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Received: 2020.08.22 Accepted: 2020.10.24 Available online: 2020.10.28 Published: 2020.11.04			Vocal Cord Ulcer Following Endotracheal Intubation for Mechanical Ventilation in COVID-19 Pneumonia: A Case Report from Northern Italy		
Authors' Co Stud Data C Statistical Data Interp Manuscript Pre Literatu Funds C	ontribution: dy Design A Collection B I Analysis C pretation D eparation E re Search F Collection G	AEF 1 DE 2 AE 3	Fabio Bertone Emanuele Robiolio Carmine Fernando Gervasio	 Department of Otolaryngology, Hospital of the Sick (Ospedale Degli Infermi), Biella, Italy Department of Otolaryngology (Ear, Nose and Throat), University of Pavia, Pavia, Italy Department of Otolaryngology (Ear, Nose and Throat), Hospital of the Sick (Ospedale Degli Infermi), Biella, Italy 	
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Patient: Final Diagnosis: Symptoms: Medication: Clinical Procedure: Specialty:		ient: osis: oms: tion: lure: alty:	Female, 57-year-old Vocal cord ulcer Dysphonia — — Otolaryngology		
Objective: Background:		tive: und:	Diagnostic/therapeutic accidents This report is of a case of vocal cord ulceration following endotracheal intubation and mechanical ventilation in a patient with severe COVID-19 pneumonia		
Case Report:		port:	A 57-year-old woman was admitted to our hospital (Ospedale Degli Infermi, Biella, Italy) presenting with symptoms of severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection. Reverse transcription real- time polymerase chain reaction from a nasopharyngeal swab, authorized and validated by the World Health Organization, confirmed the diagnosis of SARS-CoV-2 infection. The patient presented with severe respiratory distress and underwent orotracheal intubation for mechani- cal ventilation. She was extubated after 9 days in the intensive care unit. After extubation, the patient experi- enced an onset of dysphonia, and was evaluated by the otolaryngologist. The videolaryngoscopy revealed the presence of an ulceration at the level of the left vocal cord. Steroids and proton pump inhibitors were admin- istered as primary therapy for 1 week. Two weeks later, a significant improvement in the patient's voice qual- ity was observed. A second videolaryngoscopy was performed, which displayed healing of the ulcer at the lev- el of the left vocal fold and rapid re-epithelialization.		
Conclusions:		ions:	tracheal intubation and mechanical ventilation, clinical guidelines should be followed to ensure that the inci- dence of complications such as vocal cord ulceration are as low as possible.		
MeSH Keywords:		ords:	Case Reports • COVID-19 • Intubation, Intratracheal • Vocal Cords		
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Background

A variety of laryngeal and tracheal lesions secondary to endotracheal intubation for mechanical ventilation have been reported thus far, including mucosa ulcers, synechiae, laryngeal and tracheal stenosis, and granulomas. Focal ischemia, laryngeal damage, or edema of the mucosa due to prolonged intubation and high cuff pressure are the most common pathophysiological conditions of the tracheal lesion [1-5]. According to Shinn et al. [6], a 7.0-mm or larger endotracheal tube, diabetes, and large body habitus are among the main predisposing factors to lesion. On the other hand, conflicting results have been reported by Colton House et al. [7]; according to their cohort study, prolonged intubation and endotracheal tube size and type are not significantly related to the incidence of laryngeal injury. However, any differences with patients affected by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are difficult to detect at present, owing to the lack of available data.

Current evidence from China suggests that between 9.8% and 15.2% of patients with SARS-CoV-2 require invasive mechanical ventilation [8–11]. At present, insights into the prognosis, complication rate, and sequelae of this new disease are still lacking.

To date, no glottic complications have been reported in the English-language literature on patients affected by SARS-CoV-2 and undergoing invasive mechanical ventilation. However, a review aimed at alerting the scientific community to the possibility of a surge in the number of airway injuries in the short and medium term was reported to provide a narrative analysis of the main mechanisms potentially leading to laryngotracheal injuries during prolonged intubation and tracheostomy [12]. Two cases of patients with SARS-CoV-2 who presented with tracheal stenosis following prolonged intubation and then underwent tracheostomy have been reported [13]. These case reports describe the pathophysiologic mechanisms underlying the development of laryngotracheal complications in patients with SARS-CoV-2.

The current clinical guidelines recommend daily chest radiographs on mechanically ventilated patients to check endotracheal tube position [14]; nevertheless, no specific guidelines have thus far been validated for SARS-CoV-2 crisis units.

We report a rare case of vocal fold ulceration following endotracheal intubation for mechanical ventilation in a 57-year-old woman presenting with severe COVID-19 pneumonia.

Case Report

A 57-year-old woman was admitted to our hospital (Ospedale Degli Infermi, Biella, Italy) presenting with symptoms of SARS-CoV-2 infection. The patient also had type 2 diabetes mellitus, hepatic steatosis, and hypertension. Bilateral diffuse opacities consistent with interstitial pneumonia were revealed by a computer tomography scan.

SARS-CoV-2 infection was diagnosed by reverse transcription polymerase chain reaction (RT-PCR) testing with a nasopharyngeal swab using the RADI COVID-19 RT-PCR detection kit (A. Menarini Diagnostic, Firenze, Italy) for use with the CFX Opus 96 Real-Time PCR Detection System (Bio-Rad, Hercules, CA, USA), which received FDA emergency use authorization (EUA). The patient presented with severe respiratory distress and subsequently underwent orotracheal standard intubation for mechanical ventilation, with the standard sedation. The correct positioning of the 8-mm tracheal tube was promptly inspected through a videolaryngoscopy. No guiding wire was utilized and no further immediate complications were identified. The correct endotracheal tube positioning was regularly verified by a clinician and then confirmed every 3 days through chest X-ray. The patient monitoring was stable during the entire intubation period. The cuff pressure was maintained between 20 and 30 cmH₂O; furthermore, the tube was constantly monitored to avoid overinflation. The patient had never undergone intubation before, so any difficulties were unpredictable. The chest X-rays revealed no tracheal dilatation. Neither hypoxemia nor hypotension were detected during the entire intubation period of the patient or during medical maneuvers. After 9 days in the intensive care unit, the patient's clinical condition improved; therefore, she was extubated without any further complications and transferred to the semi-intensive care unit.

During the following days, the patient presented with significant dysphonia, and was therefore visited by the otolaryngologist. The videolaryngoscopy performed in the semi-intensive care unit revealed an ulceration at the level of the left vocal cord, subsequently covered with fibrin. At the same time, chordal respiratory space and laryngeal motility were preserved. Owing to the patient's conditions and to the logistical difficulties in managing a patient with COVID-19, videolaryngoscopy was performed at the patient's bed, with no possibility of reporting any photographic record of the lesion. Reduced doses of steroids (methylprednisolone 40 mg/day) and proton pump inhibitors were administered as primary treatment. After 2 weeks, a significant improvement in the patient's voice was observed, and healing of the ulcer at the level of the left vocal fold and a rapid tendency to re-epithelialization were shown by a second fibroscopy. The complete resolution of the ulcer and totally normal laryngeal findings were revealed by a third fibroscopy after 1 month.

Discussion

Vocal fold ulcers are well-known complications of prolonged intubations. Mucosal damage during intubation, larger tube size, infection, and the clasping movements between the vocal cords and the tube along with the continuous tube pressure are among the main causes of vocal cord ulcers [15,16]. These factors lead to distress of the local tissue, causing a pathophysiological condition of focal ischemia and edema of the mucosa. Prolonged intubation or elevated cuff pressure tend to increase the severity of inflammatory damage during endotracheal intubation. Therefore, there is a direct correlation between intubation time and pressure and the probability of developing vocal cord ulcers.

Vocal cord ulcers are usually clinically detected after their evolution into granulomas; nevertheless, the damage is likely to be contained and healed if discovered before its progression [16].

Published data about the possible appearance of vocal cord ulcers in patients with SARS-CoV-2 requiring invasive and prolonged mechanical ventilation are still lacking. We describe a rare case of vocal cord ulcer following prolonged endotracheal intubation for mechanical ventilation in a SARS-CoV-2 patient.

Cytokine storms in patients with SARS-CoV-2 are known to result from an immune system overreaction, which induces immune cells to release a vast number of free radicals, the major cause of multiple organ failure. Steroids, such as immunosuppressants, are widely used to treat cytokine storms and to reduce the severity of inflammatory damage in patients with SARS-Cov-2; indeed, a remarkable and decisive clinical improvement was observed in our case due to the administration of steroids in association with proton pump inhibitors for gastric prophylaxis.

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There is still insufficient data to determine whether patients undergoing prolonged intubation have a higher risk of developing vocal cord damage. However, considering the marked tendency to multi-organ tissue damage due to immune system overreaction and the high percentage of patients with SARS-CoV-2 on prolonged mechanical ventilation, we emphasize the importance of evaluating any clinical dysphonia or foreign body sensation inside the larynx through videolaryngoscopy. In particular, the endoscopic examination should be performed during the first days after extubation to obtain a prompt diagnosis and administer adequate therapy to prevent an ulceration from evolving into a granuloma and, in general, to increase the treatment benefits.

Patients with SARS-CoV-2 undergoing prolonged intubation for mechanical ventilation should be treated according to current clinical guidelines. First, the correct endotracheal tube positioning should be regularly verified by clinicians. Second, the cuff pressure should be monitored and maintained within the accepted standards. Finally, the potential tracheal dilatation should be monitored through chest X-rays.

Conclusions

Herein, a case of a vocal cord ulcer in a patient with SARS-CoV-2 who underwent prolonged intubation is presented. More data are required to determine if patients undergoing prolonged intubation have a higher risk of developing a vocal cord ulcer.

The present case demonstrates the importance of considering vocal cord ulcer as a potential complication in patients recovering from SARS-CoV-2 pneumonia and the effects of prolonged intubation. To prevent the occurrence of vocal cord ulcers in the setting of an increasing number of severe COVID-19 pneumonia cases requiring endotracheal intubation and mechanical ventilation, clinical guidelines should be carefully followed to ensure the lowest incidence of complications.

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