Research Article

Stellate ganglion block for anosmia and taste disturbance due to Long-COVID

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Anosmia and parosmia refer to loss or dysfunction of smell, respectively. There is an increased prevalence of anomia/parosmia in patients that have clinically recovered from COVID-19 infection. Anosmia could be self-limiting over a two- or three-week post- COVID-19 infection but can persist for longer. Anosmia or parosmia associated with COVID-19 has generated a lot of interesting etiological hypotheses. One such theory implicates autonomic dysregulation or dysautonomia as the underlying mechanism for anosmia. In the case of Long-COVID, dysautonomia could be induced by the autonomic nervous system's response or maladaptation to pro-inflammatory cytokines leading to excessive sympathetic nervous system activity. Stellate ganglion block can abate the symptoms of Long COVID attributed to increased sympathetic nervous system activity. The authors report successful persistent anosmia and dysgeusia resolution due to Long-COVID after stellate ganglion block.

INTRODUCTION

Anosmia and parosmia refer to loss or dysfunction of smell, respectively. There is an increased prevalence of anomia/parosmia in patients that have clinically recovered from COVID-19 infection. Current literature reports that the incidence rate of olfactory dysfunction in COVID-19 patients varies from 33.9 to 68%, with female dominance [1]. Anosmia could be self-limiting over a two- or three-week post- COVID-19 infection but can persist for longer. Despite a high recovery rate, multiple studies have reported up to 7% of the patients remain anosmic more than 12months after onset, leaving millions worldwide with severe olfactory dysfunction [2,3]. Anosmia might coexist with other symptoms such as fatigue, orthostatic hypotension, shortness of breath, insomnia, anxiety, depression, and taste disturbances. These constellations of symptoms may persist chronically and are termed "Long COVID" or formally as Post-Acute Sequalae of SARS-CoV-2 (PASC) infection [3]. The

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incidence of PASC is 30% in symptomatic and 5% in asymptomatic patients with COVID-19 infection [4]. Compared to influenza, COVID-19 is reported to have a higher prevalence of anosmia (53% vs. 17%) [5]. PASC patients with or without hospitalization often reported anosmia as one of the predominant and persisting symptoms [4].

Anosmia or parosmia associated with COVID-19 infection has generated a lot of interesting etiological hypotheses. One such theory implicates autonomic dysregulation or dysautonomia as the underlying mechanism for anosmia [6]. In the case of Long-COVID, dysautonomia could be induced by the autonomic nervous system's (ANS) response or maladaptation to pro-inflammatory cytokines leading to excessive sympathetic nervous system activity [4,6,7]. Sympathetic innervation of the head and neck consists of the cervical and upper thoracic sympathetic chain [8]. It is postulated that unrestrained cervical sympathetic activity in the head and neck region can be blocked by injecting local anesthetics in the stellate ganglion, restoring the homeostasis of the regional autonomic nervous system [9]. The stellate ganglion block (SGB) has been used clinically for medical conditions associated with increased sympathetic nervous system activity [10-12]. In this report, the authors discuss the resolution of persistent anosmia after stellate ganglion block in a patient that had completely recovered from COVID-19 infection, implicating dysautonomia in the pathophysiology of PASC.

CLINICAL VIGNETTE

A 48-year-old female patient, who consented to publish this case report, presented to our clinic four months after recovering from a COVID-19 infection. The patient didn’t have any significant comorbidities. The patient reported that her COVID-19 symptoms were like any other viral infection she had in the past, with fevers ranging from 99-to 102 degrees Fahrenheit, non-productive cough, and nasal congestion. She was placed on antiviral therapy for five days, followed by a complete resolution of symptoms. The patient reported that she first noticed the loss of smell and taste 3 to 4 days into the acute phase of COVID-19 and attributed it to nasal congestion and high fevers. The patient also reported fatigue, light-headedness, and loss of smell and taste. The patient reported that all her symptoms resolved within one month, except issues with taste and smell. The patient reported complete loss of sense of smell and altered taste sensation to various types of foods. The patient further reported that she had tried various nasal decongestants and mucolytic agents. She frequently did nasal irrigation with saline. The patient also failed olfactory threshold tests. No conductive loss of sense of smell was identified, such as nasal obstruction due to rhinosinusitis, allergic rhinitis, etc.

Anosmia was affecting her quality of life, and the patient was depressed due to a lack of therapeutic options. The patient was finally referred to our clinic by her otolaryngologist for stellate ganglion block. The patient underwent a right-sided stellate ganglion block under ultrasonographic guidance, with 4 ml of 0.25% Bupivacaine. The patient reported a partial return of her sense of smell within 24 hours. The patient underwent the left-sided SGB after 72 hours and reported a complete resolution of anomia 24 hours after the second SGB. The patient commented that her altered taste sensation resolved a few days after the last block.

DISCUSSION

Anosmia/ Parosmia as a part of COVID-19 infection could be due to neurological virulence and associated cytopathic effects [13,14]. In patients reporting resolution of anosmia post-SGB, an argument could be made that they might have undergone structural recovery and only need to reset the tone of the autonomic nervous system to produce functional recovery. Furthermore, dramatic resolution of anosmia after SGB favors dysautonomia rather than cytopathic or structural damage due to COVID-19 as underlying etiology.

Dysautonomia is also reported with other viral illnesses (Hepatitis C, HIV, Epstein-Barr virus) and other pathologies such as alcoholism, diabetes, and Parkinson's. Dysautonomia is associated with fatigue, anosmia, heart rate variability, bowel and bladder dysfunction, and orthostatic hypotension [6]. Multiple theories have been generated to explain the persistence of dysautonomia post- COVID-19 infection [15]. Current literature implicates the complex interaction between Angiotensin-Converting Enzyme 2 receptor (ACE2) and COVID-19 as the underlying mechanism for dysautonomia and subsequent anosmia. ACE-2 enzyme converts angiotensin II (Ang II) to angiotensin (1-7) [16]. Ang II feed-forwards the inflammation by stimulating AT1 receptors, whereas angiotensin (1-7) activates Mas receptors inhibiting inflammation [17]. ACE-2, expressed in membrane-bound and soluble forms, is the receptor for the spike portion of the SARS-CoV-2 virus. A link between ACE2 and the spike portion of SARS-COV-2 facilitates the viral entry into the cells while inhibiting the activity of the ACE2 enzyme. A subsequent decrease in the activity of ACE2 potentiates inflammation by perpetuating the feed-forward loop mediated by the ATII molecule [18]. Furthermore, auto-antibodies, such as anti-interferon, anti-nuclear, and anti-phospholipids, are ubiquitously detected in patients with PASC. Antibodies to ACE2 enzyme can also perpetuate inflammation and dysautonomia by reducing the activity of both membrane-bound and soluble ACE-2 [19-21]. ACE2-viral interaction theory also explains an increased incidence of anosmia in patients of European descent with an increased

expression of ACE2 compared to Asians [22]. The expression of ACE2 also increases with age, explaining the less severe prognosis of COVID-19 infection in young adults and children [23]. The female gender, with overexpression of ACE2 as compared to males, has an increased propensity for olfactory issues due to COVID-19 infection [24].

Irrespective of etiology, sequelae of COVID-19 neurotropism and tissue injury entail chronic sympathetic hyperresponsiveness, vasomotor dysfunction, persistent chronic inflammation, and aberrant neuroplasticity manifesting clinically as dysautonomia. Impaired cerebral blood flow is a common observation reported in subjects with dysautonomia [6,7,25]. Various reports have established that cerebral blood flow impairment parallels dysautonomia's clinical severity in patients with PASC [26]. SGB improves cerebral blood flow under normotensive conditions [27]. The increase in CBF leading to improved perfusion of cortical areas associated with the sense of smell or the peripheral receptors in the facial region might be responsible for an immediate resolution of anosmia seen with SGB. However, the exact mechanism of dramatic resolution of anosmia post-SGB is still unknown.

The mechanistic insights of dramatic improvement of anosmia due to SGB are still debatable; however, SGB may be an effective treatment option for patients with olfactory issues associated with PASC.

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