



Case report

Vagus nerve neuropathy related to SARS COV-2 infection

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ABSTRACT

A 38-year-old woman with confirmed SARS-CoV-2 infection developed dysphagia to both solids and liquids. A fiberoptic nasolaryngoscopy and a videofluoroscopy swallowing study showed right vocal cord paresis, tenth cranial nerve neuropathy, as well as oral, hypopharynx, and supraglottic hypoesthesia. Orotracheal intubation was not required. The patient was fully recovered after undergoing a multidisciplinary rehabilitation program that included speech and deglutition therapy.

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Background

In this report, the case of a female patient with SARS-CoV-2 infection and who developed dysphonia, dysphagia, and neuropathic pain on an area of her neck due to vagus nerve involvement is presented. Although SARS-CoV-2 infection and the resulting Coronavirus disease 2019 (COVID-19) is considered a pandemic, the course of the disease described here is infrequent. In addition, the unusual findings observed in this patient are usually associated with previous orotracheal intubation, which led us to think that they may not be always caused by traumatic injuries resulting from orotracheal intubation and prolonged mechanical ventilation since in this case there was no intubation. Also, it has been described that neurological symptoms are present in 36 % of individuals infected with SARS-CoV-2 and those include meningitis, encephalitis, epilepsy, stroke, headache, Guillain-Barré syndrome-like symptoms, anosmia and dysgeusia, the latter being more frequent [1].

Covid-19 pathophysiologic mechanism of neuropathy is diverse because it may be caused by viral infectious mechanisms, host cytokines and chemokines release as part of the inflammatory response to the infection [2]. The virus enters the nervous tissue through retrograde and anterograde transport along peripheral nerves. SARS-CoV-2 can infect the olfactory bulb and then it can be transported through the vagus and trigeminal nerves. In addition,

it has been reported that infection with this virus can lead to development of an acute inflammatory demyelinating polyneuropathy [6] associated with neuromuscular disorders characterized by weakness and peripheral neuropathies [7]. Hence, considering the pathophysiological mechanisms of the complications reported here, the therapeutic approach that contributed to the improvement of the clinical condition of the patient is presented. Finally, besides describing how the acute infection by SARS-CoV-2 was treated in this patient, this case illustrates the long-term effects of COVID-19 and highlights the importance of the rehabilitation process since the chronicity of the disease can affect the quality of life of the patient.

Case presentation

A 38-year-old female patient was admitted to the emergency room due to dry cough, mild dyspnea, severe headache, asthenia, adynamia, polyarthralgia, ageusia, anosmia, dysphonia andodynophagia. A positive PCR test result for SARS CoV-2 was obtained, and pneumonia, caused by bacterial superinfection, was radiologically confirmed. Therefore, inpatient management with the intravenous administration of dexamethasone, ceftriaxone, and bronchodilators was instituted. Then, three days after this treatment was started, the patient reported experiencing retrosternal pain and progressive difficulty swallowing solid and liquid foods. A fiberoptic nasolaryngoscopy was performed in which right vocal cord paresis and laryngeal sensory neuropathy were observed. Also, tenth nerve neuropathy, oral-hypopharyngeal and supraglottic hypoesthesia, right vocal fold paresis, and increased supraglottic and extra-laryngeal muscle activity were

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identified by means of a videofluoroscopic swallowing study. It should be noted that the patient did not require orotracheal intubation at any time during hospitalization.

During her hospital stay, she reported shock-like pain episodes on both sides of her neck, as well as perioral paresthesia. In addition, upon physical examination, facial edema, dysesthesias on her left lower jaw border and her left mandibular angle region, allodynia with superficial touch in the left preauricular region, right peripheral facial palsy, and decreased proximal muscle strength in her right lower limb were observed. Taking this into account, the following treatment was started with administration through a nasogastric tube of pregabalin 80 milligrams every 12 h, and intravenous infusion of lidocaine (1–2 mg/kg every hour), achieving a progressive improvement of both cervical and facial pain.

Investigations

Based on the signs and symptoms of the patient, and the physical examination findings, a fiberoptic nasopharyngoscopy and a videofluoroscopic swallowing study were performed to check the functionality of structures related to the dysfunction experienced by her (attached video). It should be emphasized that the different pathophysiologic mechanisms of dysphagia reported in the context of SARS-CoV-2 infection are secondary to traumatic injuries and deconditioning associated with orotracheal intubation and prolonged mechanical ventilation. However, in the case reported here, the patient did not require orotracheal intubation, so the possibility of a neuropathy secondary to the systemic inflammatory response caused by the infection was considered. Management with pregabalin and dexamethasone was established, which allowed the reduction of the systemic inflammatory response at the neuronal level to the infection, as well as the progressive resolution of the symptoms.

Differential diagnosis

This case report shows how airway involvement and neuropathy can be caused not only by orotracheal intubation, but also by the SARS-CoV-2 infection itself.

Treatment

Given that the neuropathic pain of the patient was difficult to manage, treatment with pregabalin, dexamethasone, and lidocaine was initiated. Lidocaine (1–2 mg/kg every hour) was administered intravenously. The initial pregabalin dosage was 80 mg two times per day, but later it was reduced to 40 mg every twelve hours; it was administered through a nasogastric tube. Additionally, the patient underwent a rehabilitation program that included psychological, physical, respiratory and speech therapy.

Outcome and follow-up

During her first week of hospitalization, the patient developed neurological complications such as dysphonia and dysphagia to both solids and liquids. On later tests, vocal fold paresis and neuropathy of the vagus nerve were evidenced. Therefore, a non-pharmacological management consisting of speech therapy, physical rehabilitation and nasogastric tube feeding was started due to severe dysphagia.

In the fourth week of her hospital stay, she presented neuropathic pain in both sides of her neck that was difficult to solve with analgesic treatment. Taking this into account, an intravenous infusion of lidocaine and pregabalin was started, in addition to previous steroid management. Progressive

improvement of the initial neurological symptoms and better analgesic control were achieved. Subsequently, the patient's condition improved in terms of her dysphonia and the severity of her pain episodes decreased during the next five days. Furthermore, we have witnessed significant mood improvement during her recovery process, and she continues undergoing the comprehensive rehabilitation plan.

Discussion

Neurological symptoms are present in 36 % of patients with SARS-CoV-2 infection. A multicenter study has suggested that the incidence of neurological complications of SARS-CoV-2 could be 55 % [1], and these are more common in patients with severe respiratory infection (about 46 % of cases) [2]. In the case presented here, dysphagia and dysphonia were likely caused by the inflammatory response to the infection, affecting the vagus nerve, which led to vocal fold paresis and a laryngeal sensory neuropathy.

The underlying pathophysiology of neuropathy is diverse and, in some cases, multifactorial, since it may arise from the mechanisms of virus entry, and from a systemic inflammatory response to SARS-CoV-2 infection characterized by the massive release of cytokines and chemokines [3]. The virus enters the nervous tissue through retrograde and anterograde transport along peripheral nerves. SARS-CoV-2 can infect the olfactory bulb through the TMPRSS2 (transmembrane protease serine 2) and ACE2 (angiotensin I-converting enzyme-2) receptors, which are found in neurons and then it can be transported through the vague and trigeminal nerves. Furthermore, the virus can be transferred through the extracellular vesicle (EV) in the olfactory ensheathing cells (OEC) which is independent to ACE2 receptors [4].

On the other hand, some studies have shown that one of the main risk factors for the development of dysphagia is intubation and mechanical ventilation, since 1 out of 3 patients who undergo these measures will develop it. In fact, there is a risk of laryngeal and tracheal injury, post-intubation voice disorder, and dysphagia during the passage of the tube; however, the latter has been mainly associated with duration of mechanical ventilation [5]. Post-intubation oropharyngeal and laryngeal trauma can cause mucosal abrasion, ulceration or dislocation and subluxation of the arytenoid cartilage. Another consequence of intubation is the deconditioning and atrophy of the muscles responsible for swallowing because of sedation and analgesia, the use of long-term neuromuscular blocking agents, and that these muscles are not used while on mechanical ventilation. In addition, the reduced sensitivity of the upper respiratory tract interferes with the protective reflexes of swallowing. This deprivation of sensation causes changes in chemoreceptors and mechanoreceptors that can last several days after extubation. Dysphagia can also be caused by gastroesophageal reflux, and the risk is increased by the presence of a nasogastric tube, being in supine position, high doses of sedation, and the use of neuromuscular relaxants [5]. In other words, the cause or causes of neurological symptoms must be carefully evaluated to develop an adequate rehabilitation plan. In the case reported here, SARS-CoV-2 infection was considered to be their cause.

In conclusion, it must be emphasized that the occurrence of dysphagia in the context of patients with SARS-CoV-2 infection could be a direct complication of the infection itself, and is not necessarily related to orotracheal intubation or respiratory muscles deconditioning.

Conflicts of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Ethical approval

This case report was approved by the Ethics Committee of the institution.

Consent

Informed consent was obtained from the patient.

Author contribution

Jairo Moyano: conceived the idea, wrote, and approved the final version of the manuscript.

Jonathan Espinosa: wrote the manuscript, and approved the final version.

Sara Mejía: wrote the manuscript, and approved the final version.

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