, transnasal injection, transoral injection, and percutaneous infrazygomatic injections; each has its own distinct advantages (12). Ho et al (14) evaluated the level of evidence for SPGB for various pain syndromes in a systematic review. Their group designated a high SPGB indication for cluster headaches, second-division trigeminal neuralgia, migraine headaches, and endoscopic sinus surgeries (14). Lower levels of evidence were seen for other neurological syndromes, including trigeminal neuralgia, dural puncture headache, hiccups, and complex regional pain syndrome (14).

Indications for an SPGB for PASC headaches have shown empirical evidence for relief via a transnasal topical approach in 2 case series (15,16). Our case is the first to report an infrazygomatic SPGB injection with fluoroscopy to address PASC in a patient at the time of this writing. Current evidence postulates the blockade downregulates autonomic stimuli to the head, neck, and shoulder, potentially explaining SPGB's effectiveness for PASC (17).

Direct targets of an SPGB can induce mild intracranial vasoconstriction leading to an analgesic effect or reduction in the release of vasoactive substances in the pterygopalatine fossa (i.e., calcitonin gene-related

peptide) that can be seen in COVID-19 (18). Looking into PASC and its pro-inflammatory etiology explains how an SPGB with bupivacaine and dexamethasone can result in the resolution of headaches and associated impaired concentration and fatigue. Dexamethasone has been shown to effectively suppress inflammation and promote recovery in patients with acute (19) and chronic COVID-19 (20). Using bupivacaine with dexamethasone is also advantageous in prolonging the duration of an SPGB and symptomatic relief (21).

Thus, we pursued a percutaneous infrazygomatic approach due to the success we had with the patient's previous stellate ganglion blocks, the direct application of bupivacaine and dexamethasone to the sphenopalatine ganglion, the minimal risk profile with a targeted injection, prolongation of SPGB effects, and the disadvantage of direct diffusion across mucous membranes in other techniques. The patient reported significant relief in symptoms after the right-sided SPGB, prompting a left-sided SPGB and similar results. To date, the patient still has significant relief with no refractory symptoms.

One limitation to this case is the potential confounding symptoms the patient had that arose after the initial presentation of PASC symptoms. While loss of taste and smell, sinus congestion, back pain, bilateral eye pain, and blurry vision have been previously reported in the PASC literature, other viral and infectious diagnoses could have presented similarly (10,11). Additionally, this one case is, at this point, empirical until further case reports or series can show similar benefits with SPGB via an infrazygomatic approach.

CONCLUSION

With a rising patient population experiencing PASC, further research can provide insight into SPGB's effectiveness for reating PASC and other inflammatory-related disorders as well as drive public health conversations. This case highlights PASC's relation to headaches, eye pain, blurry vision, and impaired short-term memory and concentration. Clinicians should be cognizant of additional treatment modalities such as an SPGB via an infrazygomatic approach when evaluating a patient with atypical recovery from SARS-CoV-2 infection and consider it earlier in their patients' management. Incorporation of this treatment modality can lead to improvement in morbidity earlier, avoiding unnecessary costly treatments.

Patient Perspective

I am very pleased with the results of the injections into my nose. These long-COVID symptoms have debilitated me for the longest time and being able to be functional again has been a godsend. It was so hard to concentrate and bear the pain. It was difficult to be me. The injection has changed that for me. I would recommend bringing it up as a potential treatment to others who suffered life as I have.

Author Contributions

PDV: Wrote and edited the manuscript with VB with support from ML, and BB and conducted a majority of the literature review before writing the manuscript.

VB: Wrote and edited the manuscript with PDV with support from ML and BB and assisted in the literature review before starting the manuscript.

ML: Provided discussion and edits for the manuscript and provided supervision of the patient's care.

BB: Conceived the presented idea, provided discussion and edits for the manuscript, And provided supervision of the patient's care.

Everyone participated in the patient's care. Everyone discussed and interpreted the findings and contributed to the final manuscript.

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