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Case Report

Superior Laryngeal Nerve Block Attenuates Refractory Cough in a Patient With COVID-19 on Extracorporeal Membrane Oxygenation Awaiting Lung Transplantation

Maria Yared, MD*, Kendall W. Headden, MD, William F. Barrett, DO, Drew O. Boehmer, DO, Patrick E. Britell, MD

Department of Anesthesia and Perioperative Medicine, Medical University of South Carolina, Charleston, SC

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LUNG PATHOLOGY, instrumentation of the upper airway, and oropharyngeal secretions commonly trigger the cough reflex.[1,2] Severe cough in patients on mechanical ventilation may cause ventilator dyssynchrony refractory to the adjustment of ventilator settings, exacerbating lung injury.[3,4] Treatment of dyssynchrony and refractory cough usually consists of the administration of sedatives, opiates, neuromodulating medications, such as amitriptyline, gamma-aminobutyric acid analogs (gabapentin, pregabalin), and gamma-aminobutyric acid agonists (baclofen), and may require neuromuscular blockade.[3-5]

In nonintubated patients, persistent cough has sometimes been attributed to a sensory neuropathy caused by post-viral damage to the internal branch of the superior laryngeal nerve (SLN), leading to laryngeal nerve hypersensitivity and hyperexcitability,[5] and decreased inhibitory tone regulating the magnitude and duration of the cough response.[1,6] The authors hypothesized that this mechanism might be responsible for their patient's cough. Infiltration of the SLN with local anesthetic (LA) and corticosteroids has been effective for the treatment of cough in this group of patients.[5,7] Thus, the authors tested the effectiveness of SLN block for the treatment of refractory cough.

Case Description

The authors present a 35-year-old male patient, with a history of hypertension treated with amlodipine and hydrochlorothiazide, hospitalized for the management of respiratory failure secondary to COVID-19 pneumonia. He was treated with systemic steroids, remdesivir, and convalescent plasma, but continued to deteriorate with worsening hypoxemia and respiratory acidosis that required prone positioning and mechanical ventilation a month after being admitted to the hospital. His course was complicated by tension pneumothorax and bronchopleural fistula, further impairing gas exchange. Eight days after intubation, he required additional support with venovenous extracorporeal membrane oxygenation (VV ECMO) for refractory hypoxemia and hypercarbia. Once gas exchange was optimized, a percutaneous tracheostomy was performed. The patient required deep sedation to prevent ventilator dyssynchrony and cough. This was necessary to protect his lungs from further damage, as well as prevent the associated severe decrease in VV ECMO blood flow and oxygen saturation that were frequent and life-threatening. For weeks, the patient received a propofol infusion, dexmedetomidine infusion, midazolam infusion, ketamine infusion, fentanyl infusion

Address correspondence to Maria Yared, MD, Department of Anesthesia and Perioperative Medicine, Medical University of South Carolina, 167 Ashley Avenue Suite 301 MSC 912, Charleston, SC 29425-9120.

E-mail address: yared@musc.edu (M. Yared).

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that was later changed to hydromorphone infusion, and scheduled quetiapine along with as needed doses of haloperidol. Additional problems included coagulopathy and upper airway bleeding likely due to repeated oral suctioning, multiple transesophageal echocardiograms, and recent tracheostomy. Despite not being on heparin or other anticoagulants, the patient's activated partial thromboplastin time ranged between 55 and 77 seconds.

The case was presented to the authors' hospital Lung Transplantation Committee. The consensus was that this patient's lung damage was irreversible and incompatible with survival and that he would be listed for lung transplantation once the authors demonstrated that his neurologic function was preserved and he could participate in rehabilitation therapy. Unfortunately, all attempts by the intensive care unit (ICU) team to reduce sedation without exacerbating the coughing spells that were causing life-threatening decreases in VV ECMO blood flow and oxygen saturation were ineffective. Interventions included modification of the sedative regimen, minimization of polypharmacy, and, once pharyngeal bleeding was controlled, nebulization of lidocaine 2% and topical application of lidocaine-soaked pads in the oropharynx. The ICU team elected to defer the addition of neuromodulators, such as gabapentin and amitriptyline, in order to mitigate their potential negative impact on neurologic function.

At the request of the ICU team and after obtaining informed consent from the patient's wife, fellowship-trained regional anesthesia physicians performed a SLN block at bedside. The presence of a tracheostomy tube, left internal jugular vein large-bore introducer, and right internal jugular vein ECMO cannula significantly reduced the space available to perform the block, making ultrasound guidance difficult. The authors opted for an anatomic approach (Fig 1). Instead of the typical

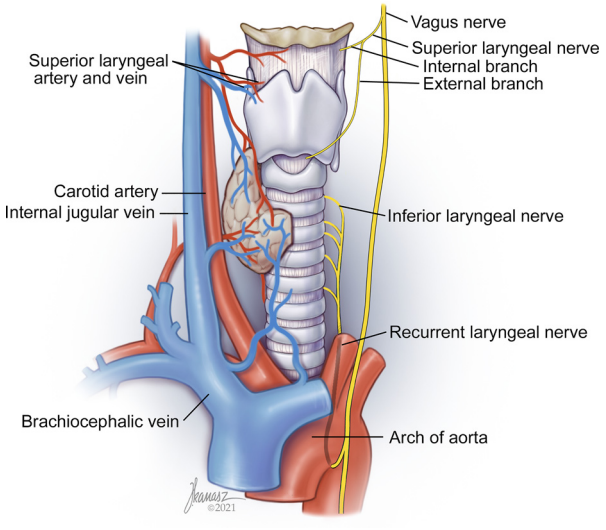

Fig 1. Anatomy surrounding the superior laryngeal nerve (SLN). When performing the block, it is important to palpate for the carotid artery and note the location of the external jugular vein. The superior laryngeal artery and vein pierce the thyrohyoid membrane along with the internal branch of the SLN. The SLN innervates the mucosa of the larynx above the vocal cords to the epiglottis. Image provided by Joseph Kanasz.

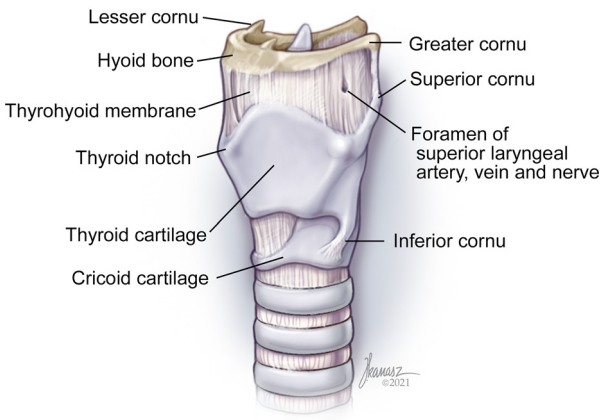

Fig 2. Anatomic landmarks for performing the superior laryngeal nerve block. Image provided by Joseph Kanasz.

21-gauge or 22-gauge nerve block needle, a 25-gauge injection needle was chosen to minimize bleeding risk. With the patient supine and neck extended, the authors identified the thyroid notch and then palpated posteriorly along its upper border until the superior cornu (Fig. 2 and 3). The needle was inserted from the lateral aspect of the neck, and once it hit the superior cornu, it was walked off the cartilage, aiming cephalad. At this location, a total of 5 mL of lidocaine and ropivacaine mixture were injected per side after aspiration yielded no blood or air.

Coordination between the ICU and regional anesthesia teams enabled progressive weaning of sedation so that the effectiveness of the bilateral SLN blocks could be assessed. One day after the procedure, the bedside nurse reported that the patient tolerated weaning of propofol sedation, and that there was a decrease in the frequency, duration, and intensity of his cough as well as decrease in ventilator dyssynchrony and alteration of VV ECMO blood flow. The patient had become more alert and was able to use nonverbal communication to answer questions. Ten minutes after repeating the injections with the same LA mixture, the patient reported a marked decrease in throat discomfort. Propofol was weaned off, and the weaning of other sedatives continued, allowing the

Fig 3. Surface anatomy of the hyoid bone, thyroid cartilage, and the cricoid cartilage, along with the path of the superior laryngeal nerve.[8]

mobilization and reorientation of the patient. About 18 hours after the second SLN block, the patient reported recurrence of throat discomfort and started having coughing spells again that required additional sedation while awaiting the subsequent SLN block.

The authors repeated the SLN blocks on 4 consecutive days with a mixture of ropivacaine and dexamethasone, which provided relief from ventilator dyssynchrony and throat discomfort for about 24 hours after each set of injections. The authors then transitioned to ropivacaine alone in decreasing concentrations for 3 days (Table 1). After several days of injections, skin bruising at the nerve block injection sites was noted.

The patient progressed well with rehabilitation, and, after 64 intubation days, 56 VV ECMO days, and 1 month after the first bilateral SLN blocks, he underwent bilateral lung transplantation and VV ECMO decannulation. His recovery was uncomplicated and free from refractory cough. His trachea was decannulated 19 days after the transplant, and he was discharged from the hospital without evidence of vocal cords dysfunction or dysphagia. There were no adverse effects related to the SLN blocks.

Discussion

Ventilator dyssynchrony is common in patients with acute respiratory distress syndrome and is sometimes accompanied by severe coughing spells. It may increase the risk of barotrauma and volutrauma.[3] In the authors' patient, dyssynchrony and cough also caused acute, repetitive changes in intrathoracic pressure and venous return that decreased blood flow and oxygen delivery through the VV ECMO circuit. Several methods were used to prevent ventilator dyssynchrony and achieve blood gases within physiological range, including sedation and optimization of ventilator and VV ECMO settings. The authors' patient's cough was refractory to these interventions, thus requiring deep sedation and sometimes neuromuscular blockade. They sought a solution that would block his cough reflex to hopefully alleviate dyssynchrony and cough, minimize sedation, and initiate rehabilitation. Achieving these goals was essential for the authors' Lung Transplantation Committee to consider him for lung transplantation.

Since the patient was unable to tolerate a reduction in the depth of sedation, the ICU team tried to attenuate his cough by nebulizing lidocaine and applying lidocaine-soaked pads in the oropharynx to block the glossopharyngeal nerve and branches of the vagus nerve that innervates the airway. These interventions were ineffective. The authors hypothesized that the combination of pneumonia, tracheostomy, and frequent suctioning for secretion clearance triggered their patient's cough and might have caused SLN neuropathy that amplified the cough reflex, thus leading to refractory coughing spells, ventilator dyssynchrony, and cardiorespiratory instability.

Thus, the ICU team felt that SLN blocks, as used by otolaryngologists in the outpatient setting for the treatment of chronic neurogenic cough due to the inflammation of the SLN, might help this patient. This is achieved with a 2 mL mixture of LA (either lidocaine 1% with 1:100,000 epinephrine or

Table 1
Local Anesthetic Mixture Used for Daily Superior Laryngeal Nerve Blocks

Day	1	2	3	4	5	6	7	8	9	10
LA mixture	Lido 2% 2.5 mL + Ropi 1% 2.5 mL	Lido 2% 2.5 mL + Ropi 1% 2.5 mL	Ropi 0.5% 4.9 mL + 1 mg dex	Ropi 0.2% 4.9 mL + 1 mg dex	Ropi 0.5% 3.9 mL + 1 mg dex	Ropi 0.375% 3.9 mL + 1 mg dex	Ropi 0.375% 4 mL	Ropi 0.25% 4 mL	Ropi 0.1% 4 mL	No block
Volume injected per side	5 mL	5 mL	5 mL	5 mL	4 mL	4 mL	4 mL	4 mL	4 mL	
Mobility	Decrease in propofol drip off pressors	Stopped propofol Got up on feet once	Got up on feet twice with assist			Walked 15-20 feet		Walked 80 feet	Walked 90 feet	

Abbreviations: DEX, dexamethasone; LA, local anesthetic; LIDO, lidocaine; ROPI, ropivacaine.

bupivacaine 0.5%) to assess the short-term success of the block and a long-acting particulate steroid (triamcinolone or methylprednisolone) to stop the inflammatory process thought to perpetuate the cough.[5] Inhibition of the inflammatory process and sensory feedback from the SLN leading to cough improvement usually requires 1 to 2 weeks.[5,7]

The authors' Pain Management team was consulted about the appropriateness of performing an SLN block.[8] The consensus was that although SLN blocks have not been described in this setting, their potential benefit in allowing the patient to be considered for lung transplantation outweighed the risks of bleeding or nerve damage. The coagulopathy could not be reversed without risks of clot formation in the VV ECMO circuit.

The authors were unable to confirm the diagnosis of SLN neuropathy because available tests are not applicable in the critical care setting. Videostroboscopy and laryngeal electromyography have limited reliability.[6] Moreover, they require the patient to phonate, which would not have been possible for this intubated, sedated patient in severe respiratory failure.[6] The use of surface evoked laryngeal sensory action potentials is less invasive since it involves transcutaneous stimulation; although it shows promise in assisting the diagnosis of neuropathy in the sensory branch of the SLN, it has not been determined to be the standard for diagnosis.[9]

Determining the daily dose of LA and the number of injections needed to terminate the hypersensitized cough cycle was a challenge, as the SLN block was being used in a novel setting. Since cough suppression was essential and time-sensitive, daily administration of long-acting LA seemed to achieve the goal more efficiently than waiting a couple of weeks for the effect of steroid injections, as is done in the outpatient setting. The first 2 blocks used lidocaine 1% and ropivacaine 0.5% within the range of concentrations used by anesthesiologists for airway blocks,[8] as well as a higher volume to provide room for error in a situation where anatomic precision could be compromised by the presence of the tracheostomy and bilateral internal jugular vein cannulas. Lidocaine allowed the initial block to be diagnostic because its rapid onset of action allowed immediate evaluation of the block's success, whereas other variables that can trigger or inhibit cough, such as suctioning or alteration of sedation, were kept at a minimum. The mixture was changed subsequently to include dexamethasone to prolong the duration of the block and possibly decrease inflammation and hypersensitized cough cycle associated with SLN neuropathy. The team was concerned that repeated injections of dexamethasone might cause nerve atrophy. It was therefore administered for 4 days only. Interestingly, no noticeable decrease in the duration of the block was observed when ropivacaine alone was used for the block, possibly because small nerves are more sensitive to LA or because of the persistent anti-inflammatory effect of the steroid.

Similarly, the authors were concerned about the potential for dose- and duration-related LA neurotoxicity.[10] On day 4, they decreased the concentration of ropivacaine from 0.5% to 0.2%. The patient reported inadequate relief of throat discomfort, and coughing spells recurred, requiring additional sedation. The authors, therefore, administered 4 mL of ropivacaine 0.5% the next day and gradually decreased it to 0.1% while keeping the volume unchanged. The nerve block remained effective during the taper and was discontinued on day 10.

Bilateral SLN blocks attenuated the cough reflex in a critically ill patient in respiratory failure and on VV ECMO support, allowing for the successful decrease in sedation requirements and increased mobility, which ultimately led him to being accepted for lung transplantation. The novel application of this block deserves further investigation to determine whether the authors' findings can be replicated. If effective, SLN blocks may be useful for facilitating the weaning of intubated patients with ventilator dyssynchrony and refractory cough. Future studies are needed to determine the volume, concentration, and duration of treatment, as well as the role of corticosteroids and other airway blocks in the ICU setting.

Conflict of Interest

None.

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