A case report of laryngeal edema caused by COVID-19

Mintong Liang  
Southern Medical University

Tong Li  
Southern Medical University

Xiaolin He  
Southern Medical University

Lishan Ding  
Southern Medical University

Lei He  
Zhujiang Hospital

Rui Yang (yangrui91@163.com)  
Zhujiang Hospital

Research Article

Keywords: COVID-19, laryngeal edema, secondary infection

Posted Date: April 3rd, 2023

DOI: https://doi.org/10.21203/rs.3.rs-2749778/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License. 
Read Full License
Abstract

Background

Laryngeal edema is caused by the exudation of submucosal tissue fluid from the laxity of the pharynx and can lead to obstruction of the upper airway. It is commonly caused by post-extubation, drug allergy, and bacterial infection. During the current COVID-19 pandemic situation, laryngeal edema is a relatively rare but fatal complication of COVID-19. Taking measures to prevent laryngeal edema can reduce the incidence of sudden life-threatening events in the course of treatment.

Case presentation:

Here, we report a case in a Chinese male with COVID-19 complicated with laryngeal edema. The initial diagnosis of COVID-19 was followed by a sudden onset of inspiratory dyspnea during hospitalization. At the time of tracheal intubation, laryngeal edema was seen, and a positive bacterial culture suggested a secondary bacterial infection.

Conclusion


1. Background

In December 2019, an outbreak of novel coronavirus pneumonia (coronavirus disease 19, COVID-19), caused by a novel coronavirus (novel coronavirus 2019, 2019-nCoV), was reported in Wuhan, China. The disease then spread rapidly around the world. The 2019-nCoV is mainly transmitted via aerosol, droplets or direct contact. It colonizes the mucous membrane of the human upper respiratory tract and causes mainly respiratory symptoms. The first clinical manifestations of the infection are commonly fever, dry cough, fatigue, chest tightness and shortness of breath. Meanwhile, it has been found that COVID-19 is often associated with bacterial infections [1–3], causing complications such as pharyngeal abscess [4]. This can aggravate the condition in a short time and can even be life-threatening. Compared with previous variants, the variants currently prevalent in China, Omicron, mainly causes upper respiratory symptoms. However, laryngeal disease is less commonly reported. This paper reports a case of laryngeal edema caused by COVID-19. We share our test results and treatment process to provide a reference for the clinical diagnosis and adjunctive treatment of patients with laryngeal edema caused by COVID-19.

2. Clinical Data
2.1 Case introduction

An 80-year-old male was admitted to our hospital on 1 January 2023 with complaints of "fever, cough, sputum and vomiting for more than 10 days". On 22 December 2022, the patient started to have a fever with a maximum temperature of 39 degrees. It was accompanied by discomfort such as sore throat, cough, dyspnea and vomiting, and the vomit was stomach contents. Tests for IgG and IgM antibodies specific for COVID-19 were positive. This patient had a previous history of type 2 diabetes mellitus, hypertension and coronary atherosclerotic heart disease for many years.

2.2 Physical examination of admission

On admission, a physical examination was performed on the patient. The patient had temperature of 36.5°C, pulse of 73 times per minute, respiratory rate of 20 breaths per minute, blood pressure of 155/76mmHg, finger pulse oxygen saturation of 86% and fingertip random blood glucose of 3.8 mmol/L. Breath sounds were coarse in both lungs. And wet rales could be heard in both lungs.

2.3 Accessory examination

Complete Blood Count(CBC) showed leukocytosis of 7.01G/L, lymphocyte of 0.98G/L, ESR-T of 91mm/h, PCT-F 0.05. Blood gas analysis showed PH was 7.39, PCO2 was 5.07Kpa, PO2 was 8.26Kpa and SPO2 was 91.9%. CRP was high(82.72mg/L). Chest CT showed multiple patchy, nodular and small patchy shadows of increased density in both lungs, as well as partial ground glass lesions. This suggested viral pneumonia.

2.4 Treatment and clinical manifestations

From January 1 to January 9, the patient's temperature was normal. He was conscious, with mild wheeze and cough. His heart rate fluctuated from 60 to 88 beats per minute and respiration from 18 to 23 breaths per minute. Cefoperazone sulbactam sodium was given as an antibacterial agent and methylprednisolone as an anti-inflammatory agent. Anti-spasmodic and anti-asthmatic treatment and nebulized inhalation was also given, supplemented by sputumification and oxygen care (3L/min). The patient's symptoms improved during this period. On the night of January 9, the patient complained of throat discomfort and sore throat, and the symptoms were slightly improved after receiving Jinhoujian spray. Sputum culture showed both Gram-positive and Gram-negative bacteria. A fever developed on 10 January, with maximum temperature of 37.8°C. At night he complained of pharyngeal discomfort and dysphagia. Nebulisation was given but there was no significant relief of symptoms.

At 6am on 11 January, the patient suddenly developed shortness of breath and his oxygen saturation dropped to 70-81%. He presented with inspiratory dyspnea and the three concave sign was obvious. An emergency tracheotomy was immediately performed by Anesthesia Department. Obvious redness and swelling of the throat tissue were seen at the time of intubation. After intubation, the blood oxygen level recovered to 94%-95%. Hormone anti-inflammatory and meropenem anti-infective treatment were continued.
His condition improved (Table 1.) and was discharged 16 days after receiving the tracheotomy.

<table>
<thead>
<tr>
<th>Test Item</th>
<th>1.1</th>
<th>1.9</th>
<th>1.11</th>
<th>1.12</th>
<th>1.13</th>
</tr>
</thead>
<tbody>
<tr>
<td>HSCRP</td>
<td>82.72↑</td>
<td>37.42↑</td>
<td>142.03↑</td>
<td>118.33↑</td>
<td>38.9↑</td>
</tr>
<tr>
<td>WBC</td>
<td>7.01↑</td>
<td>13.36↑</td>
<td>20.71↑</td>
<td>22.69↑</td>
<td>11.96↑</td>
</tr>
<tr>
<td>NEUT#</td>
<td>4.89</td>
<td>11.08↑</td>
<td>18.06↑</td>
<td>20.67↑</td>
<td>9.93↑</td>
</tr>
<tr>
<td>NEUT</td>
<td>69.7</td>
<td>82.9↑</td>
<td>87.2↑</td>
<td>91.1↑</td>
<td>83↑</td>
</tr>
<tr>
<td>PCT-F</td>
<td>0.05</td>
<td>0.05</td>
<td>0.39↑</td>
<td>0.42↑</td>
<td>-</td>
</tr>
</tbody>
</table>

3. Discussion

This case report focuses on the clinical manifestation of secondary laryngeal edema in a patient with COVID-19, and has an in-depth discussion about laryngeal edema caused by secondary bacterial infection after the patient infected 2019-nCoV.

3.1 Analysis of the correlation between bacterial infection and laryngeal edema secondary to COVID-19

In this case, the patient was admitted with fever and cough. CT examination on admission showed scattered in multiple patchy, nodular and small patchy shadows of increased density in both lungs. Partial lung showed ground-glass opacity. These signs and symptoms were consistent with the clinical features of COVID-19. After treatment in hospital, his condition improved, and his vital signs were stable.

On 9 January, the patient complained of throat discomfort and pharyngalgia. Sputum bacterial culture showed positive for both Gram-positive bacteria and Gram-negative bacteria. On 10 January, the patient developed dysphagia and fever, with a maximum temperature of 37.8°C. In the early morning of 11 January, the patient suffered sudden onset of shortness of breath, wheezing, with blood oxygen saturation dropping to 70% to 81%. Laryngeal edema was found when trachea intubating. Compared with his previous results, we found his High - sensitivity C - reactive protein and white blood cell count spiked on 11 January. After symptomatic anti-inflammatory treatment, the inflammatory indicators decreased and the sputum culture was free of bacteria on 12 January.

Examination related to laryngeal edema: (1) Laryngofiberscope: indirect or direct laryngoscopy for direct visualization to judge. (2) Laboratory examination: complete blood count (elevated white blood cell count, suggesting signs of infection or inflammation). (3) Arterial blood gas analysis (decreased oxygen saturation and other signs of hypoxia).
3.1.1 Corresponding situation of the patient

(1) When the patient was intubated by the Anesthesiology Department on 11 January, it was directly visible that the larynx was red and swollen, obstructing the airway. (2) Inflammatory indexes were significantly increased. (see secondary infection specific analysis below) (3) Between 9 January and 12 January, blood gas analysis showed a decrease in partial pressure of oxygen and partial pressure of carbon dioxide. The patient’s dyspnea presentation was highly similar to that of dyspnea caused by the pre-laryngeal edema and the occurrence stage. (4) The dyspnea symptoms of the patient were relieved after intubation, which ruled out the possibility of pulmonary insufficiency due to COVID-19. In addition, this suggests that the signs of a sudden drop in the patient’s oxygen saturation, heart rate, and blood pressure may be due to obstructive dyspnea.

Edema of the larynx refers to exudation of tissue fluid below the mucous membrane in the larynx relaxation area. There are many causes of laryngeal edema, commonly caused by acute infection of the larynx, such as acute laryngitis, acute epiglottitis, laryngeal abscess and other pharyngeal inflammation. Infectious diseases can cause an inflammation response in the body. When an inflammatory response occurs, a variety of inflammation-mediating factors are activated. The release of vasoactive substances such as histamine and 5-hydroxytryptamine (5-TH) from mast cells acts on H2 receptors, producing a vasodilatory effect and leading to tissue fluid leakage [6–7] In addition, sensory nerve endings release Neurotransmitter P(SP) and calcitonin gene-related peptide (CGRP) to further increase vascular permeability [8–10] (Fig. 1.).

Severe leakage of tissue fluid from the submucosa of the larynx can induce laryngeal edema. Secondary infections often occur in severe and critically ill COVID-19 cases. One study reported that secondary infections occurred in 22 (57.89%) of 38 COVID-19 patients, 21 (95.45%) of whom developed respiratory infections. And the rate of secondary infection was much higher in critically ill patients than that in severely ill patients. In this report, the patient was critically ill before and after onset of laryngeal edema. [11]

3.1.2 Test results of patients with secondary infection in control patients

(1) Inflammatory index: Inflammation-associated cell count and cytokine levels showed a significant increase between January 9 and January 12, indicating the presence of laryngeal edema in the patient closely associated with infectious disease.

(2) Sputum culture: Gram-positive and Gram-negative bacteria were cultured in sputum on 9 January, indicating the presence of bacterial infection in respiratory system. After resuscitation, anti-infection treatment was intensified. The sputum specimen culture on 12 January was free of bacteria, indicating that secondary bacterial infection was suppressed (Table 2).

Table 2 Sputum culture result
It has been reported that the coronavirus infection has a strong correlation with laryngeal edema. The bacterial culture described in this report, identified Gram-positive pathogens as a strong predictor of laryngeal edema [12], suggesting that secondary bacterial infection of coronavirus is a potential factor which causes laryngeal edema [13].

According to the patient's clinical symptoms and previous studies, we speculated that the patient had a secondary bacterial infection causing laryngeal edema. And this was the result of a decrease in autoimmunity 21 days after infection with 2019-nCoV. [14]

### 3.2 Treatment and care

Under the post-epidemic era, the sudden onset of symptoms such as dyspnea in advanced patients with COVID-19 and multiple complications often indicates an aggravation of pneumonia. However, in this case, the patient suffered from laryngeal edema and consequent dyspnea. This is the result of a secondary infection, which is less common in patients with COVID-19, rather than an aggravation of pneumonia. If a patient has significant symptoms or signs such as dyspnea, three concave sign and a rapid drop in blood oxygen, immediate symptomatic measures such as airway intubation should be taken to prevent sudden onset of laryngeal edema leading to airway obstruction and hypoxia.

Therefore, when a patient with neoclonal pneumonia presents with symptoms such as dyspnoea and decreased blood oxygen, a possible laryngopharyngeal lesion secondary to bacterial infection should be considered. In this case, the patient's sudden onset of laryngeal edema was treated with symptomatic resuscitation, intensified anti-infective therapy and symptomatic treatment, and the patient's condition was alleviated. When COVID-19 induces laryngeal edema of unknown origin, we can provide comprehensive treatment for patients to relieve the edema. For instance, intensive antibacterial, anti-inflammatory and anti-infection therapy, as well as using antibiotics and other medicines. Once the patient has dyspnea and decrease in blood oxygen, the condition should be judged quickly and the treatment should be adjusted appropriately to relieve the hypoxic state. After symptoms have resolved, tests should be refined. Samples should be collected for bacterial culture of body fluids to further determine the cause for targeted treatment.

All the above results are subject to further validation as there are few reports of secondary bacterial infections causing laryngeal edema in patients with COVID-19. The subsequent presentation of similar signs could be studied in depth for earlier intervention and more effective treatment.

### 4. Conclusion
Laryngeal edema has been reported in several cases as an acute complication of COVID-19, particularly in patients with multiple complications. In this case, although the patient's lung condition improved during the initial treatment, the patient is elderly and has multiple chronic conditions, which presents a risk of bacterial infection and should therefore be closely monitored. Laryngeal edema often presents as shortness of breath and dyspnea, which are similar to the symptoms of lung infection in COVID-19. This makes it difficult to differentiate during treatment. This case report highlights the importance of observing for edema in the larynx and sudden abnormalities in inflammatory indicators in COVID-19 patients with multiple co-morbidities who have sudden onset of dyspnea. Direct visualisation of the patient can be performed by laryngoscopy if necessary.

**Abbreviations**


CBC: Complete Blood Count; ESR-T: Erythrocyte Sedimentation Rate

PCT-F: Procalcitonin; HSCRP: High-Sensitivity C-Reactive Protein

WBC: White Blood Cell; NEUT: Neutrophil

5-TH: 5-hydroxytryptamine; SP: Neurotransmitter P

CGRP: Calcitonin Gene-related Peptide

**Declarations**

**Acknowledgements**

We would like to thank to the instruction given by Dr. He Lei as well as Dr. Yang Rui's immediate treatment to the patient in critical condition. We would also appreciate the Zhujiang Hospital of Southern Medical University, Guangdong, China.

**Authors’ contributions**

Mintong Liang, Tong Li and Xiaolin He contributed equally to this work.

Mintong Liang: Preparation, creation and/or presentation of the published work, specifically writing the initial draft (including substantive translation), data collection and collation.

Tong Li: Preparation, creation and/or presentation of the published work, specifically writing the initial draft (including substantive translation), data collection and collation.

Xiaolin He: Preparation, creation and/or presentation of the published work, specifically writing the initial draft (including substantive translation) and visualization presentation, data collection and collation.
Lishan Ding: Critical review, commentary or revision, Partial translation.

Lei He: Critical review, commentary or revision.

Rui Yang responsible for ensuring that the descriptions are accurate and agreed by all authors.

All authors contributed this study equally. All authors read and approved the final manuscript.

**Funding**

Not applicable.

**Availability of data and materials**

All data generated or analyzed during this study are included in this published article.

**Ethics approval and consent to participate**

Not applicable.

**Consent for publication**

Written informed consent for publication of details was obtained from the patient.

**Competing interests**

The authors declare that they have no competing interests.

**References**


**Figures**
Figure 1

The cause of the induced laryngeal edema