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【 CASE REPORT 】

Two Cases of Post-intubation Laryngotracheal Stenosis Occurring after Severe COVID-19

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Abstract:

We experienced two cases of post-intubation laryngotracheal stenosis (PILS) occurring in patients after acute coronavirus disease (COVID)-19 in a relatively narrow time period. The patients required mechanical ventilation for 9 days in one and 28 days in the other. In both cases, the patients were discharged but later developed symptoms of cough and dyspnea, which were later diagnosed as PILS. Persistent cough and dyspnea are common symptoms in both PILS and the recovery phase of severe COVID-19. For this reason, PILS should be considered in the differential diagnosis post-COVID-19 patients. In addition, the prevalence of PILS may be greater than that of other critical diseases in severe COVID-19 patients.

Key words: coronavirus disease 19, COVID-19, SARS-CoV-2, mechanical ventilation, post-intubation laryngotracheal stenosis, tracheal stenosis

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Introduction

While a potentially life-saving procedure, tracheal intubation poses the inherent risk of inducing mucosal damage and inflammation, granulation tissue formation, cartilage destruction, tracheomalacia and tracheal stenosis (1). The rate of post-intubation laryngotracheal stenosis (PILS) ranges from 10% to 22% according to previous studies (2). Only 1-2% of PILS patients present with severe or symptomatic clinical presentations, such as inspiratory dyspnea that fail to improve regardless of treatment with corticosteroids (2). A longitudinal population-level epidemiological study reported that post-intubation tracheal stenosis is a rare event, with an estimated incidence of 4.9 cases per million per year (3).

Coronavirus disease 2019 (COVID-19), which is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has spread rapidly to become a major global public health emergency (4). In a small fraction of patients, COVID-19 results in severe illness compounded by serious complications, including severe pneumonia, acute respiratory distress syndrome, acute respiratory failure, pulmonary edema, sepsis, septic shock or multiple organ failure and even death (5). COVID-19 patients admitted to the intensive-care unit (ICU) often require prolonged mechanical ventilation with high positive end-expiratory pressure through an endotracheal tube (6). Patients with prolonged ventilation may require a tracheostomy to optimize weaning from ventilatory support (7). A recent comprehensive review of a database including 109 ICUs found that tracheostomy placement occurred at a median of 9 (interquartile range, 5-14) days after ICU admission (8). However, the global trend observed for COVID-19 patients admitted to the ICU is an undeniable procrastination of tracheostomy when feasible (6). One reason for this delay is consideration of the risk of cross-infection among healthcare professionals.

Although the Laryngotracheal Stenosis Committee of the European Laryngological Society sounded the alarm regarding the potential risk of a rising number of COVID-19-related PILS cases, the prevalence of COVID-19 patients who go on to develop PILS remains unknown. We herein report two patients presenting with this unique and relatively unfamiliar phenomenon during the recovery phase of COVID-19.

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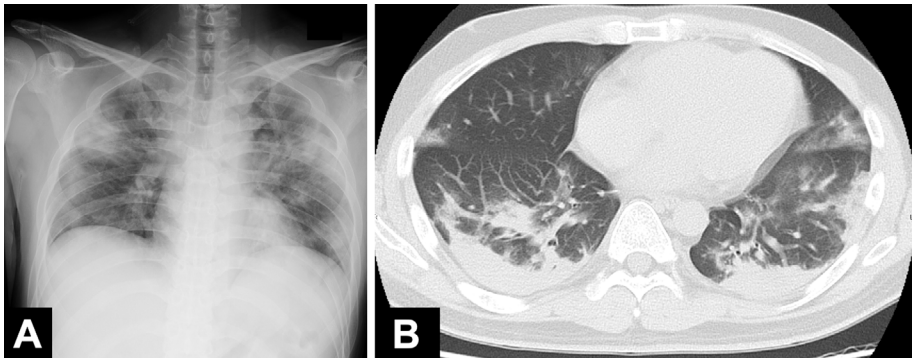

Figure 1. **Case 1 chest X-ray (A) and CT (B) findings on admission. Bilateral patchy infiltrates were observed.**

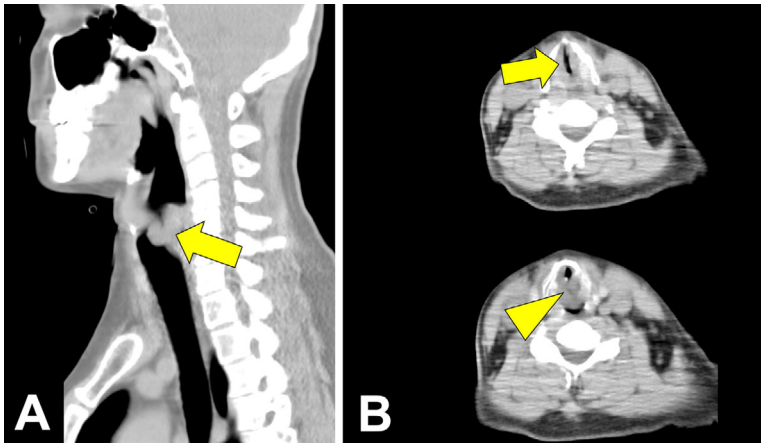

Figure 2. **Case 1 CT findings of the larynx and trachea on readmission. Sagittal CT (A) showed laryngeal stenosis (arrow). Axial CT (B) revealed laryngeal stenosis (arrow) with granulation tissue at the larynx (arrowhead).**

Case Reports

Case 1

A 42-year-old Japanese man presented to a local clinic with complaints of a fever, cough and dyspnea that had first appeared 13 days prior to admission. The patient had no significant medical history and received scheduled medical checkups regularly. There was no family history of cardiovascular disease, sudden death or lung disease. No history of smoking was documented.

On a physical examination, his general appearance was poor. Oxygen saturation was 85% on room air, improving to 92% on 4 L/min on nasal-cannula. His height was 172 cm, weight 70 kg, and he had a body mass index of 23.7 kg/m^2. His oropharyngeal mucous membranes were dry. A cardiovascular examination was unremarkable, and lung auscultation revealed bilateral rhonchi. Chest X-ray and computed tomography (CT) revealed bilateral patchy infiltrates (Fig. 1). Real-time reverse transcriptase-polymerase chain reaction (RT-PCR) for SARS-CoV-2 was positive.

Despite our best efforts, the patient's respiratory condition rapidly deteriorated. He was subsequently admitted to the ICU and intubated on the day of admission. The cuffed tube size was 8.0 mm in internal diameter. During mechanical ventilation, the highest positive end-expiratory pressure (PEEP) level was 10 cmH_2O, and the highest driving pressure was 14 cmH_2O. The tube cuff pressure was between 20 and 30 cmH_2O. With the consent of the patient, off-label use of favipiravir was initiated. The patient was extubated on the 9th hospital day and discharged on the 17th hospital day. Although exertional dyspnea was not apparent, residual symptoms of persistent dry cough and hoarseness remained at the time of discharge.

On the 34th day after discharge, the patient presented to our hospital with complaints of dyspnea. These symptoms initially emerged 17 days after discharge and were compounded by stridor and dysphagia. Oxygen saturation was 95% on room air. CT of the larynx and trachea showed airway stenosis (Fig. 2). Flexible laryngoscopy revealed swelling of the vestibular fold and stenosis of the airway with granulation tissue at the larynx on the superior and inferior aspects of the glottis (Fig. 3). Tracheostomy was immediately performed, and the granulomatous tissue at the larynx was successfully removed. The post-surgical course was un-

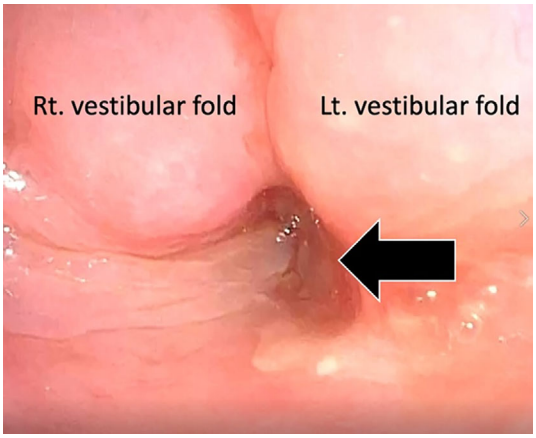

Figure 3. **Case 1 flexible laryngoscopy findings on readmission. Laryngoscopy revealed swelling of the vestibular fold and stenosis of the larynx on the superior aspect of the glottis (arrow).**

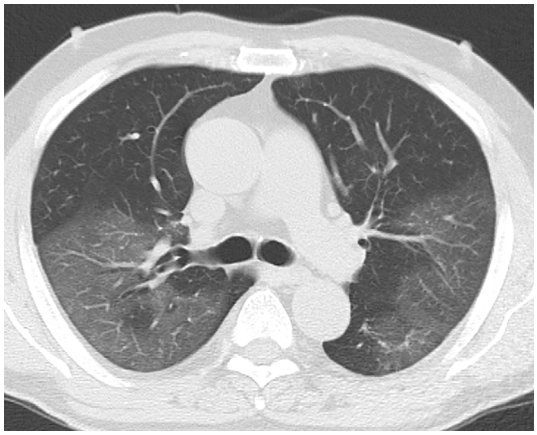

Figure 4. **Case 2 chest CT findings on admission. Bilateral ground-glass opacities were observed in the lungs.**

remarkable, and the patient made a full recovery.

Case 2

A 69-year-old Japanese man presented with complaints of a fever, cough and dyspnea to a local hospital. The symptoms first appeared 10 days prior to admission. His medical history included severe type 2 diabetes mellitus, but he had discontinued medications based on self-judgment. He had never smoked. His height was 166 cm, weight 70.0 kg, and he had a body mass index of 25.4 kg/m^2.

At the local hospital, he presented with poor oxygen saturation (90% on 15 L/min on non-rebreather mask). CT demonstrated bilateral ground-glass opacities in the lungs (Fig. 4). RT-PCR for SARS-CoV-2 was positive. Due to his poor condition, the decision was made to transfer him to our hospital. Upon arrival, progressively worsening oxygenation was noted, and the patient was subsequently admitted to the ICU and intubated on the day of admission. The cuffed tube size was 8.0 mm in internal diameter. The highest PEEP level was 10 cmH_2O, and the highest driving pressure was 16 cmH_2O. The tube cuff pressure was maintained between 20 and 30 cmH_2O during mechanical ventilation. The off-label use of favipiravir was started after patient consent was obtained on the day of admission. Prednisolone was commenced on the 8th hospital day. The loading dose was 40 mg and was gradually tapered by 5 mg every 5 days. The patient could not be liberated from the ventilator, and tracheotomy was performed on the 14th hospital day. The patient showed gradual improvement and was discontinued from mechanical ventilation on the 28th hospital day. He used a tracheal cannula without a ventilator for an additional 17 days, and prednisolone was discontinued on the 32nd hospital day. The tracheal tube was removed on the 45th hospital day, and he was discharged home in good condition on the 54th hospital day. The only apparent residual symptom at discharge was a persistent dry cough.

On the 47th day after discharge, he presented to our hospital with complaints of progressive dysphagia and dyspnea. Oxygen saturation was 95% on room air. CT revealed tracheal stenosis (Fig. 5). Flexible laryngoscopy confirmed the diagnosis of tracheal stenosis (Fig. 6). Granulation tissue was observed in the trachea at the exact site where the flap of the recent tracheostomy was created. He underwent emergency tracheostomy again, aiming 1 cm under the previous tracheostomy site, and the stenotic granulation tissue was successfully excised via electrocautery.

Discussion

Early clinical reports suggest that COVID-19 patients experience extended stays in the ICU with prolonged intubations, stretching from one to two weeks or longer (9). In the present case report, one patient required 9 days and the other 28 days of ventilation. Although laryngotracheal stenosis is associated with prolonged mechanical ventilation, we herein report cases representing both relatively short and prolonged intubations with tracheostomy.

Previous reports have shown that 11% of patients in the general population who underwent tracheal intubation developed PILS (10). The length of time to the onset of PILS varied on a case by case basis. Past case reports have shown times to onset of 28 days, 2 months and 6 months (11-13). The risk factors of PILS were prolonged intubation, endotracheal tube material, over-inflation of the tracheal cuff, trauma induced during intubation, tube displacement after intubation and endotracheal tube size (1, 14, 15). In another previous report, orotracheal intubation in excess of 10 days prior to tracheostomy was associated with increased rates of PILS (16). Regardless of the fact that we used a standard cuff pressure and appropriate tube sizes, we experienced two cases of PILS in patients who recently underwent mechanical ventilation due to COVID-19 in a relatively short period of time. PILS is a rarely encountered condition, and its incidence is estimated to be 4.9 cases per million per year (3). Our facility experienced 20 patients with severe COVID-19 who required mechanical ventilation in the ICU from March

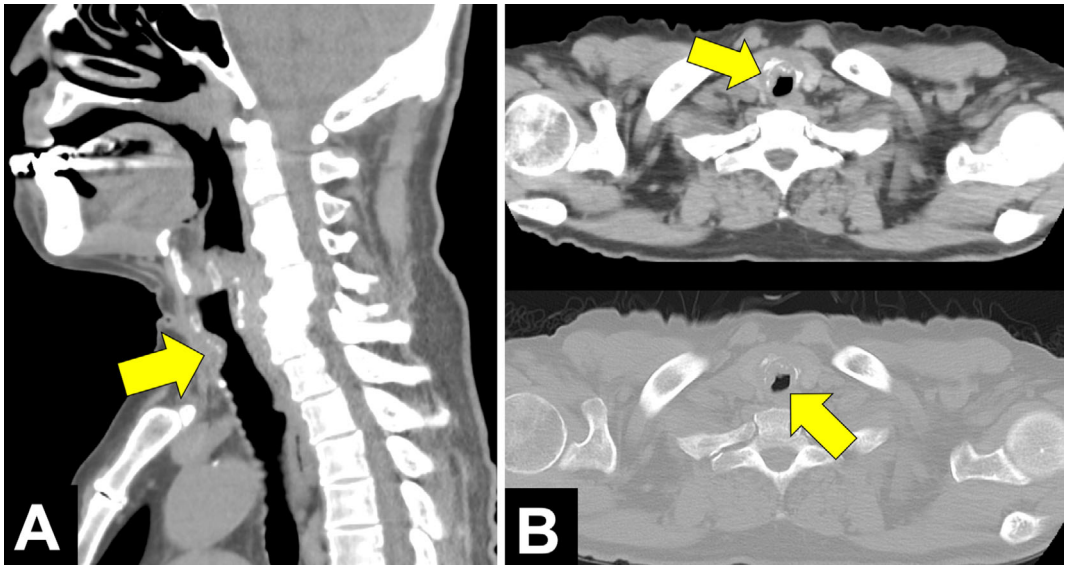

Figure 5. **Case 2 CT findings on readmission. CT revealed tracheal stenosis (arrows). (A: sagittal, B: axial)**

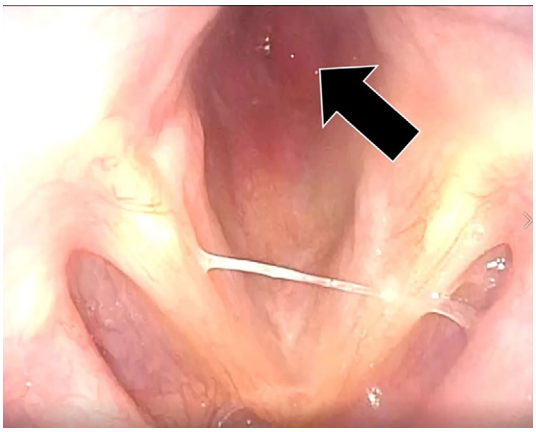

Figure 6. **Case 2 flexible laryngoscopy findings on readmission. Retrograde perspective on tracheal stenosis observed from tracheal stoma (arrow).**

to June 2020. Although the exact prevalence of PILS after acute COVID-19 is unknown, 2 out of 20 patients developed PILS at our facility.

There was no evidence to suggest that the observed damage to the larynx and trachea was directly caused by COVID-19. However, in COVID-19 patients, long-term intubation and a persistent cough may cause laryngotracheal mucosal damage and inflammation, leading to tracheal stenosis. Furthermore, obesity was associated with increased rates of developing post-intubation tracheal stenosis (17). The most common and frequently reported symptoms of COVID-19 are a fever (88-98%) and cough (59-68%) (17, 18). A strong and persistent cough, in addition to increased inspiratory effort, may pose an inherent risk for developing PILS after prolonged intubation. It should be noted that the clinical manifestations of PILS closely resemble those of severe COVID-19 in the recovery phase.

In conclusion, PILS should be considered when a COVID-19 patient complains of prolonged cough or dysphagia after liberation from mechanical ventilation. Although the prevalence of PILS remains unknown in patients after severe COVID-19 infection, it may be higher in these patients than in those with other critical diseases.

The authors state that they have no Conflict of Interest (COI).

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